Zynerba Pharmaceuticals Reports Third Quarter 2021 Financial Results and Operational Highlights

November 15, 2021

– Initiated RECONNECT, a confirmatory pivotal Phase 3 trial of Zygel™ in patients with Fragile X Syndrome (FXS); topline results expected second-half 2023 –

– Cash runway well into the first half of 2024; $75.6 million at September 30, 2021 –

DEVON, Pa., Nov. 15, 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 reported financial results for the third quarter ended September 30, 2021, and provided an overview of recent operational highlights and a pipeline update.

"We remain focused on enrolling patients into our confirmatory pivotal Phase 3 RECONNECT trial in children and adolescents with Fragile X Syndrome," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "If the results from RECONNECT are positive, Zygel has the potential to become the first FDA approved treatment option for the significant unmet medical need that affects FXS patients and their families."

Third Quarter 2021 and Recent Highlights and Zygel Pipeline Update

Zygel in Fragile X Syndrome (FXS)

- Zynerba initiated a pivotal, multinational randomized, double-blind, placebo-controlled, multiple-center, efficacy and safety (RECONNECT) Phase 3 trial during the third quarter of 2021. The RECONNECT trial is designed to evaluate the efficacy and safety of Zygel (cannabidiol formulated in a transdermal gel) in children and adolescents with FXS. The trial is planned to confirm the positive results observed in a population of responders in the Company's CONNECT-FX trial. (Press Release)
- RECONNECT is an 18-week trial that is expected to enroll approximately 200 children and adolescents, aged three through 17 years, at approximately 25 clinical sites in the United States, Australia, the UK and Ireland. Approximately 160 of the patients enrolled will have complete (100%) methylation of their *FMR1* gene and approximately 40 patients will have partial methylation of their *FMR1* gene. Patients will be randomized 1:1 to either Zygel or placebo. Randomization will be stratified by gender, methylation status and weight.
- The primary endpoint for the trial will be the change from baseline to the end of the treatment period in the Aberrant Behavior Checklist-Community FXS Specific (ABC-C_{FXS}) Social Avoidance subscale in patients who have complete methylation of their *FMR1* gene. The ABC-C_{FXS} Social Avoidance subscale is the same primary endpoint used in the CONNECT-FX trial. The Company believes that the results from RECONNECT, if positive, will be sufficient to support the submission of a New Drug Application for Zygel in patients with FXS.
- Presented data at the American Academy of Child and Adolescent Psychiatry (AACAP) Annual Meeting demonstrating that more patients on Zygel attained and maintained clinically meaningful improvement in social avoidance as compared to placebo-treated patients during the double-blind treatment phase of CONNECT-FX. In addition, patients who received blinded Zygel in CONNECT-FX continued to improve on open-label Zygel with approximately two-thirds of patients achieving sustained meaningful improvement in social avoidance at 16 weeks and 24 weeks on Zygel.
- Presented data at the 2021 National Organization for Rare Disorders (NORD) Rare Diseases and Orphan Products Breakthrough Summit describing the design of the Phase 3 RECONNECT trial of Zygel in children and adolescents with FXS based on learnings from CONNECT-FX.

Zygel in Autism Spectrum Disorder (ASD)

- Presented data at The Society for the Study of Behavioural Phenotypes (SSBP) Conference 2021 demonstrating that through 38 weeks of treatment, the Phase 2 BRIGHT trial suggests initial evidence of a positive benefit-risk profile for Zygel when administered in addition to stable standard of care in children and adolescents with moderate-to-severe ASD. Furthermore, in patients who completed the 38-week treatment period in BRIGHT, statistically significant improvements compared to baseline were sustained in all efficacy measures of ASD compared to baseline. (Press Release)

Zygel in 22q11.2 Deletion Syndrome (22q)

- The Company continues to screen patients for the 14-week open-label Phase 2 INSPIRE trial in children and adolescents with genetically confirmed 22q.

Zygel in Developmental and Epileptic Encephalopathies (DEE)

- Published results from the Company's open-label Phase 2 BELIEVE study in the *Journal of the American Medical Association (JAMA) Network Open*. 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 Zygel was safe, well tolerated, and was associated with reductions in focal impaired awareness seizures (FIAS) and tonic-clonic seizure (TCS) frequency and disease burden. (Press Release)

Zynerba will provide an update on its development path forward in ASD, 22q and DEE by the end of 2021.

Corporate

- In November 2021, Stephen O'Quinn, Pharm.D. was appointed as the Vice President, Medical Affairs. Dr. O'Quinn is a senior pharmaceutical executive with more than 30 years of experience in clinical development, medical affairs and commercialization of medicines in multiple therapy areas, including neurology and psychiatry. Dr. O'Quinn spent over 20 years with GlaxoSmithKline in senior leadership roles. He most recently served as a consultant to pharmaceutical clients, including Zynerba Pharmaceuticals, supporting clinical development and medical affairs activities. Dr. O'Quinn earned a Doctor of Pharmacy, with highest honors, from the University of North Carolina at Chapel Hill. He completed a post-doctoral fellowship in Cardiovascular Pharmacotherapy with the UNC School of Pharmacy and Division of Cardiology. He also completed marketing and executive leadership training at The Wharton School of the University of Pennsylvania.

Third Quarter 2021 Financial Results

Research and development expenses were $6.3 million for the third quarter of 2021, including stock-based compensation of $0.8 million. General and administrative expenses were $3.9 million in the third quarter of 2021, including stock-based compensation expense of $0.8 million. The net loss for the third quarter of 2021 was $10.6 million, with basic and diluted loss per share of $(0.26).

Financial Outlook

As of September 30, 2021, cash and cash equivalents were $75.6 million, compared to $59.2 million as of December 31, 2020. Management believes that the Company's cash and cash equivalents as of September 30, 2021 are sufficient to fund operations and capital requirements well into the first half of 2024.

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.

CONSOLIDATED STATEMENTS OF OPERATIONS

	(unaudited)			
	Three months ended September 30,		Nine months ended September 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 6,341,171	$ 5,805,948	$ 16,402,129	$ 30,038,582
General and administrative	3,869,481	3,425,831	11,531,824	11,834,434
Total operating expenses	10,210,652	9,231,779	27,933,953	41,873,016
Loss from operations	(10,210,652)	(9,231,779)	(27,933,953)	(41,873,016)
Other income (expense):				
Interest income	5,038	10,781	16,614	239,066
Foreign exchange (loss) gain	(376,637)	172,467	(576,619)	(85,171)
Total other expense	(371,599)	183,248	(560,005)	153,895
Net loss	$ (10,582,251)	$ (9,048,531)	$ (28,493,958)	$ (41,719,121)
Net loss per share - basic and diluted	$ (0.26)	$ (0.31)	$ (0.73)	$ (1.59)
Basic and diluted weighted average shares outstanding	40,092,128	29,243,375	38,933,209	26,258,626
Non-cash stock-based compensation included above:				
Research and development	$ 818,390	$ 544,909	$ 2,443,667	$ 1,590,285
General and administrative	751,603	717,716	2,325,512	2,343,125
Total	$ 1,569,993	$ 1,262,625	$ 4,769,179	$ 3,933,410

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	(unaudited) September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 75,642,498	$ 59,157,187
Incentive and tax receivables	8,535,607	9,042,586
Prepaid expenses and other current assets	3,880,014	5,166,401
Total current assets	88,058,119	73,366,174
Property and equipment, net	447,728	585,403
Incentive and tax receivables	868,083	—
Right-of-use assets	622,240	105,199
Total assets	$ 89,996,170	$ 74,056,776
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,636,350	$ 2,522,716
Accrued expenses	8,053,949	11,280,843
Lease liabilities	207,635	109,689
Total current liabilities	10,897,934	13,913,248
Lease liabilities, long-term	411,237	—
Total liabilities	11,309,171	13,913,248
Stockholders' equity:		
Common stock	41,282	29,975
Additional paid-in capital	309,312,130	262,286,008
Accumulated deficit	(230,666,413)	(202,172,455)
Total stockholders' equity	78,686,999	60,143,528

Total liabilities and stockholders' equity	$ 89,996,170	$ 74,056,776

Zynerba Contacts

Jim Fickenscher, CFO and VP Corporate Development
Zynerba Pharmaceuticals
484.581.7483
fickenscherj@zynerba.com

Peter Vozzo
ICR Westwicke
Office: 443.213.0505
Cell: 443.377.4767
Peter.Vozzo@Westwicke.com