Zynerba Pharmaceuticals Reports Second Quarter 2020 Financial Results and Operational Highlights

August 10, 2020

DEVON, Pa., Aug. 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 second quarter ended June 30, 2020, and provided an overview of recent operational highlights.

“We have made solid progress over the past few months towards our core mandate of developing important new therapies for patients suffering from underserved rare and near rare neuropsychiatric disorders,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “Regarding our pivotal CONNECT-FX data in Fragile X Syndrome, we continue to evaluate the data and believe that we have identified an important and severely impacted patient population that responded well to Zygel™ CBD gel. We also announced positive data from the Phase 2 BRIGHT trial in autism spectrum disorder during the quarter. We expect to meet with the U.S. Food and Drug Administration in the second half of this year to discuss the results from both trials and to clarify the paths forward.”

Second Quarter 2020 and Recent Highlights

Zygel in Fragile X Syndrome (FXS)

Reported Topline Results from Pivotal CONNECT-FX Trial; Pre-planned Ad Hoc Analysis Showed Statistically Significant Improvements (p=0.020) in Primary Endpoint in Children and Adolescents with Full Methylation of FMR1 Gene

Zygel did not achieve statistical significance versus placebo in the primary or secondary endpoints in the full analysis set (n=210). However, a pre-planned ad hoc analysis of the most severely impacted patients in the trial (n=167), as defined by full methylation of the impacted FMR1 gene (FMet), demonstrated that Zygel achieved statistical significance in the primary endpoint of improvement at 12 weeks of treatment in the Social Avoidance subscale of the ABC-C_{FXS} compared to placebo (p=0.020). The median improvement in this subscale after twelve weeks of treatment was 40% for patients on Zygel and 21% for patients on placebo. This group comprised 80% of the patients enrolled in the CONNECT-FX study and approximately 60% of the overall FXS patient population. Zygel was very well tolerated in CONNECT- FX, and the safety profile was consistent with previously released data from other Zygel clinical trials. Zynerba intends to meet with the FDA to discuss a regulatory path forward. (Press release)

Presented CONNECT-FX Data Showing Statistically Significant Caregiver-Reported Improvements in Most Impactful FXS Behaviors at the 17th NFXF International Conference Research Roundup; Results Support Statistically Significant Results of Pre-planned Ad Hoc Analysis in FMet Patients

Consistent with guidance from the FDA on capturing the voice of the patient in drug development, the Company collected additional qualitative data on the clinical relevance of various FXS behaviors to caregivers during CONNECT-FX. The results of the Qualitative Caregiver Reported Behavioral Survey indicate that caregivers found anxiety, socially avoidant behaviors (including elopement and isolation seeking), and disruptive behaviors (including aggression and temper tantrums) to be the most challenging. The results of the Caregiver Global Impression – Change survey show a broad shift toward global improvement from baseline to week 12 in FMet patients, with three of the four behavioral domains (social avoidance and isolation, irritable and disruptive behaviors, and social interactions) showing statistically significant improvements in favor of patients on Zygel compared to placebo and the fourth domain (overall behavior) trending toward significance. (Press release)

Presented New Two-Year Data from the Open Label Extension of the Phase 2 FAB-C Trial in Patients with Fragile X at 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

At the completion of the 12-week Phase 2 FAB-C study (Period 1), patients could enter an open label extension study (Period 2). Statistically significant improvements from baseline were observed at week 12 in all subscale scores of the ABC-C_{FXS} in Period 1 and these statistically significant improvements were sustained through two years in subjects who entered Period 2. In this analysis, the majority of patients who completed Period 1 met important criteria for therapeutic response (≥25% or ≥50% improvement from baseline in ABC-C_{FXS} domains) at weeks 4, 8, and 12 of the Phase 2 trial; this response was sustained or continued to improve through two years in patients who entered Period 2. Zygel was very well tolerated over two years. (Press release)

Zygel in Autism Spectrum Disorder (ASD)

Reported Positive Topline Results from Phase 2 BRIGHT Trial of Zygel in ASD; Statistically Significant Improvements from Baseline Observed in All Subscales of the Aberrant Behavior Checklist – Community (ABC-C)

Thirty-seven children and adolescents with moderate-to-severe ASD were enrolled in the 14-week open label exploratory Phase 2 BRIGHT trial. The clinical trial was designed to evaluate the safety, tolerability and efficacy of Zygel as an add-on to standard-of-care for the treatment of pediatric and adolescent patients 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. The results of other efficacy assessments reinforce the results demonstrated in the ABC-C, including a mean improvement of 46% at week 14 from baseline as measured by the Parent Reported Anxiety Scale for ASD (PRAS-ASD; $p<0.0001$) and 57% of patients were assessed as “very much improved” or “much improved” at week 14 as measured by the Clinical Global Impression - Improvement scale (CGI-I). Zygel was very well tolerated. (Press release)

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

Recruitment into Phase 2 INSPIRE Trial of Zygel in 22q Delayed Due to the Impact COVID-19 in Australia

Recruitment into the 14-week open label Phase 2 INSPIRE trial in children and adolescents (ages six through 17) with genetically confirmed 22q has been delayed due to the impact of COVID-19 in Australia and resulting travel restrictions. As a result of the uncertainty of the scope, duration and impact of the COVID-19 pandemic in Australia, the Company has withdrawn its guidance on the timing of data from this trial, and will provide updated guidance as soon as possible.

Zygel in Developmental and Epileptic Encephalopathies (DEE)

Presented Additional Phase 2 BELIEVE Safety, Efficacy and Quality of Life Data at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

Over the Phase 2 BELIEVE 26-week treatment period, the median percentage reduction from baseline in monthly frequency of focal impaired awareness seizures (FIAS) and tonic clonic seizures (CS) was 43.5% (primary efficacy endpoint). Monthly (28-day) reductions from baseline in seizure frequency ranged from 44% to 58% from month two of the treatment period onward using monthly seizure frequency normalized to 28 days (SF28). At six months of treatment in the BELIEVE trial, 62% of patients achieved a ≥35% reduction in FIAS and TCS from baseline, and 55% of patients achieved a ≥50 reduction. Statistically significant reductions from baseline in mean Epilepsy and Learning Disabilities Quality of Life (ELDQOL)-modified subscale scores for seizure severity, behavior, and mood were observed at week 26 ($p<0.01$ for all measures). At month six, the combined proportion of “good day” and “fantastic day” reports increased from 52% at baseline to 70%, and the combined proportion of “terrible day” and “bad day” reports decreased from 12% at baseline to 4%. (Press release)

Outcome of Discussions with FDA on Clinical Pathway for Zygel in DEE Expected in the Third Quarter of 2020

Based on the Phase 2 trial design and positive efficacy and safety results, Zynerba anticipates that it will pursue an indication that includes the syndromes and encephalopathies in the DEE category that present with FIAS and/or TCS, the most common and debilitating seizure types representing 75% to 80% of all seizures. Zynerba expects to announce the results of its ongoing discussions with the FDA on the clinical path forward in DEE in the third quarter of 2020.

Second Quarter 2020 Financial Results

As of June 30, 2020, cash and cash equivalents were $77.0 million, compared to $70.1 million as of December 31, 2019. In the second quarter of 2020, the Company sold and issued 5,682,784 shares of its common stock in the open market at a weighted-average selling price of $4.92 per share, for gross proceeds of $27.9 million and net proceeds, after deducting commissions and offering expenses, of $27.2 million under an a Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co., Canaccord Genuity, LLC, H.C. Wainwright & Co. LLC and Ladenburg Thalmann & Co. Inc.

Our Australian subsidiary, Zynerba Pharmaceuticals Pty Ltd, or the Subsidiary, is incorporated in Australia and is eligible to participate in an Australian research and development tax incentive program. As part of this program, the Subsidiary is eligible to receive a cash refund from the Australian Taxation Office, or ATO, for a percentage of the research and development costs expended by the Subsidiary in Australia. In July 2019, the Australian government’s Department of Industry, Innovation and Science, or AusIndustry, responded to an Advance Overseas Finding, or AOF, application submitted by Zynerba that AusIndustry would allow certain research and development expenses incurred with respect to our product candidate Zygel outside of Australia to be eligible for the Australian research and development tax incentive program. During the year ended December 31, 2019, we recorded $8.3 million as an incentive and tax receivable and a corresponding credit to research and development expense for amounts expected to be received through the AOF for the period January 1, 2018 through December 31, 2019. As of June 30, 2020, incentive and tax receivables included $8.1 million related to the AOF. The reduction of $0.2 million versus December 31, 2019 was due to unrealized foreign currency losses related to the remeasurement of the Subsidiary’s assets and liabilities. In June 2020, the ATO informed us that we may not qualify for the AOF program based on their interpretation of certain eligibility requirements.

We evaluate our eligibility under the Australian tax incentive programs as of each balance sheet date based on the most current and relevant data available. While a numeric standard does not exist, accounting practice generally considers an event that has a 75% or greater likelihood of occurrence to be probable. Although we continue to believe that we comply with the relevant conditions of the AOF program that were in place when we received our original approval from AusIndustry, based on this probability standard we have determined it is no longer probable that the AOF credits will be received. As a result, during the three months ended June 30, 2020, we recorded a full reserve against the $8.1 million AOF receivable. Discussions between the Company and the ATO are ongoing with respect to this issue.

The following table summarizes research and development expenses for the three months ended June 30, 2020 and 2019.

	Three months ended June 30,	
	2020	**2019**
Research and development expenses (before impact of AOF)	9,242,146	8,223,783
Amounts reserved against AOF refund	8,107,695	—
Total research and development expenses	$ 17,349,841	$ 8,223,783

Excluding the $8.1 million increase in research and development expenses for amounts reserved against the AOF refund, research and development expenses for the second quarter of 2020 were $9.2 million, including stock-based compensation expense of $0.5 million.

General and administrative expenses for the second quarter of 2020 were $4.5 million, including stock-based compensation expense of $0.8 million.

The net loss for the second quarter of 2020 was $20.3 million with basic and diluted net loss per share of $(0.78). During the three months ended June 30, 2020, we recognized a $1.5 million non-cash foreign exchange gain, which is primarily due to the remeasurement of our Australian subsidiary’s assets and liabilities, which are denominated in the local currency to the Subsidiary’s functional currency (the U.S. dollar).

Financial Outlook

Management believes that the current cash and cash equivalents is sufficient to fund operations and capital requirements into the fourth quarter of 2021.

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, 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 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.

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited)

	Three months ended June 30,		Six months ended June 30,	
	2020	2019	2020	2019
Operating expenses:				
Research and development	$ 17,349,841	$ 8,223,783	$ 24,232,634	$ 14,530,495
General and administrative	4,492,034	3,287,276	8,408,603	6,446,933
Total operating expenses	21,841,875	11,511,059	32,641,237	20,977,428
Loss from operations	(21,841,875)	(11,511,059)	(32,641,237)	(20,977,428)
Other income (expense):				
Interest income	26,601	439,201	228,285	790,152
Foreign exchange gain (loss)	1,482,513	(63,327)	(257,638)	(94,926)
Total other income (expense)	1,509,114	375,874	(29,353)	695,226
Net loss	$ (20,332,761)	$ (11,135,185)	$ (32,670,590)	$ (20,282,202)
Net loss per share - basic and diluted	$ (0.78)	$ (0.50)	$ (1.32)	$ (0.98)
Basic and diluted weighted average shares outstanding	26,100,264	22,116,758	24,749,851	20,791,784
Non-cash stock-based compensation included above:				
Research and development	$ 534,900	$ 675,953	$ 1,045,376	$ 1,342,132
General and administrative	812,533	805,752	1,625,409	1,635,865
Total	$ 1,347,433	$ 1,481,705	$ 2,670,785	$ 2,977,997

ZYNERBA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	(unaudited) June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 77,006,040	$ 70,063,242
Incentive and tax receivables	6,528,682	14,613,969
Prepaid expenses and other current assets	1,804,243	2,378,812
Total current assets	85,338,965	87,056,023
Property and equipment, net	641,263	362,724
Incentive and tax receivables	1,274,382	—
Right-of-use assets	227,529	345,849
Total assets	$ 87,482,139	$ 87,764,596
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,882,768	$ 4,740,981
Accrued expenses	8,936,501	7,073,506
Lease liabilities	237,406	243,677
Total current liabilities	13,056,675	12,058,164
Lease liabilities, long-term	—	109,689
Total liabilities	13,056,675	12,167,853
Stockholders' equity:		
Common stock	29,255	23,211
Additional paid-in capital	257,902,423	226,409,156
Accumulated deficit	(183,506,214)	(150,835,624)
Total stockholders' equity	74,425,464	75,596,743
Total liabilities and stockholders' equity	$ 87,482,139	$ 87,764,596

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