Zynerba Pharmaceuticals Reports Second Quarter 2022 Financial Results and Operational Highlights

August 10, 2022

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

Announced positive topline results from Phase 2 trial of Zygel in patients with 22q11.2 deletion syndrome (22q)

Company focusing resources on orphan neuropsychiatric disorders, FXS and 22q

$62.5 million in cash and cash equivalents at June 30, 2022; Cash runway through the end of 2023 / early 2024

DEVON, Pa., Aug. 10, 2022 (GLOBE NEWSWIRE) -- Zynerba Pharmaceuticals, Inc. (Nasdaq: ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for orphan neuropsychiatric disorders, today reported financial results for the second quarter ended June 30, 2022, and provided an overview of recent operational highlights and a pipeline update.

“During the second quarter, we were pleased to announce positive topline results from our Phase 2 trial of Zygel in patients with 22q. In addition to further progressing 22q, we are focused on completing the Phase 3 RECONNECT trial for children and adolescents with Fragile X syndrome, with topline results expected in the second half of 2023,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “With a cash runway extending past expected availability of topline results from our RECONNECT trial, we remain well-positioned on achieving our goal of bringing the first pharmaceutical product indicated for the treatment of behavioral symptoms of Fragile X syndrome to market.”

Operational Highlights and Pipeline Update

Zygel in Fragile X Syndrome (FXS)

- The Company continues to expect topline results from RECONNECT, a confirmatory pivotal Phase 3 trial of Zygel in patients with FXS, in the second half of 2023. The Company believes that the results from RECONNECT, if positive, will be sufficient to support the submission of a New Drug Application (NDA) for Zygel in patients with FXS.

- Presented data at the *18th NFXF International Fragile X Conference* in July and the *American Society of Clinical Psychopharmacology Annual Meeting* in June demonstrating that in the long-term safety and efficacy study of Zygel in children and adolescents with FXS, improvement was seen in Social Avoidance in the full population, with the greatest improvement in patients with complete methylation of the *FMR1* gene. Patients with complete methylation, who match the primary efficacy population in the ongoing confirmatory trial, RECONNECT, achieved and maintained clinically meaningful change in Social Avoidance, supporting one of the key design enhancements for RECONNECT. Zygel was well-tolerated during long-term administration up to 38 months of exposure. (Poster and Presentation)

- Presented data at the *18th NFXF International Fragile X Conference* in July and the *American Society of Clinical Psychopharmacology Annual Meeting* in June describing how learnings from CONNECT-FX, the first randomized, double-blind, placebo-controlled trial of Zygel in the treatment of FXS, shaped the design of RECONNECT. In addition to the primary endpoint of the RECONNECT trial being measured in patients who have a completely methylated *FMR1* gene, the treatment period of the trial has been extended by four weeks and an additional weight-based dose has been added for participants weighing greater than 50kg. RECONNECT is expected to provide key data to determine the effectiveness of Zygel in FXS while using a design intended to reduce the burden of participation in a clinical trial for families with children and adolescents with FXS. (Poster)

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

- In June, the Company announced positive topline results from the exploratory, open label Phase 2 INSPIRE trial of Zygel in children and adolescents with 22q. The INSPIRE trial achieved statistically significant and clinically meaningful improvements from baseline in multiple efficacy assessments. Zygel was shown to be well tolerated, and the safety profile was consistent with previously released data from other Zygel clinical trials. (Press Release)

- Based on the positive Phase 2 data, the Company plans to meet with the U.S. Food and Drug Administration (FDA) to discuss the data and the regulatory path forward. The Company plans to move forward in 22q as an orphan indication and has previously received orphan drug designation from the FDA for cannabidiol, the active ingredient in Zygel, for the treatment of 22q.

Zygel in Autism Spectrum Disorder (ASD)

- As previously disclosed, while data from the Company's ASD clinical development program to date are compelling, given the difficult financing market, the Company has deferred the start of the Phase 3 development program in ASD as it has prioritized its resources on FXS and 22q in the near term.

Second Quarter 2022 Financial Results

Research and development expenses were $5.4 million for the second quarter of 2022, including stock-based compensation of $0.5 million. General and administrative expenses were $3.7 million in the second quarter of 2022, including stock-based compensation expense of $0.6 million. Net loss for the second quarter of 2022 was $9.9 million, with basic and diluted loss per share of $(0.24).

Financial Outlook

As of June 30, 2022, cash and cash equivalents were $62.5 million, compared to $67.8 million as of December 31, 2021.

On May 11, 2021, the Company entered into a Controlled Equity Offering^{SM} Sales Agreement, or the 2021 Sales Agreement", with Cantor Fitzgerald & Co., Canaccord Genuity, LLC, H.C. Wainwright & Co. LLC and Ladenburg Thalmann & Co. Inc., as sales agents, pursuant to which the Company may sell, from time to time, up to $75.0 million of its common stock. In the second quarter of 2022, the Company sold and issued 488,892 shares of its common stock under the 2021 Sales Agreement in the open market resulting in gross proceeds of $0.9 million and net proceeds of $0.8 million, after deducting commissions and offering expenses. From July 1, 2022 through August 8, 2022, the Company sold and issued 1,469,714 shares of its common stock under the 2021 Sales Agreement in the open market resulting in gross proceeds of $1.8 million, and net proceeds of $1.6 after deducting commissions and offering expenses

On July 21, 2022, the Company entered into an equity purchase agreement for up to $20 million with Lincoln Park Capital Fund, LLC (LPC), a Chicago-based institutional investor. Under the terms of the agreement, Zynerba will have the right in its sole discretion, but not the obligation, to sell to LPC shares of its common stock over the 36-month term of the agreement. Zynerba controls the timing and amount of any future sales of its shares of common stock and LPC is obligated to make purchases in accordance with the terms of the purchase agreement, subject to various limitations including those under the Nasdaq listing rules.

Management believes that the Company's cash and cash equivalents are sufficient to fund operations and capital requirements through the end of 2023 or into early 2024, after the expected availability of topline results from its confirmatory pivotal Phase 3 RECONNECT trial of Zygel in patients with FXS.

About Zygel

Zygel is the first and only pharmaceutically-manufactured cannabidiol formulated as a patent-protected permeation-enhanced clear gel, designed to provide controlled drug delivery into the bloodstream transdermally (i.e. through the skin). Recent studies suggest that cannabidiol may modulate the endocannabinoid system and improve certain behavioral symptoms associated with neuropsychiatric conditions. Zygel is an investigational drug product in development for the potential treatment of behavioral symptoms associated with Fragile X syndrome (FXS), 22q11.2 deletion syndrome (22q) and autism spectrum disorder (ASD). The Company has received orphan drug designation for cannabidiol, the active ingredient in Zygel, from the FDA and the European Commission in the treatment of FXS and by the FDA for the treatment of 22q. Additionally, Zygel has been designated a Fast Track development program for treatment of behavioral symptoms of FXS.

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, 22q11.2 deletion syndrome and autism spectrum disorder. 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 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; and the extent to which inflation or global instability, including political instability, may disrupt our business operations or our

financial condition. 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 month ended June 30,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	$ 5,446,317	$ 5,451,948	$ 10,592,922	$ 10,060,958
General and administrative	3,722,453	4,386,546	7,479,763	7,662,343
Total operating expenses	9,168,770	9,838,494	18,072,685	17,723,301
Loss from operations	(9,168,770)	(9,838,494)	(18,072,685)	(17,723,301)
Other income (expense):				
Interest income	91,691	5,943	187,735	11,576
Foreign exchange gain (loss)	(775,927)	(117,528)	(458,675)	(199,982)
Total other income (expense)	(684,236)	(111,585)	(270,940)	(188,406)
Net loss	$ (9,853,006)	$ (9,950,079)	$ (18,343,625)	$ (17,911,707)
Net loss per share - basic and diluted	$ (0.24)	$ (0.25)	$ (0.45)	$ (0.47)
Basic and diluted weighted average shares outstanding	41,406,803	40,065,715	40,858,688	38,344,145
Non-cash stock-based compensation included above:				
Research and development	$ 488,645	$ 1,005,886	$ 1,018,141	$ 1,625,277
General and administrative	619,898	928,463	1,250,884	1,573,909
Total	$ 1,108,543	$ 1,934,349	$ 2,269,025	$ 3,199,186

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	(unaudited)	
	June 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 62,489,635	$ 67,808,000
Incentive and tax receivables	1,474,328	9,580,468
Prepaid expenses and other current assets	1,707,738	2,831,392
Total current assets	65,671,701	80,219,860
Property and equipment, net	322,713	385,833
Incentive and tax receivables	560,745	—
Right-of-use assets	451,800	565,814
Total assets	$ 67,006,959	$ 81,171,507
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,674,841	$ 1,798,813
Accrued expenses	7,640,866	7,896,598
Lease liabilities	211,965	209,068
Total current liabilities	9,527,672	9,904,479
Lease liabilities, long-term	237,414	353,694
Total liabilities	9,765,086	10,258,173
Stockholders' equity:		

Common stock	43,936	41,218
Additional paid-in capital	315,023,041	310,353,595
Accumulated deficit	(257,825,104)	(239,481,479)
Total stockholders' equity	57,241,873	70,913,334
Total liabilities and stockholders' equity	$ 67,006,959	$ 81,171,507

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