# Zynerba Pharmaceuticals Reports Fourth Quarter and Full Year 2021 Financial Results and Operational Highlights

March 1, 2022

*– European Commission granted orphan drug designation for Zygel™ in Fragile X syndrome (FXS) –*

*– Continued enrollment in RECONNECT, a confirmatory pivotal Phase 3 trial of Zygel in patients with FXS; topline results expected second-half 2023 –*

*– Completed enrollment in Phase 2 trial of Zygel in patients with 22q11.2 deletion syndrome (22q); topline results expected mid-year 2022 –*

*– $67.8 million in cash and cash equivalents at December 31, 2021; Cash runway into second-half 2023 –*

DEVON, Pa., March 01, 2022 (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 fourth quarter and full year ended December 31, 2021, and provided an overview of recent operational highlights and a pipeline update.

“In 2022, we look to build on last year’s progress as we continue to enroll patients in our confirmatory pivotal Phase 3 trial in Fragile X syndrome, initiate a Phase 3 program in autism spectrum disorder and report topline results in our Phase 2 trial in 22q11.2 deletion syndrome,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “We are committed to achieving our goal of bringing the first pharmaceutical product indicated for the treatment of behavioral symptoms of Fragile X syndrome to market, as well as advancing Zygel in other rare and near rare neuropsychiatric indications.”

**Operational Highlights and Pipeline Update**

**Zygel in Fragile X Syndrome (FXS)**

- In February 2022, the European Commission granted orphan drug designation to cannabidiol, the active ingredient in Zygel, for the treatment of FXS. As previously announced, the Company believes, based on the scientific advice of the European Medicines Agency, that the successful completion of the current development program for Zygel in FXS will satisfy the requirements of a marketing authorization application in the European Union.
- 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.

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

- In February 2022, the Company announced completion of enrollment for the 14-week open-label Phase 2 INSPIRE trial in children and adolescents with genetically confirmed 22q. The Company continues to expect topline data from INSPIRE mid-year 2022. A total of 20 patients have been enrolled in the INSPIRE trial.
- The Company plans to move forward in 22q as an orphan indication pending results from the INSPIRE trial, and subsequent discussion with the FDA on the regulatory path forward. The Company has previously received orphan drug designation for Zygel in 22q from the FDA.

**Zygel in Autism Spectrum Disorder (ASD)**

- The Company expects to initiate the first of two Phase 3 trials in patients with ASD in the second half of 2022. The Company is finalizing the Phase 3 study protocol and will submit an Investigational New Drug application to the U.S. Food and Drug Administration (FDA) prior to commencing the pivotal program.
- As previously announced, earlier discussions with 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 pivotal trials for the two existing FDA approved treatments for ASD.

**Corporate**

- In February 2022, Albert P. Parker was appointed Chief Legal Officer and Corporate Secretary. Mr. Parker is an accomplished legal and business executive with over 25 years of pharmaceutical, biotech and healthcare experience. He assumed the duties of Suzanne Hanlon, who retired from her position at the end of February 2022.

**Fourth Quarter and Full Year 2021 Financial Results**

Research and development expenses were $5.0 million for the fourth quarter of 2021, including stock-based compensation of $0.4 million. General and administrative expenses were $3.8 million in the fourth quarter of 2021, including stock-based compensation expense of $0.7 million. The net loss for the fourth quarter of 2021 was $8.8 million, with basic and diluted loss per share of $(0.22).

Research and development expenses were $21.4 million for full year 2021, including stock-based compensation of $2.8 million. General and administrative expenses were $15.3 million for full year 2021, including stock-based compensation of $3.0 million. The net loss for the full year 2021 was $37.3 million, with basic and diluted net loss per share of $(0.95).

**Financial Outlook**

As of December 31, 2021, cash and cash equivalents were $67.8 million, compared to $59.2 million as of December 31, 2020. Management believes that the Company's cash and cash equivalents as of December 31, 2021 are sufficient to fund operations and capital requirements into the second half of 2023.

**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), autism spectrum disorder (ASD), and 22q11.2 deletion syndrome (22q). Zygel has been granted orphan drug designation by 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, autism spectrum disorder, 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 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; 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 December 31, | | Year ended December 31, | |
| | 2021 | 2020 | 2021 | 2020 |
| Operating expenses: | | | | |
| Research and development | $ 5,022,360 | $ 5,616,412 | $ 21,424,489 | $ 35,654,994 |
| General and administrative | 3,814,077 | 4,573,114 | 15,345,901 | 16,407,548 |
| Total operating expenses | 8,836,437 | 10,189,526 | 36,770,390 | 52,062,542 |
| Loss from operations | (8,836,437) | (10,189,526) | (36,770,390) | (52,062,542) |

| | | | | |
|---|---|---|---|---|
| Other income (expense): | | | | |
| Interest income | 4,433 | 4,926 | 21,047 | 243,992 |
| Foreign exchange gain (loss) | 16,938 | 566,890 | (559,681) | 481,719 |
| Total other expense | 21,371 | 571,816 | (538,634) | 725,711 |
| Net loss | $ (8,815,066) | $ (9,617,710) | $ (37,309,024) | $ (51,336,831) |
| Net loss per share - basic and diluted | $ (0.22) | $ (0.33) | $ (0.95) | $ (1.90) |
| Basic and diluted weighted average shares outstanding | 40,227,715 | 29,299,233 | 39,259,495 | 27,022,931 |
| Non-cash stock-based compensation included above: | | | | |
| Research and development | $ 384,304 | $ 604,603 | $ 2,827,971 | $ 2,194,888 |
| General and administrative | 657,097 | 639,514 | 2,982,609 | 2,982,639 |
| Total | $ 1,041,401 | $ 1,244,117 | $ 5,810,580 | $ 5,177,527 |

**ZYNERBA PHARMACEUTICALS, INC.**
**CONSOLIDATED BALANCE SHEETS**

| | December 31, 2021 | December 31, 2020 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 67,808,000 | $ 59,157,187 |
| Incentive and tax receivables | 9,580,468 | 9,042,586 |
| Prepaid expenses and other current assets | 2,831,392 | 5,166,401 |
| Total current assets | 80,219,860 | 73,366,174 |
| Property and equipment, net | 385,833 | 585,403 |
| Right-of-use assets | 565,814 | 105,199 |
| Total assets | $ 81,171,507 | $ 74,056,776 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,798,813 | $ 2,522,716 |
| Accrued expenses | 7,896,598 | 11,280,843 |
| Lease liabilities | 209,068 | 109,689 |
| Total current liabilities | 9,904,479 | 13,913,248 |
| Lease liabilities, long-term | 353,694 | — |
| Total liabilities | 10,258,173 | 13,913,248 |
| Stockholders' equity: | | |
| Common stock | 41,218 | 29,975 |
| Additional paid-in capital | 310,353,595 | 262,286,008 |
| Accumulated deficit | (239,481,479) | (202,172,455) |
| Total stockholders' equity | 70,913,334 | 60,143,528 |
| Total liabilities and stockholders' equity | $ 81,171,507 | $ 74,056,776 |

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