Zynerba Pharmaceuticals Announces Clinical Development Updates for FXS, ASD, 22q and DEE

January 4, 2022

– Company plans to focus development of Zygel™ in FXS, ASD and 22q –

– Company plans to initiate Phase 3 trial with Zygel in ASD in the second half of 2022 –

– Zynerba to hold conference call tomorrow, January 5, 2022 at 9:00 a.m. ET –

DEVON, Pa., Jan. 04, 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 provided program updates for Fragile X syndrome (FXS), autism spectrum disorder (ASD), 22q11.2 deletion syndrome (22q) and developmental and epileptic encephalopathies (DEE). In addition to the continued clinical development of Zygel in FXS, the Company plans to focus on the development of Zygel in ASD and 22q. Based on Company research and strategic prioritization, the decision has been made to not move forward in DEE at this time.

“Committing to a Phase 3 development program for patients with autism spectrum disorder is a key step in the advancement of a new treatment option for patients who have high unmet medical needs and limited FDA approved treatment options,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “Data from our ASD clinical development program to date are compelling and, with a clear regulatory path toward potential approval, we are excited to move forward with this program.”

Anido added, “In addition, we are making good progress towards completing enrollment in the INSPIRE trial for patients with 22q11.2 deletion syndrome and expect to have topline results mid-year 2022. Putting resources behind a second indication beyond FXS and completing the INSPIRE trial is consistent with our mission of being a leader in rare and near-rare neuropsychiatric disorders, including FXS, ASD and 22q.”

Pipeline Updates

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 received written scientific advice from the European Medicines Agency (EMA) providing clarity and guidance on the clinical and regulatory requirements for the submission of a marketing authorization application (MAA) in the European Union (EU) for Zygel for the treatment of behavioral symptoms associated with FXS. Based on the EMA’s scientific advice, the Company believes that the successful completion of the current development program for Zygel in FXS will satisfy the requirements of an MAA in the EU.
- Presented data at the BRAIN Foundation Synchrony 2021 Symposium describing how Zygel may provide therapeutic benefit in FXS through its effects on the endocannabinoid system. The presentation included results from the Phase 3 CONNECT-FX trial demonstrating that Zygel was superior to placebo in multiple analyses in the groups of patients with either ≥90% methylation or complete methylation (100%) of their *FMR1* gene. Data also showed that in the Company’s ongoing open label extension study, Zygel continued to be well-tolerated, without reports of clinically significant changes in vital signs, ECGs or laboratories (including liver function) with a median length of treatment of 21 months. (Presentation)

Zygel in Autism Spectrum Disorder (ASD)

- The Company plans to advance its program in ASD with two Phase 3 trials, the first of which is expected to start 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.
- Previous 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.
- In the Company’s exploratory, open-label Phase 2 BRIGHT trial in 37 children and adolescents with ASD, all five subscales of the ABC-C showed both statistically significant ($p<0.0002$) and clinically meaningful improvements at 14 weeks of treatment from baseline, including the irritability subscale which showed a 39.1% improvement ($p<0.0001$). Furthermore, as previously reported, the 18 patients who continued through 38 weeks of treatment in the extension portion of the BRIGHT trial saw a 56.1% improvement in the ABC-C irritability subscale compared to baseline ($p<0.0001$).
- In the United States, new estimates published in the U.S. Centers for Disease Control and Prevention’s Morbidity and

Mortality Weekly Report confirm an increasing trend in the prevalence of ASD, with approximately one in 44 eight year old children (or approximately 1.4 million children in total, if extrapolated to include children ages 3 to 17 years) identified with ASD. This increasing prevalence underscores the significant unmet medical need, as well as opportunity, to develop effective and well-tolerated treatment alternatives for these patients, especially considering that there are currently only two FDA approved treatments available for patients with ASD, each of which are antipsychotics.

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

- The Company continues to screen and enroll patients for the 14-week open-label Phase 2 INSPIRE trial, and expects topline data mid-year 2022.
- In the fourth quarter of 2021, the Company initiated an additional clinical site in the United States to assist completion of enrollment.
- The Company plans to move forward in 22q as an orphan indication pending results from the ongoing Phase 2 INSPIRE trial in children and adolescents with genetically confirmed 22q, and subsequent discussion with the FDA on the regulatory path forward.

Zygel in Developmental and Epileptic Encephalopathies (DEE)

- Feedback received from the FDA indicated that selecting a specific DEE syndrome will be required for a pediatric indication in epilepsy rather than evaluating improvements in certain seizure types across all DEEs. During 2021, the Company evaluated individual syndromes and conducted a feasibility study. Based on Company research and strategic prioritization, the decision has been made to maintain focus on other important neuropsychiatric behavioral conditions and not to pursue further development in DEE at this time.

Financial Outlook

As a result of the pipeline update and anticipated additional clinical studies in ASD, management now believes the Company's $75.6 million of cash and cash equivalents as of September 30, 2021 are sufficient to fund operations and capital requirements into the second half of 2023.

Conference Call Information

Zynerba management will host a live conference call and webcast tomorrow, January 5, 2022, at 9:00 a.m. Eastern Time to discuss updates to its clinical development plans. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 4181504. To access the live webcast or the replay, visit the investor page of the Company's website at http://ir.zynerba.com/. The webcast will be recorded and available on the Company's website for 30 days.

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; 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.

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