Zynerba Pharmaceuticals Reports Second Quarter 2021 Financial Results and Operational Highlights

August 9, 2021

- *On track to initiate RECONNECT, a confirmatory pivotal trial of Zygel™ in patients with FXS, in the third quarter of 2021*
- *Positive feedback from FDA clarifies potential path forward in ASD*
- *Cash runway well into the first half of 2024; $85.8 million at June 30, 2021*

DEVON, Pa., Aug. 09, 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 second quarter ended June 30, 2021, and provided an overview of recent operational highlights and a pipeline update.

"We continue to make progress across our portfolio, particularly in FXS in which our confirmatory pivotal Phase 3 trial, RECONNECT, is expected to start in the third quarter of 2021," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "Following a positive meeting with the FDA on our development program in autism spectrum disorder (ASD), we are evaluating and prioritizing our development options for ASD, 22q and developmental and epileptic encephalopathies and we expect to provide guidance on the path forward in each of these indications by the end of 2021."

Second Quarter 2021 and Recent Highlights and Zygel Pipeline Update

Zygel in Fragile X Syndrome (FXS)

- Zynerba expects to initiate RECONNECT (A **R**andomize**d**, Double-Blind, Pla**c**ebo-C**on**trolled, Multiple-Ce**n**t**e**r, Effi**c**acy and Safe**t**y Study of ZYN002 Administered as a Transdermal Gel to Children and Adolescents with Fragile X Syndrome), a pivotal, multi-national confirmatory Phase 3 trial of Zygel in children and adolescents with FXS, in the third quarter of 2021. The trial is designed to confirm the positive results observed in a population of responders in the Company's previously conducted CONNECT-FX trial. (Press release)
- The RECONNECT trial will be an 18-week trial which will enroll approximately 200 children and adolescents of which approximately 160 patients will have complete (100%) methylation of their *FMR1* gene and approximately 40 patients will have partial methylation of their *FMR1* gene. The primary endpoint for the trial will be the change in the Aberrant Behavior Checklist-Community FXS Specific (ABC-C_{FXS}) Social Avoidance subscale in patients who have complete methylation of their *FMR1* gene. All patients, including the cohort of partially methylated patients, will be included in a key secondary endpoint analysis. 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 International Society for Pharmacoeconomic and Outcomes Research (ISPOR) Virtual 2021 Conference demonstrating the ABC-C_{FXS} subscales capture behaviors that are impactful and understandable to caregivers of children with FXS and are fit for purpose for measuring clinical trial endpoints in FXS. (Press release)

Zygel in Autism Spectrum Disorder (ASD)

- In the first half of 2021, Zynerba discussed data supporting the potential efficacy of Zygel in ASD, including the results of the Phase 2 BRIGHT trial, with the U.S. Food and Drug Administration (FDA) to determine the regulatory path forward. The guidance from the FDA included agreement on utilizing the irritability subscale of the Aberrant Behavior Checklist – Community (ABC-C) as the primary endpoint to support an indication for the treatment of irritability in ASD. This is the same primary endpoint utilized in the previously completed BRIGHT open label Phase 2 trial.
- Presented data at the 2021 American Society of Clinical Psychopharmacology (ASCP) Annual Meeting demonstrating that Zygel may provide important clinical promise across a spectrum of endpoints, including, behavior, seizure reduction and sleep in children with ASD, children with developmental epileptic encephalopathies (DEE) with comorbid ASD, and children with FXS with comorbid ASD. These previously disclosed data are from two open-label Phase 2 trials and one double-blind placebo-controlled trial when added to standard of care in children and adolescents. (Press release)

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

- Despite constantly changing COVID-19-related restrictions in Australia, the Company has resumed screening of patients for the 14-week open label Phase 2 INSPIRE trial in children and adolescents with genetically confirmed 22q. Once enrollment is complete, a timeframe for disclosing topline results of the trial will be provided.

Zygel in Developmental and Epileptic Encephalopathies (DEE)

- Zynerba is conducting an observational trial that will help finalize target syndrome selection in one or more DEE syndromes in 2021. Due to the heterogeneity of patients who fall under the DEE umbrella, the FDA suggested the company pursue individual syndromes rather than considering DEE as a single disorder or condition (Press release).
- Presented data at the Associated Professional Sleep Societies SLEEP 2021 Annual Meeting demonstrating in an open-label Phase 2 trial with patients with DEE, treatment with Zygel was associated with improved sleep in children with clinically significant sleep disorders at baseline. Furthermore, the children with both DEE and ASD appeared to show more wide-ranging benefits on sleep compared to those with DEE alone. The Company believes that because epilepsy and sleep disorders have a bidirectional relationship and co-occur in individuals with ASD, improvements in sleep may result in better seizure control and behavior in these medically fragile children with DEE. (Press release)

Second Quarter 2021 Financial Results

Research and development expenses were $5.5 million for the second quarter of 2021, including stock-based compensation of $1.0 million. General and administrative expenses were $4.4 million in the second quarter of 2021, including stock-based compensation expense of $0.9 million. The net loss for the second quarter of 2021 was $10.0 million, with basic and diluted loss per share of $(0.25).

Financial Outlook

As of June 30, 2021, cash and cash equivalents were $85.8 million, compared to $59.2 million as of December 31, 2020. Management believes that the Company's cash and cash equivalents as of June 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.

ZYNERBA PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	(unaudited)			
	Three months ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 5,451,948	$ 17,349,841	$ 10,060,958	$ 24,232,634
General and administrative	4,386,546	4,492,034	7,662,343	8,408,603
Total operating expenses	9,838,494	21,841,875	17,723,301	32,641,237
Loss from operations	(9,838,494)	(21,841,875)	(17,723,301)	(32,641,237)

Other income (expense):				
Interest income	5,943	26,601	11,576	228,285
Foreign exchange (loss) gain	(117,528)	1,482,513	(199,982)	(257,638)
Total other expense	(111,585)	1,509,114	(188,406)	(29,353)
Net loss	$ (9,950,079)	$ (20,332,761)	$ (17,911,707)	$ (32,670,590)
Net loss per share - basic and diluted	$ (0.25)	$ (0.78)	$ (0.47)	$ (1.32)
Basic and diluted weighted average shares outstanding	40,065,715	26,100,264	38,344,145	24,749,851
Non-cash stock-based compensation included above:				
Research and development	$ 1,005,886	$ 534,900	$ 1,625,277	$ 1,045,376
General and administrative	928,463	812,533	1,573,909	1,625,409
Total	$ 1,934,349	$ 1,347,433	$ 3,199,186	$ 2,670,785

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	(unaudited) June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 85,780,711	$ 59,157,187
Incentive and tax receivables	8,906,379	9,042,586
Prepaid expenses and other current assets	1,767,989	5,166,401
Total current assets	96,455,079	73,366,174
Property and equipment, net	509,623	585,403
Incentive and tax receivables	552,922	—
Right-of-use assets	678,280	105,199
Total assets	$ 98,195,904	$ 74,056,776
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,819,761	$ 2,522,716
Accrued expenses	8,002,290	11,280,843
Lease liabilities	206,211	109,689
Total current liabilities	10,028,262	13,913,248
Lease liabilities, long-term	468,385	—
Total liabilities	10,496,647	13,913,248
Stockholders' equity:		
Common stock	41,252	29,975
Additional paid-in capital	307,742,167	262,286,008
Accumulated deficit	(220,084,162)	(202,172,455)
Total stockholders' equity	87,699,257	60,143,528
Total liabilities and stockholders' equity	$ 98,195,904	$ 74,056,776

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