Zynerba Pharmaceuticals Reports First Quarter 2023 Financial Results and Operational Highlights

May 15, 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

$44.4 million in cash and cash equivalents at March 31, 2023; Cash runway to mid-year 2024

Proposal for a reverse stock split is on the agenda for June 13, 2023 annual meeting of stockholders to satisfy the minimum bid price requirement for continued listing on the Nasdaq Capital Market

DEVON, Pa., May 15, 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 first quarter ended March 31, 2023, and provided an overview of recent operational highlights and a pipeline update.

"The first quarter of 2023 was a period of continued focus and execution on our two lead programs with Zygel," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "During the quarter we continued to enroll patients in our confirmatory pivotal Phase 3 RECONNECT trial as we are committed to bringing the first pharmaceutical product indicated for the treatment of behavioral symptoms of Fragile X syndrome to market. In addition, we expect continued dialogue with the U.S. Food and Drug Administration (FDA) in 2023 regarding an acceptable trial design for our Phase 3 program in patients with 22q deletion syndrome, with the goal of finalizing a trial design by the end of 2023."

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.
- The Company presented data at the *55th Gatlinburg Conference* in April 2023 demonstrating that in the ongoing long-term safety and efficacy trial of Zygel in children and adolescents with FXS, Zygel was well-tolerated with long-term administration with up to 45 months of exposure. Patients with complete methylation, who match the primary efficacy population in the ongoing confirmatory trial, RECONNECT, achieved and maintained clinically meaningful changes in Social Avoidance over 24 months, further supporting this design enhancement for RECONNECT. (Press Release)

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

- As previously disclosed, based on the positive Phase 2 INSPIRE trial data announced in June 2022 (Press Release), the Company held an initial meeting with the 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.
- The Company presented data at the *55th Gatlinburg Conference* in April 2023 that showed through 38-weeks of treatment, 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 other behavioral symptoms in children and adolescents with 22q when added to standard of care. (Press Release).

Corporate – Reverse Stock Split

- Zynerba intends to seek approval of a reverse stock split at its Annual Meeting of Stockholders in June (Annual Meeting), which it would effect any time prior to November 1, 2023. Details of the reverse stock split are included in the Company's Proxy Statement for the Annual Meeting. The primary objective of implementing a reverse split is to satisfy the minimum bid price requirement for continued listing on the Nasdaq Capital Market. The Company's Board believes that effecting the reverse split would increase the price of our common stock which would, among other things, help the Company to:
  - Meet certain continued listing requirements of the Nasdaq Capital Market;
  - Appeal to a broader range of investors to generate interest in the Company; and

- Improve perception of the Company's common stock as an investment security.

Stockholders of record are encouraged to review the proxy materials filed with the SEC before voting. If stockholders have any questions or need assistance with processing their vote, please contact MacKenzie Partners, Inc. (email: proxy@mackenziepartners.com, or call toll free: 1-800-322-2885), Zynerba's proxy solicitor.

First Quarter 2023 Financial Results

Research and development expenses were $7.1 million for the first quarter of 2023, including stock-based compensation of $0.4 million. General and administrative expenses were $3.4 million in the first quarter of 2023, including stock-based compensation expense of $0.4 million. Net loss for the first quarter of 2023 was $10.1 million, with basic and diluted loss per share of $(0.21).

Financial Outlook

As of March 31, 2023, cash and cash equivalents were $44.4 million, compared to $50.6 million as of December 31, 2022.

On May 11, 2021, the Company entered into a Controlled Equity Offering℠ 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. We are currently subject to General Instruction I.B.6 of Form S-3, and the amount of funds we can raise through primary public offerings of securities in any twelve-month period using our existing registration statement on Form S-3 is limited to one-third of the aggregate market value of the voting and non-voting common equity held by non-affiliates. We will be subject by this limit until such time as our public float exceeds $75.0 million. In the first quarter of 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 (2022 Purchase Agreement) and registration rights agreement for up to $20.0 million with Lincoln Park Capital Fund, LLC (LPC), a Chicago-based institutional investor. In the first quarter of 2023, the Company sold and issued 2,100,000 shares of its common stock under the 2022 Purchase Agreement resulting in gross and net proceeds of $1.1 million. From April 1, 2023 through May 11, 2023, the Company sold and issued 150,000 shares of common stock under the Purchase Agreement resulting in gross and net proceeds of $0.1 million.

Management believes that the Company's cash and cash equivalents are sufficient to fund operations and capital requirements to 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 consistent 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) and 22q11.2 deletion syndrome (22q). 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 Company's ability to regain compliance with the requirements for continued listing on the Nasdaq Capital Market, including the risk of not obtaining stockholder approval for a potential reverse stock split; 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, banking stability 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 March 31,	
	2023	**2022**
Operating expenses:		
Research and development	$ 7,078,081	$ 5,146,605
General and administrative	3,393,094	3,757,310
Total operating expenses	10,471,175	8,903,915
Loss from operations	(10,471,175)	(8,903,915)
Other income (expense):		
Interest income	447,315	96,044
Foreign exchange (loss) gain	(89,983)	317,252
Total other income (expense)	357,332	413,296
Net loss	$ (10,113,843)	$ (8,490,619)
Net loss per share - basic and diluted	$ (0.21)	$ (0.21)
Basic and diluted weighted average shares outstanding	48,430,567	40,304,484
Non-cash stock-based compensation included above:		
Research and development	$ 373,626	$ 529,496
General and administrative	448,360	630,986
Total	$ 821,986	$ 1,160,482

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	(unaudited) March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 44,400,344	$ 50,640,993
Incentive and tax receivables	1,174,817	1,225,383
Prepaid expenses and other current assets	2,001,086	2,908,731
Total current assets	47,576,247	54,775,107
Property and equipment, net	473,270	409,572
Incentive and tax receivables	309,190	—
Right-of-use assets	277,826	336,215
Total assets	$ 48,636,533	$ 55,520,894
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,142,216	$ 1,942,830
Accrued expenses	7,251,414	7,014,882
Lease liabilities	216,385	214,901
Total current liabilities	9,610,015	9,172,613
Lease liabilities, long-term	59,967	119,524
Total liabilities	9,669,982	9,292,137
Stockholders' equity:		

Common stock	53,503	47,896
Additional paid-in capital	323,544,176	320,698,146
Accumulated deficit	(284,631,128)	(274,517,285)
Total stockholders' equity	38,966,551	46,228,757
Total liabilities and stockholders' equity	$ 48,636,533	$ 55,520,894

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