Zynerba Pharmaceuticals Reports Fourth Quarter and Full Year 2022 Financial Results and Operational Highlights

March 28, 2023

Enrollment continues in RECONNECT, a confirmatory pivotal Phase 3 trial of Zygel™ in patients with Fragile X syndrome; topline results expected first-half 2024

European Commission granted orphan drug designation for cannabidiol, the active ingredient in Zygel, in 22q11.2 deletion syndrome

$50.6 million in cash and cash equivalents at December 31, 2022; Cash runway to mid-year 2024

DEVON, Pa., March 28, 2023 (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 fourth quarter and full year ended December 31, 2022, and provided an overview of recent operational highlights and a pipeline update.

"We remain focused on enrolling patients in our confirmatory pivotal Phase 3 RECONNECT trial, and expect topline results in the first half of 2024," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "We are committed to bringing the first pharmaceutical product indicated for the treatment of behavioral symptoms of Fragile X syndrome to market, and with a cash runway to mid-year 2024, we remain well-positioned on achieving that goal."

Operational Highlights and Pipeline Update

Zygel in Fragile X Syndrome (FXS)

- The Company expects topline results from RECONNECT, a confirmatory pivotal Phase 3 trial of Zygel in patients with FXS, in the first half of 2024. The Company believes that the results from RECONNECT, if positive, will be sufficient to support the submission of a New Drug Application (NDA) in the U.S. and a Marketing Authorization Application (MAA) in Europe for Zygel in patients with FXS.
- Published data in the *Journal of Neurodevelopmental Disorders* describing the role of the endocannabinoid system and cannabidiol therapy in FXS. The review of evidence suggests a central role for the endocannabinoid system in neuronal development and cognitive function and in the pathogenesis of FXS, and the potential role of cannabidiol as a treatment for FXS. (Press Release).
- Published data from the Phase 3 CONNECT-FX study of Zygel in the *Journal of Neurodevelopmental Disorders.* The Phase 3 study demonstrated that patients with FXS who have a highly methylated *FMR1* gene that were treated with Zygel showed a significant reduction in behavioral symptoms compared to those treated with placebo, and that Zygel was well tolerated. (Press Release).
- The Company announced that the U.S. Patent and Trademark Office (USPTO) issued a patent titled "Treatment of Fragile X Syndrome With Cannabidiol," which includes claims directed to methods of treating FXS with cannabidiol. This new patent, which expires in 2038, is part of an expanding international intellectual property portfolio covering Zygel. (Press Release)

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

- Based on the positive Phase 2 INSPIRE trial data announced in June 2022 (Press Release), the Company held an initial meeting with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2022 to obtain feedback on the Phase 2 data and regulatory pathway for Zygel in patients with 22q. The Company expects to continue its productive dialogue with the FDA on this topic and arrive at an acceptable trial design by the end of 2023. The Company currently plans to initiate a Phase 3 program in children and adolescents with 22q following topline results from RECONNECT.
- In November 2022, the Company announced that the European Commission granted orphan drug designation to cannabidiol, the active ingredient in Zygel, for the treatment of 22q.
- The Company presented positive long-term 38-week data from the Phase 2 INSPIRE trial with Zygel in children and adolescents with 22q at the *61st Annual Meeting of the American College of Neuropsychopharmacology.* The data showed that through 38-weeks of treatment, sustained, statistically significant improvements were seen in children and adolescents treated with Zygel in the Pediatric Anxiety Rating Scale (PARS-R), all five scales of the Anxiety, Depression and Mood Scale (ADAMS), and all five subscales of the Aberrant Behavior Checklist – Community (ABC-C). These results are

consistent with the previously reported 14-week treatment data suggesting a positive risk-benefit profile for Zygel in improving anxiety-related and behavioral symptoms in children and adolescents with 22q when added to a stable standard of care. (Press Release).

- During the fourth quarter of 2022, the Company announced that the USPTO issued a patent titled “Treatment of 22q11.2 Deletion Syndrome With Cannabidiol,” which includes claims directed to methods of treating one or more behavioral symptoms of 22q with cannabidiol, and expires in 2040. (Press Release).

Fourth Quarter and Full Year 2022 Financial Results

Research and development expenses were $5.5 million for the fourth quarter of 2022, including stock-based compensation of $0.5 million. General and administrative expenses were $3.2 million in the fourth quarter of 2022, including stock-based compensation expense of $0.5 million. Net loss for the fourth quarter of 2022 was $8.0 million, with basic and diluted loss per share of $(0.18).

Research and development expenses were $21.1 million for full year 2022, including stock-based compensation of $2.0 million. General and administrative expenses were $14.2 million for full year 2022, including stock-based compensation expense of $2.4 million. Net loss for full year 2022 was $35.0 million, with basic and diluted loss per share of $(0.82).

Financial Outlook

As of December 31, 2022, cash and cash equivalents were $50.6 million, compared to $67.8 million as of December 31, 2021. On March 13, 2023, the Company issued a statement confirming that it does not hold cash deposits or securities at Silicon Valley Bank.

On May 11, 2021, the Company entered into a Controlled Equity Offering^{SM} Sales Agreement (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. During the year ended December 31, 2022, the Company sold and issued 4,608,274 shares of its common stock under the 2021 Sales Agreement in the open market resulting in gross proceeds of $6.2 million and net proceeds of $5.8 million, after deducting commissions and offering expenses. From January 1, 2023 through March 22, 2023, the Company sold and issued 1,179,077 shares of its common stock under the 2021 Sales Agreement in the open market resulting in gross proceeds of $0.7 million and net proceeds of $0.6 million, after deducting commissions and offering expenses.

On July 21, 2022, the Company entered into a Purchase Agreement and registration rights agreement for up to $20 million with Lincoln Park Capital Fund, LLC (LPC), a Chicago-based institutional investor. During the year ended December 31, 2022, the Company sold and issued 350,000 shares of its common stock under the 2022 Purchase Agreement with LPC in the open market resulting in gross proceeds of $0.3 million and net proceeds of $0.2 million, after deducting offering expenses. From January 1, 2023 through March 22, 2023, the Company sold and issued 1,950,000 shares of its common stock under the Purchase Agreement, resulting in gross and net proceeds of $1.0 million.

Management believes that the Company’s cash and cash equivalents are sufficient to fund operations and capital requirements into mid-year 2024. Top-line results from the Company’s confirmatory pivotal Phase 3 RECONNECT trial of Zygel in patients with FXS are expected in the first half of 2024.

About Zygel

Zygel is the first and only pharmaceutically-manufactured cannabidiol formulated as a patent-protected permeation-enhanced clear gel, designed to provide 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 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 orphan neuropsychiatric disorders. We are committed to improving the lives of patients and their families living with severe, chronic health conditions including Fragile X syndrome and 22q11.2 deletion syndrome. 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, the European Medicines Agency and other 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 December 31,		Year ended December 31,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	$ 5,467,516	$ 5,022,360	$ 21,099,666	$ 21,424,489
General and administrative	3,218,463	3,814,077	14,151,874	15,345,901
Total operating expenses	8,685,979	8,836,437	35,251,540	36,770,390
Loss from operations	(8,685,979)	(8,836,437)	(35,251,540)	(36,770,390)
Other income (expense):				
Interest income	407,270	4,433	846,860	21,047
Foreign exchange gain (loss)	262,677	16,938	(631,126)	(559,681)
Total other income (expense)	669,947	21,371	215,734	(538,634)
Net loss	$ (8,016,032)	$ (8,815,066)	$ (35,035,806)	$ (37,309,024)
Net loss per share - basic and diluted	$ (0.18)	$ (0.22)	$ (0.82)	$ (0.95)
Basic and diluted weighted average shares outstanding	45,127,998	40,227,715	42,662,770	39,259,495
Non-cash stock-based compensation included above:				
Research and development	$ 472,447	$ 384,304	$ 1,972,894	$ 2,827,971
General and administrative	549,155	657,097	2,358,833	2,982,609
Total	$ 1,021,602	$ 1,041,401	$ 4,331,727	$ 5,810,580

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 50,640,993	$ 67,808,000
Incentive and tax receivables	1,225,383	9,580,468
Prepaid expenses and other current assets	2,908,731	2,831,392
Total current assets	54,775,107	80,219,860
Property and equipment, net	409,572	385,833
Right-of-use assets	336,215	565,814
Total assets	$ 55,520,894	$ 81,171,507
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,942,830	$ 1,798,813
Accrued expenses	7,014,882	7,896,598
Lease liabilities	214,901	209,068
Total current liabilities	9,172,613	9,904,479

Lease liabilities, long-term	119,524	353,694
Total liabilities	9,292,137	10,258,173
Stockholders' equity:		
Common stock	47,896	41,218
Additional paid-in capital	320,698,146	310,353,595
Accumulated deficit	(274,517,285)	(239,481,479)
Total stockholders' equity	46,228,757	70,913,334
Total liabilities and stockholders' equity	$ 55,520,894	$ 81,171,507

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