Zynerba Pharmaceuticals Reports Fourth Quarter and Year End 2019 Financial Results and Operational Highlights

March 10, 2020

- Key Recent Clinical Milestones Include Completion of Enrollment in Pivotal CONNECT-FX Trial in Fragile X Syndrome and Phase 2 BRIGHT Trial in Autism Spectrum Disorder -

DEVON, Pa., March 10, 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 reported financial results for the fourth quarter and full year ended December 31, 2019 and provided an overview of recent operational highlights.

“The fourth quarter of 2019 capped off a year of strong execution by Zynerba,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “With a number of shots-on-goal in our clinical pipeline, each with near term milestones, our outlook is promising for the remainder of 2020 and beyond. We are positioned for major news events throughout this year and next, including the topline results from our pivotal CONNECT-FX trial of Zygel™ in patients with Fragile X syndrome which are expected late next quarter.”

Fourth Quarter 2019 and Recent Highlights

Zygel in Fragile X Syndrome (FXS)

Enrollment Complete in Pivotal FXS Trial; Topline Results Expected in the Second Quarter of 2020

Enrollment is complete with 212 patients randomized into CONNECT-FX, a pivotal, multi-national, randomized, double blind, placebo-controlled trial evaluating the efficacy and safety of Zygel in treating common behavioral symptoms of FXS. The primary endpoint is the change from baseline to the end of the treatment period in the Aberrant Behavior Checklist-Community FXS Specific (ABC-C_{FXS}) Social Avoidance subscale. Key secondary endpoints are the change from baseline to the end of the treatment period in the ABC-C_{FXS} Irritability subscale score and the ABC-C_{FXS} Socially Unresponsive/Lethargic subscale score, and Clinical Global Impression - Improvement (CGI-I) at the end of the treatment period. The Company expects to report topline results late in the second quarter of 2020. If the results are positive, Zynerba intends to request a meeting with the FDA to determine the acceptability of the data as a basis for a New Drug Application (NDA) and to seek advice on preparation of the marketing authorization. The Company expects to submit its NDA for Zygel in FXS to the U.S. Food and Drug Administration (FDA) in the second half of 2020, with potential approval by mid-year 2021. (Press release)

Robust Enrollment Continues into Open Label Extension Study

During the screening phase of CONNECT-FX, caregivers of patients in the trial were informed that their participating child may have the opportunity to receive Zygel in an open label extension trial following the child’s compliant completion of CONNECT-FX, regardless of their child’s perceived response or actual blinded drug assignment at randomization in CONNECT-FX. As of March 9, 2020, 97% of the 163 patients who have completed the 14-week blinded portion of the CONNECT-FX trial have enrolled in the open label extension trial.

New U.S. Patent Received for Treatment of FXS with Transdermal Cannabidiol (CBD)

The U.S. Patent and Trademark Office issued U.S. Patent No. 10,471,022 titled “Treatment of Fragile X Syndrome with Cannabidiol” which includes claims directed to a method of treating Fragile X syndrome, comprising transdermally administering 250 mg or 500 mg of CBD daily via a gel or cream. This new patent expires in 2038 and is part of an expanding intellectual property portfolio covering Zygel. (Press release)

Poster Describing Health State Utility Indices (HUI) that Estimate the Severity of FXS and Other Pediatric Disorders Presented at the American Society for Experimental Neurotherapeutics (ASENT) 2020 Meeting

An HUI specific to FXS, known as the ABC-UI, was derived from the ABC-C_{FXS} to measure the health-related quality of life (HRQoL) benefit of treatments for FXS (Kerr C et al. Qual Life Res.2015;24(2):305-314); HUI are measured on a scale of 0 to 1 and used in clinical and economic analyses of therapies with potential impact on HRQoL. This poster described the evaluation of the potential benefit of Zygel on the ABC-UI in FXS through post hoc analysis of data from the FAB-C trial. The mean ABC-UI for FXS patients was calculated to be 0.57 at baseline, estimating a significant disease-related impact on HRQoL in FXS despite the children and adolescents in the study being maintained on standard of care for FXS, and suggesting an impact similar or worse than other debilitating pediatric conditions as described in the published literature in measures of HUI. Additionally, compared to baseline, patients receiving Zygel experienced significant ($P < 0.01$) and sustained improvement in their mean ABC-UI from week 4 to 12. (Press release)

Poster Describing Caregivers’ Perspectives on FXS Diagnosis and Patient Journey Perspective Presented at the American Society for Experimental Neurotherapeutics (ASENT) 2020 Meeting

The poster described the results of a caregiver survey that found an average age of 3 years at initial diagnosis, a high prevalence of comorbid conditions including ASD and attention-deficit/hyperactivity disorder, and standard of care consisting primarily of counseling/therapy and prescription medications that are not indicated for FXS. While caregivers of children with FXS often notice a variety of initial symptoms early and seek help from a health care professional, it is not until subsequent physician visits, often involving a specialist, that a formal diagnosis is made. (Press release)

Zygel in Autism Spectrum Disorder (ASD)

Completed Enrollment in Phase 2 Open Label Trial of Zygel in ASD; Topline Results Expected in the Second Quarter of 2020

Enrollment is complete in the Phase 2 BRIGHT trial assessing the safety, tolerability and efficacy of Zygel for the treatment of pediatric and adolescent patients with ASD. The 14-week trial is evaluating the efficacy and safety of Zygel in 37 children and adolescents (ages four through 17) with moderate-to-severe ASD. The efficacy assessments include the Aberrant Behavior Checklist, Parent Rated Anxiety Scale – Autism Spectrum Disorder, Autism Impact Measure, and Clinical Global Impression – Severity and Improvement. The mean age of the 37 patients enrolled in the BRIGHT trial is 9.2 years. Ninety-two (92) percent of the enrolled patients are male, accurately reflecting the overall prevalence and gender ratio of moderate-to-severe ASD in the United States and in other studies. Zynerba expects to report topline results from this study in the second quarter of 2020. (Press release)

New U.S. Patent Received for Treatment of ASD with Transdermal Cannabidiol

The U.S. Patent and Trademark Office has issued U.S. Patent No. 10,568,848, titled “Treatment of Autism with Cannabidiol” which includes claims directed to methods of treating ASD by transdermally administering, via a gel or cream, a therapeutically effective amount of purified CBD. The patent expires in 2038. (Press release)

Poster Describing the Baseline Characteristics of Patients in Phase 2 BRIGHT Trial in ASD Presented at the American Society for Experimental Neurotherapeutics (ASENT) 2020 Meeting

The poster further describes the baseline characteristics of the pediatric and adolescent patients in the fully-enrolled Phase 2 BRIGHT trial, indicating that the trial enrolled a broad patient population and was enriched for disease severity to avoid floor effects on outcome measures. At baseline, at least 92% of patients have moderate to severe symptoms of ASD as measured by the Autism Diagnostic Observation Schedule (ADOS®-2) comparison score and the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) severity level score; this severity is further confirmed by an ABC-C Irritability subscale score of 30. In addition, 24% of patients enrolled in the BRIGHT trial had a PRAS-ASD score of >52, indicating possible clinical anxiety. (Press release)

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

Phase 2 Open Label Trial of Zygel in 22q Ongoing; Data Now Expected in the Third Quarter of 2020

The Company is conducting the 14-week Phase 2 INSPIRE trial to evaluate the safety, tolerability and efficacy of Zygel in approximately 20 children and adolescents (ages six through 17) with genetically-confirmed 22q. The efficacy assessments include the Aberrant Behavior Checklist-Community (ABC-C), the Anxiety, Depression and Mood Scale (ADAMS), the Qualitative Caregiver Reported Behavioral Problem Survey, and Clinical Global Impression – Severity and Improvement. Zynerba now expects to report topline results from this study in the third quarter of 2020.

Zygel in Developmental and Epileptic Encephalopathies (DEE)

Meeting with U.S. Food and Drug Administration (FDA) to Discuss Pathway for Zygel in DEE Expected in the First Half of 2020

Zynerba expects to meet with the FDA to discuss the clinical path forward in DEE. Based on the Phase 2 trial design and positive efficacy and safety results, Zynerba anticipates that it will discuss the pursuit of an indication that includes all syndromes and encephalopathies in the DEE category that present with focal impaired-awareness seizures (FIAS; previously known as complex partial seizures) and/or convulsive seizures (CS), the most common and debilitating seizure types representing 75% to 80% of all seizures.

Corporate

Enhanced Senior Management Team

Paul M. Kirsch joined Zynerba as Vice President of Regulatory Affairs and Quality Assurance, bringing 30 years of regulatory affairs management experience with companies including Trevena, Inc., Iroko Pharmaceuticals, LLC, Teva Pharmaceuticals, and Cephalon, Inc. He has extensive regulatory experience with orphan and neuroscience products, and has led five successful NDAs into commercialization in multiple indications.

Fourth quarter and full year 2019 Financial Results

As of December 31, 2019, cash and cash equivalents were $70.1 million, compared to $59.8 million as of December 31, 2018. Research and development expenses for the fourth quarter of 2019 were $7.5 million, including stock-based compensation of $0.5 million. General and administrative expenses for the fourth quarter of 2019 were $4.0 million, including stock-based compensation expense of $0.8 million. The net loss for the fourth quarter of 2019 was $10.7 million with basic and diluted net loss per share of $(0.46).

Research and development expenses for the year ended December 31, 2019 were $20.4 million, including stock-based compensation of $2.4 million. General and administrative expenses for the year ended December 31, 2019 were $13.9 million, including stock-based compensation expense of $3.2 million. The net loss for the full year of 2019 was $32.9 million with basic and diluted net loss per share of $(1.50).

Financial Outlook

The Company’s cash and cash equivalents as of December 31, 2019 was $70.1 million. Management believes that the cash runway is sufficient to fund operations and capital requirements beyond the expected NDA submission and potential approval of Zygel in FXS and into the second half of 2021.

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 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 timing and outcome of current and future legal proceedings. 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,	
	2019	**2018**	**2019**	**2018**
Revenue	$ —	$ 86,000	$ —	$ 86,000
Operating expenses:				
Research and development	7,457,953	4,876,162	20,384,049	27,245,043
General and administrative	3,958,211	3,256,044	13,935,761	13,238,787
Total operating expenses	11,416,164	8,132,206	34,319,810	40,483,830
Loss from operations	(11,416,164)	(8,046,206)	(34,319,810)	(40,397,830)
Other income (expense):				
Interest income	295,140	321,621	1,522,138	961,323
Foreign exchange gain (loss)	406,033	(65,658)	(145,911)	(474,668)
Total other income	701,173	255,963	1,376,227	486,655
Net loss	$ (10,714,991)	$ (7,790,243)	$ (32,943,583)	$ (39,911,175)
Net loss per share - basic and diluted	$ (0.46)	$ (0.44)	$ (1.50)	$ (2.61)
Basic and diluted weighted average shares outstanding	23,191,428	17,616,373	22,000,203	15,308,886
Non-cash stock-based compensation included above:				
Research and development	$ 456,420	$ 819,715	$ 2,371,998	$ 3,087,498
General and administrative	751,253	778,915	3,189,897	3,538,245
Total	$ 1,207,673	$ 1,598,630	$ 5,561,895	$ 6,625,743

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	December 31, 2019	**December 31, 2018**
Assets		
Current assets:		
Cash and cash equivalents	$ 70,063,242	$ 59,763,773
Incentive and tax receivables	14,613,969	3,444,620
Prepaid expenses and other current assets	2,378,812	3,747,087
Total current assets	87,056,023	66,955,480
Property and equipment, net	362,724	371,963
Right-of-use assets	345,849	—
Total assets	$ 87,764,596	$ 67,327,443
Liabilities and Stockholders' Equity		

Current liabilities:		
Accounts payable	$ 4,740,981	$ 4,461,567
Accrued expenses	7,073,506	5,264,215
Lease liabilities	243,677	—
Total current liabilities	12,058,164	9,725,782
Lease liabilities, long-term	109,689	—
Total liabilities	12,167,853	9,725,782
Stockholders' equity:		
Common stock	23,211	17,627
Additional paid-in capital	226,409,156	175,476,075
Accumulated deficit	(150,835,624)	(117,892,041)
Total stockholders' equity	75,596,743	57,601,661
Total liabilities and stockholders' equity	$ 87,764,596	$ 67,327,443

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