Zynerba Pharmaceuticals Provides Regulatory Update on Zygel™ in Fragile X Syndrome

December 17, 2020

- Single Trial to be Conducted in Patients with Fragile X Syndrome to Confirm Positive Results Seen in the Population of Responders in the CONNECT-FX Trial -

- Conference Call and Webcast Today, December 17, 2020 at 8:30 am ET -

DEVON, Pa., Dec. 17, 2020 (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 an update on its meeting with the U.S. Food and Drug Administration (FDA) regarding its Fragile X syndrome (FXS) program. The Company plans to conduct a double-blind, placebo-controlled pivotal trial in patients with FXS who have a highly methylated *FMR1* gene to confirm the positive results observed in this population of responders in the CONNECT-FX trial. In the first half of 2021, Zynerba will review the trial design and protocol for the new trial through a Type C meeting with the FDA and expects to initiate the pivotal trial before the end of 2021. Zynerba believes that positive results from this confirmatory trial would be sufficient to support the submission of a New Drug Application (NDA) for Zygel™ in FXS.

“We believe that Zygel has the potential to meaningfully relieve the behavioral symptoms of the most impacted individuals with Fragile X syndrome. We are committed to bringing this important therapy to patients and their families within the Fragile X community,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “We are thankful for our ongoing constructive dialogue with the FDA on our path forward to NDA submission. Completing the development of Zygel in FXS and preparing for a successful launch will be the primary focus of the Company.”

“The results reported in the analysis of children with a highly methylated *FMR1* gene are a source of considerable hope for the patients and their families who are impacted by Fragile X syndrome,” said Linda Sorensen, Executive Director of the National Fragile X Foundation (NFXF). “Zynerba has been an important partner to the families of children with Fragile X. We thank them for their continued dedication and commitment to bringing an FDA-approved treatment to our families and look forward to helping with the recruitment of patients for this study.”

The Company’s development plan for Zygel in other indications includes the following:

- **Developmental and epileptic encephalopathies (DEE):** Evaluation of potential target indications is ongoing, and Zynerba now expects to finalize target syndrome selection in 2021 in one or more DEE syndromes.
- **22q11.2 deletion syndrome (22q):** Zynerba expects to resume recruitment for the 14-week open label Phase 2 INSPIRE trial in children and adolescents with genetically confirmed 22q once COVID-19-related restrictions in Australia are eased. After recruitment has resumed, the Company will be able to provide a timeframe for completion of this trial.
- **Autism spectrum disorder (ASD):** In the first half of 2021, Zynerba intends to discuss data supporting the potential efficacy of Zygel in ASD, including the results of the Phase 2 BRIGHT trial in children and adolescents with moderate-to-severe ASD with the FDA to determine the regulatory path forward.

Financial Impact on Cash
The Company expects that its cash runway will extend into the beginning of 2023 as a result of these changes to its development plans.

Conference call information
Zynerba management will host a live conference call and webcast today at 8:30 am Eastern Time to discuss the recent FDA meeting and the regulatory pathway for Zygel in FXS. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 4088027. 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 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, 22q11.2 deletion syndrome, and a heterogeneous group of rare and ultra-rare epilepsies known as developmental and epileptic encephalopathies. 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 planned clinical trial evaluating Zygel™ in patients with a highly methylated *FMR1* gene may not confirm the results of the CONNECT-FX trial or may not be determined to be sufficient to support an NDA submission; 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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