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): **October 15, 2020**

ZYNERBA PHARMACEUTICALS, INC.

(Exact Name of Issuer as Specified in Charter)

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

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

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

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)
Securities registered pursuant to Section 12(b) of the Act:

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 October 15, 2020, Zynerba Pharmaceuticals, Inc. ("the Company") issued a press release announcing that it is presenting a poster titled, "ZYN002 Cannabidiol Transdermal Gel in Children and Adolescents With Fragile X Syndrome: Role of Methylation Status as a Correlate to Disease Severity and as a Prognostic Biomarker," at the Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting. Data from this poster will also be presented as an oral presentation during the "Research Pipeline: New Findings on Diagnostic and Therapeutics" session of the virtual American Academy of Child and Adolescent Psychiatry (AACAP) 2020 Annual Meeting on Friday, October 23rd, 2020.

On October 15, 2020, the Company issued a second press release announcing that it is presenting a poster titled "Tolerability and Efficacy of ZYN002 Cannabidiol (CBD) Transdermal Gel in Children and Adolescents With Autism Spectrum Disorder: An Open-Label Phase 2 Study [BRIGHT (ZYN2-CL-030)]," at the Joint 16th International Child Neurology Congress (ICNC) and 49th Annual Child Neurology Society (CNS) Meeting. Data from this poster will also be presented as an oral presentation during the "Research Pipeline: New Findings on Diagnostic and Therapeutics" session of the virtual American Academy of Child and Adolescent Psychiatry (AACAP) 2020 Annual Meeting on Friday, October 23rd, 2020.

Copies of the two press releases are attached hereto as Exhibits 99.1 and 99.2 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 October 15, 2020
99.2	Press Release, dated October 15, 2020
104	The cover page from this current report on Form 8-K, formatted in Inline XBRL

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: October 15, 2020

ZYNERBA PHARMACEUTICALS, INC.

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

Exhibit 99.1

Zynerba Pharmaceuticals Presents Data Supporting *FMR1* Methylation Status as a Correlate to Fragile X Syndrome Severity at the Virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting

DEVON, Pa., October 15, 2020 – Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, is presenting a poster describing data from the CONNECT-FX (**C**linical study **O**f Ca**NN**abidiol (CBD) in Childr**E**n and Adoles**C**en**T**s with **F**ragile **X**) trial describing the role of *FMR1* methylation status in children and adolescents with Fragile X syndrome (FXS) as a correlate to disease severity and as a prognostic biomarker. These data are being presented at the virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting. These data will also be presented as an oral presentation during the "Research Pipeline: New Findings on Diagnostic and Therapeutics" session of the virtual American Academy of Child and Adolescent Psychiatry (AACAP) 2020 Annual Meeting on Friday October 23rd, 2020.

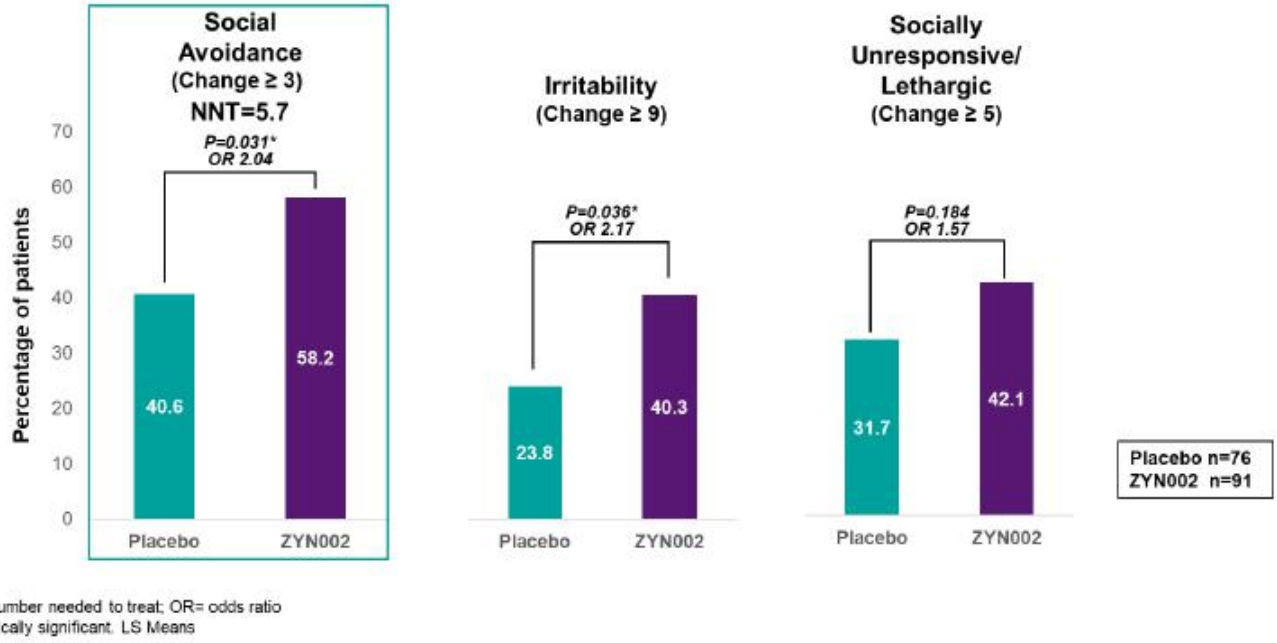
A copy of the poster entitled, "*ZYN002 Cannabidiol Transdermal Gel in Children and Adolescents With Fragile X Syndrome: Role of Methylation Status as a Correlate to Disease Severity and as a Prognostic Biomarker"* is available on the Zynerba corporate website at http://zynerba.com/publications/.

"We are excited to provide an update on the potential role of methylation status of the *FMR1* gene as a predictive biomarker of preferential response to Zygel™ (ZYN002) in the treatment of the behavioral symptoms of FXS," said Zynerba's Chief Medical Officer, Joseph M. Palumbo, MD, FAPA, MACPsych. "These new data demonstrate that in patients diagnosed with FXS with a fully methylated *FMR1* gene significantly more patients who received Zygel achieved a clinically meaningful improvement in their behavioral symptoms compared to patients who received placebo."

CONNECT-FX is a randomized, double-blind, multinational, 14-week pivotal study to evaluate the efficacy and safety of Zygel in children/adolescents aged 3 to 17 years. Although the CONNECT-FX full analysis set did not achieve statistical significance in its endpoints, building on current scientific evidence, a pre-planned ad hoc analysis of patients having at least 90% methylation ("full methylation" or FMet) of the impacted *FMR1* gene, representing 80% of the overall study population, was performed. The results, including the achievement of statistical significance (p=0.020) in the primary endpoint of improvement at 12 weeks of treatment in the Social Avoidance subscale of the ABC-C_{FXS} compared to placebo, suggest that Zygel may have benefit in patients with full methylation of the *FMR1* gene.

Zynerba utilized psychometric analyses to determine what constitutes a clinically meaningful change from baseline as measured by subscales of the ABC-C_{FXS}. New results described today include the results of these analyses which support the definition of a clinically meaningful treatment response over 12 weeks of treatment as an improvement of three points or greater for the Social Avoidance subscale, nine points or greater for the Irritability subscale, and five points or greater for the Socially Unresponsive / Lethargic subscale. The Company determined that 58.2% of FMet patients receiving Zygel achieved a clinically meaningful change in their socially avoidant behavior compared to 40.6% of patients receiving placebo (statistically significant; p=0.031), and 40.3% of patients receiving Zygel achieved a clinically meaningful change in Irritability compared to 23.8% of patients receiving placebo (statistically significant; p=0.036).

Figure 1: Greater Percentages of Participants Achieved Meaningful Change in ABC-C_{FXS} Social Avoidance and Irritability with ZYN002 vs Placebo



NNT=number needed to treat; OR= odds ratio
*Statistically significant. LS Means

The authors of the poster concluded that:

- To our knowledge, CONNECT-FX is the largest controlled study ever performed in FXS.
- These results may represent an important step forward in biomarker-driven prediction of response in FXS and neuroscience.
  - Zygel was well tolerated, and the safety profile was consistent with previously reported clinical trials.
  - In the FMet group, Zygel was superior to placebo in multiple analyses, including:
    - Statistically significant mean change in Social Avoidance vs placebo;
    - Proportion of patients attaining threshold of clinically meaningful change in Social Avoidance and Irritability;
    - Caregiver reported improvements, including statistically significant improvements in Social Avoidance and Isolation, Social Interaction, and Irritable and Disruptive Behaviors.
- Zynerba will be meeting with the FDA in the fourth quarter of 2020 to discuss these data.

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; 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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Exhibit 99.2

New Data Describing Statistically Significant Results from the Phase 2 BRIGHT Trial in Patients with Autism Spectrum Disorder (ASD) Presented at the Virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting

DEVON, Pa., October 15, 2020 – Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, is presenting a poster describing data from the Phase 2 BRIGHT (An Open-La**b**el Tole**r**abi**l**ity and Efficacy Study of ZYN002 Administered as a Transdermal **G**el to C**h**ildren and Adolescen**t**s with Autism Spectrum Disorder) trial further demonstrating the potential for Zygel™ (ZYN002) to improve the core behavioral symptoms of autism when administered in addition to stable standard of care in children and adolescents with moderate-to-severe ASD. These open label data are being presented at the virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting. These data will also be presented as an oral presentation during the "Research Pipeline: New Findings on Diagnostic and Therapeutics" session of the virtual American Academy of Child and Adolescent Psychiatry (AACAP) 2020 Annual Meeting on Friday October 23rd, 2020.

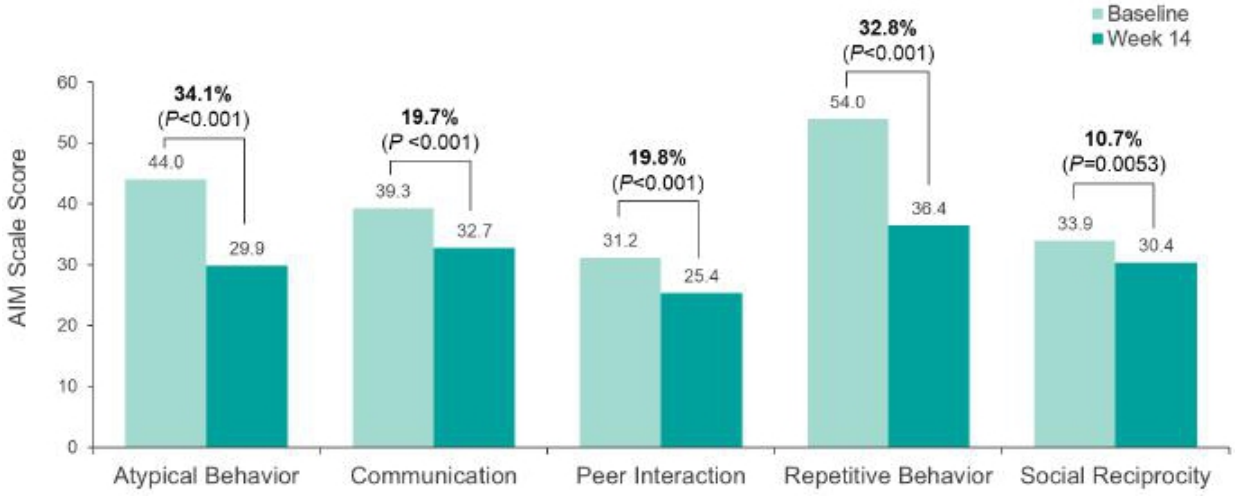
A copy of the poster entitled, "*Tolerability and Efficacy of ZYN002 Cannabidiol (CBD) Transdermal Gel in Children and Adolescents With Autism Spectrum Disorder: An Open-Label Phase 2 Study [BRIGHT (ZYN2-CL-030)]"* is available on the Zynerba corporate website at http://zynerba.com/publications/.

"The Phase 2 BRIGHT trial provides the first clinical evidence of the potential for Zygel to improve behavioral symptomology in a group of highly symptomatic pediatric and adolescent patients with ASD," said Helen Heussler, FRACP, Associate Professor at Children's Health Queensland, Medical Director Child Development and principal investigator in the BRIGHT trial. "In these children receiving Zygel, the observed changes from baseline are promising. In particular, the improvements seen in core symptoms of autism, as specifically assessed by the Autism Impact Measure, are of special interest. Though open label, these results are compelling and we look forward to continuing the evaluation of Zygel in ASD in future placebo-controlled clinical trials."

The BRIGHT Phase 2 trial is an exploratory, single-center, open-label Phase 2 study evaluating the safety and tolerability and efficacy of Zygel in children and adolescents with ASD who are 3 to <18 years old. The study enrolled patients with Clinical Global Impression (CGI)-Severity score ≥4 (moderate or greater) and Aberrant Behavior Checklist-Community (ABC-C) Irritability score ≥18. The primary objective of the trial was to evaluate the safety and tolerability of Zygel for up to 38 weeks (14-week treatment period and a 6 month extension period). Secondary objectives comprised evaluation of the efficacy of Zygel in the treatment of symptoms of ASD, including measuring parental/caregiver stress, Autism Impact Measure (AIM), and caregiver reported behavioral problems. The results provided in the poster are after 14 weeks of treatment with Zygel.

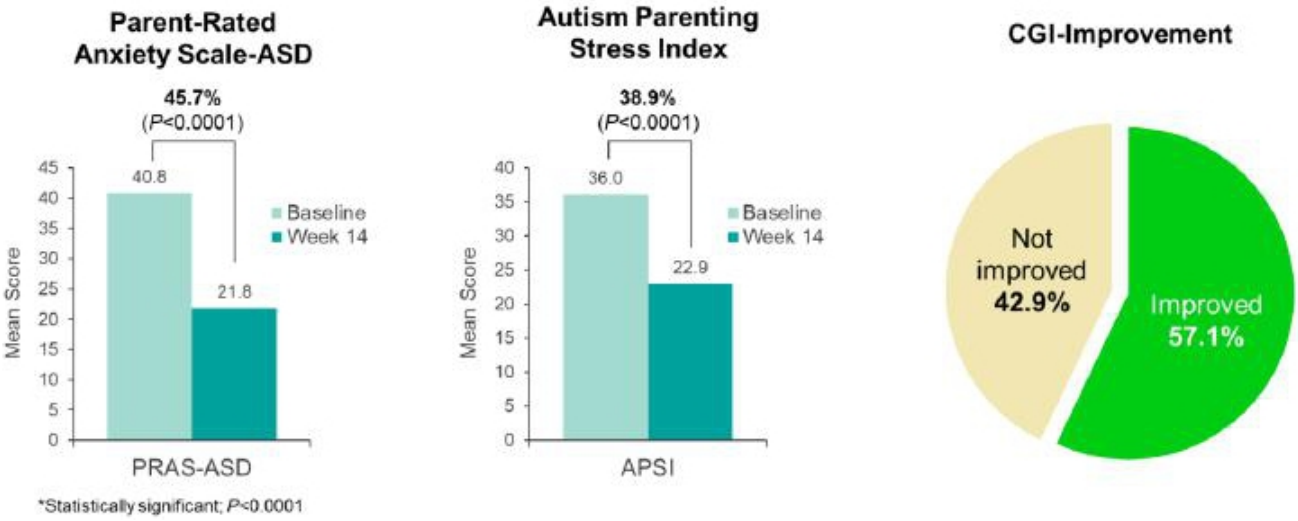
New data presented today include that patients receiving Zygel in this study achieved statistically significant caregiver-reported improvements compared to baseline across all subscales of the AIM, which was designed to track incremental change in frequency and impact of core ASD symptoms: Atypical behavior (p<0.001), Communication (p<0.001), Peer Interaction (p<0.001), Repetitive Behavior (p<0.001), and Social Reciprocity (p=0.0053).

Figure 1. Statistically Significant Improvements in Autism Impact Measure Scores



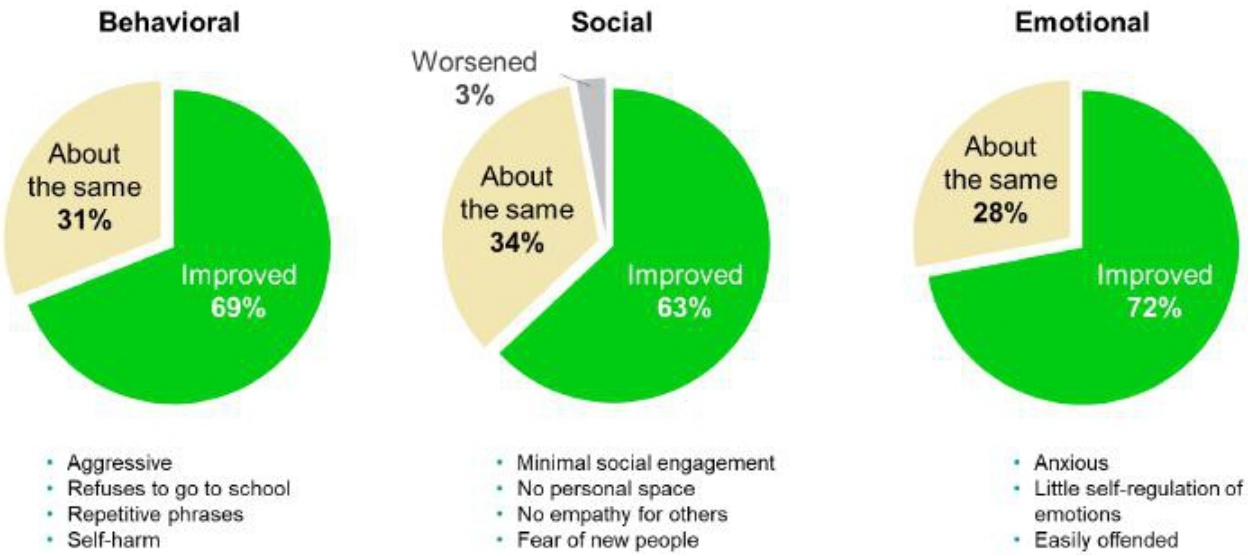
In addition, statistically significant improvements compared to baseline were observed at week 14 of treatment with Zygel in the Autism Parenting Stress Index (p<0.0001).

Figure 2. Statistically Significant Improvements in PRAS-ASD, APSI, and CGI-I



Zynerba also measured notable improvements in behaviors utilizing the Qualitative Caregiver Behavioral Problems Survey after 14 weeks of study drug. Clinically meaningful improvements were observed by a majority of surveyed caregivers in behavioral, social and emotional behavioral problems.

Figure 3. Notable Improvements in the Qualitative Caregiver Behavioral Problems Survey at Week 14



The authors of the poster concluded that:

- The BRIGHT trial provides initial evidence suggesting a positive benefit-risk profile for Zygel when administered in addition to stable standard of care in children and adolescents with moderate-to-severe ASD;
- Zygel showed improvement in all ASD measures (ABC-C, AIM, PRAS-ASD, CGI and Qualitative Caregiver Assessments);
- Further controlled studies are warranted in this difficult-to-treat population.

These results supplement the topline data initially disclosed by the Company in May 2020 (Press release), including that:

- 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 in this trial and the safety profile was consistent with previously released data from other Zygel clinical trials. No serious or severe adverse events were reported.

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