UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15 (d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **September 18, 2019**

ZYNERBA PHARMACEUTICALS, INC.

(Exact Name of Issuer as Specified in its Charter)

Delaware	**001-37526**	**26-0389433**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

80 W. Lancaster Avenue, Suite 300
Devon, PA 19333
(Address of Principal Executive Offices) (Zip Code)

(484) 581-7505
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8—K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	ZYNE	The NASDAQ Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 8.01 Other Events

On September 18, 2019, Zynerba Pharmaceuticals, Inc. (the "Company") issued a press release announcing positive top line data from the BELIEVE 1 Open Label Phase 2 Study of Zygel™ in Developmental and Epileptic Encephalopathies (DEE). A copy of this press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

The following exhibits are being filed herewith:

(d) Exhibits

Exhibit No.	Document
99.1	Press Release, dated September 18, 2019

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 18, 2019

ZYNERBA PHARMACEUTICALS, INC.

By: /s/ Suzanne Hanlon
Name: Suzanne Hanlon
Title: Secretary, Vice President and General Counsel

Exhibit 99.1

Zynerba Pharmaceuticals Announces Positive Top Line Data from BELIEVE 1 Open Label Phase 2 Study of Zygel™ in Developmental and Epileptic Encephalopathies (DEE)

- Study Achieves a 44% Median Seizure Reduction in Focal Impaired Awareness (Complex Partial) and Convulsive Seizures in DEE Patients by Month Two; Reductions were Sustained through Month Six of Treatment with Zygel -

- At Least 42% of these Patients Experienced a ≥50% Improvement from Month Two through Month Six -

- Qualitative Assessments Demonstrate Improvements in Seizure Intensity and Duration, and Socio-behavioral and Cognitive Impairments -

DEVON, Pa., September 18, 2019 — Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, today announced positive top line results from the open label Phase 2 BELIEVE 1 (Open La**b**el Study to Assess the Safety and **E**fficacy of Zygel™ (ZYN002) Administered as a Transdermal **l** Gel to Ch**i**ldren and Adol**e**scents with De**v**elopmental and **E**pileptic Encephalopathy) clinical trial. The trial assessed the safety and efficacy of Zygel in developmental and epileptic encephalopathies (DEE), a heterogeneous group of rare pediatric epilepsy syndromes, including Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS). DEE is characterized by the presence of multiple focal and generalized seizure types and severe cognitive and behavioral impairment. The most common and debilitating seizure types in people with epilepsy are focal impaired-awareness and convulsive seizures. Patients who experienced these seizure types achieved 44% to 58% monthly median reductions in seizures compared to baseline from month two to month six of treatment with Zygel. Further, qualitative assessments by caregivers in the study demonstrate that use of Zygel may result in improved socio-behavioral and cognitive symptoms of DEE. Zygel was also well tolerated in this study.

“The data from the BELIEVE 1 clinical trial are promising and suggest that Zygel may reduce seizure frequency in many types of difficult to treat developmental and epileptic encephalopathies and improve important behavior deficits, alertness, social interactions, and enable the child to be well enough to attend school more consistently,” said Ingrid Scheffer, AO, MBBS, PhD, FRACP, Professor and Chair, Paediatric Neurology Research, The University of Melbourne, and an investigator in the BELIEVE 1 trial. “DEE are the most challenging and poorly controlled epilepsy disorders with many symptoms that adversely affect patient and family function. I believe that this drug holds promise as a potential treatment for DEE.”

“We are encouraged by the positive top line results of the BELIEVE 1 trial of Zygel in children and adolescents with DEE, and we believe these data represent an important step forward for these patients and their families,” said Armando Anido, Zynerba’s Chairman and Chief Executive Officer. “These results suggest that Zygel may produce clinically meaningful reductions in seizures and may improve many of the difficult behaviors and symptoms, such as seizure intensity, fatigue, social isolation, poor cognition,

and language deficits. Once we complete our analyses of the data, we intend to seek a meeting with the FDA, likely in the first half of next year, to discuss the clinical pathway to approval."

Study Design

The six-month BELIEVE 1 clinical trial is an exploratory open label multi-dose Phase 2 clinical trial designed to evaluate the safety and efficacy of Zygel in children and adolescents (three to <18 years) with DEE as classified by the International League Against Epilepsy (ILAE) (Scheffer et al. 2017). Forty-eight patients with confirmed DEE were enrolled in the clinical trial and are included in the safety data for the trial. Forty-six patients are included in the modified intent-to-treat population (mITT). The two patients excluded from the intent-to-treat population included one patient who did not complete 80% of their seizure diaries and a second patient who did not complete a minimum of eighty days of treatment. Enrolled patients received weight-based initial doses of 250 mg or 500 mg daily of Zygel. Patients could be titrated up to 1,000 mg daily.

Baseline Patient Demographics

The BELIEVE 1 trial enrolled 48 patients between the ages of three and 16 (mean=10.5; median=10.0). Fifty-four percent of patients were male, and 46% were female. Patients weighed between 14.3 and 110 kilograms (mean=39.3; median=36.1). Patient BMI ranged between 12.5 and 35.4 (mean=19.2; median=18.6).

Top-line Efficacy Results

Of the 46 patients in the mITT population, 33 (72%) had focal impaired-awareness seizures (FIAS; previously known as complex partial seizures) and/or convulsive seizures (focal to bilateral tonic-clonic seizures and generalized tonic-clonic seizures) at baseline. These patients experienced a mean baseline seizure count of 64 FIAS and/or convulsive seizures, and a median baseline seizure count of 8.2 FIAS and/or convulsive seizures. Compared to baseline seizure frequency, these patients experienced a ≥44% median reduction in seizures from month two onwards using monthly seizure frequency normalized to 28 days (SF28).

Fifty-five percent (55%) of patients with FIAS and/or convulsive seizures experienced a ≥50% median reduction in seizures at month six of treatment with Zygel.

FIAS and convulsive seizures	Month 1 (n=33)	Month 2 (n=33)	Month 3 (n=33)	Month 4 (n=32)	Month 5 (n=32)	Month 6 (n=29)
Median % reduction in seizure frequency	16%	44%	44%	47%	58%	51%
≥50% responder rate	30%	42%	46%	47%	63%	55%

Thirteen of the 46 patients had a variety of non-FIAS and non-convulsive seizure types at baseline. The number of individual seizure types in these patients was too small to draw definitive conclusions and further analyses are warranted.

Patients with either DS or LGS who experienced FIAS and/or convulsive seizures (n=11) experienced a 51% median reduction in FIAS and/or convulsive seizures at month six of treatment compared to baseline. Sixty percent (60%) of patients with DS or LGS experienced a ≥50% median reduction in FIAS or convulsive seizures at month six of treatment with Zygel.

Lennox-Gastaut and Dravet syndromes	Month 1 (n=11)	Month 2 (n=11)	Month 3 (n=11)	Month 4 (n=11)	Month 5 (n=11)	Month 6 (n=10)
Median % reduction in seizure frequency	18%	6%	46%	23%	63%	51%
≥50% responder rate	36%	36%	46%	40%	64%	60%

Safety data

Zygel was well tolerated, and the safety profile was consistent with previously released data from Zygel clinical trials. Eight patients discontinued the study; one discontinued as a result of an application site reaction, and seven discontinued as a result of withdrawal of consent or perceived lack of efficacy. Through six months of therapy, ninety-six percent (96%) of patients experienced a treatment emergent adverse event (TEAE) and 60% of patients experienced a treatment related adverse event. Most were mild to moderate. The most common treatment related adverse events (in >5% of patients) are application site dryness (8.3%), application site pain (8.3%), and somnolence (8.3%). Ten patients reported a serious adverse event (SAE); most were infection-related. Two SAEs (lower respiratory tract infection and status epilepticus) were determined to be possibly related to treatment. There were no patient deaths during the study.

Qualitative analysis of the impact of Zygel on behavioral and cognitive symptoms

Parents and caregivers were asked to provide a qualitative assessment regarding their child's overall experiences during treatment with Zygel. The experiences of 43 patients are summarized below.

- 58% reported improved vitality (e.g. alertness / awareness, energy)
- 51% reported improvement in seizures
- 47% reported improved cognition and concentration
- 44% reported improved socially avoidant behaviors
- 28% reported that their child attended school on time / more often
- 26% reported difficulty in application of the gel to their child (e.g. time it takes for gel to dry)

About Developmental and Epileptic Encephalopathies (DEE)

DEE is a heterogeneous group of epilepsy syndromes that may be associated with severe cognitive impairment and behavioral disturbances. These disorders are often progressive, and are highly resistant to treatment. DEE includes a number of rare and ultra-rare epilepsy syndromes including early myoclonic encephalopathy, epileptic encephalopathy with continuous spike and wave during sleep, and certain syndromes including Ohtahara, West, Landau-Kleffner, Lennox-Gastaut, Doose and Dravet. Improved seizure control may have a positive impact on development and quality of life.

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. For example, there can be no guarantee that the Company will obtain approval for Zygel from the U.S. Food and Drug Administration (FDA) or foreign regulatory authorities; even if Zygel is approved, the Company may not be able to obtain the label claims that it is seeking from the FDA. 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 FDA 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; and the Company's expectations regarding its ability to obtain and adequately maintain sufficient intellectual property protection for its product candidates. 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 Contact
William Roberts, Vice President, Investor Relations and Corporate Communications
Zynerba Pharmaceuticals
484.581.7489
robertsw@zynerba.com

Media contact
Molly Devlin
Evoke KYNE
215.928.2199
Molly.Devlin@evokegroup.com