Corporate Overview

June 2, 2020

Forward-Looking Statements

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Zynerba Pharmaceuticals (NASDAQ: ZYNE)

A Rare/Near-Rare Neuropsychiatric Company

- Deep pipeline focused on high unmet medical needs; translating into multi-billion dollar market opportunity with Zygel™(CBD gel)
  - Four clinical shots on goal: FXS, DEE, ASD, 22q
  - Positive results announced in BRIGHT trial in ASD including statistically significant and clinically meaningful improvements from baseline in all subscales of the ABC-C
  - Enrollment complete in pivotal CONNECT-FX trial in FXS with topline results expected in late June 2020
- Experienced team
  - Proven development and commercialization track record in transdermal delivery, orphan diseases, neurology, psychiatry
- Well capitalized
  - Cash runway expected into the second half of 2021 - beyond the expected NDA filing and potential approval in FXS
- Multiple expected near term milestones

COVID-19 Preparedness

- We believe we have made smart and actionable adjustments in response to COVID-19:
  - These include remote site monitoring and remote visits using telemedicine where needed
  - Our approach is consistent with FDA's Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic
- As of now, our timelines for delivery of top line results from all of our ongoing trials remain unchanged
  - Includes our expectation of results from our pivotal CONNECT-FX trial in FXS late in late June 2020

Deep Clinical Pipeline

Zygel
Cannabidiol Gel

Indication	Preclinical	Phase 1	Phase 2	Pivotal	Expected Milestones
Fragile X Syndrome (FXS)*					
	CONNECT-FX: Enrollment complete				Topline pivotal data in late June 2020
Developmental and Epileptic Encephalopathies (DEE)					
	BELIEVE: Positive data released				Results of discussions with FDA on clinical path forward in 3Q2020
Autism Spectrum Disorder (ASD)					
	BRIGHT: Positive data released				Meet with FDA to discuss clinical path forward in 2H2020
22q Deletion Syndrome (22q)					
	INSPIRE				Topline Phase 2 data in 3Q2020

*Orphan Drug Designation

Zygel (ZYN002) Cannabidiol (CBD) Gel

Differentiated

First & only patent-protected, permeation-enhanced, pharmaceutically-produced CBD gel

Transdermal

Formulation delivers CBD through the epidermis and into the circulatory system

Unique MOA

CBD modulates multiple receptors and mediates numerous pathways, including the endocannabinoid pathway

Neuropsych Indications

Potential utility in rare / near-rare neuropsychiatric conditions

FDA Fast Track and Orphan Drug designations in FXS

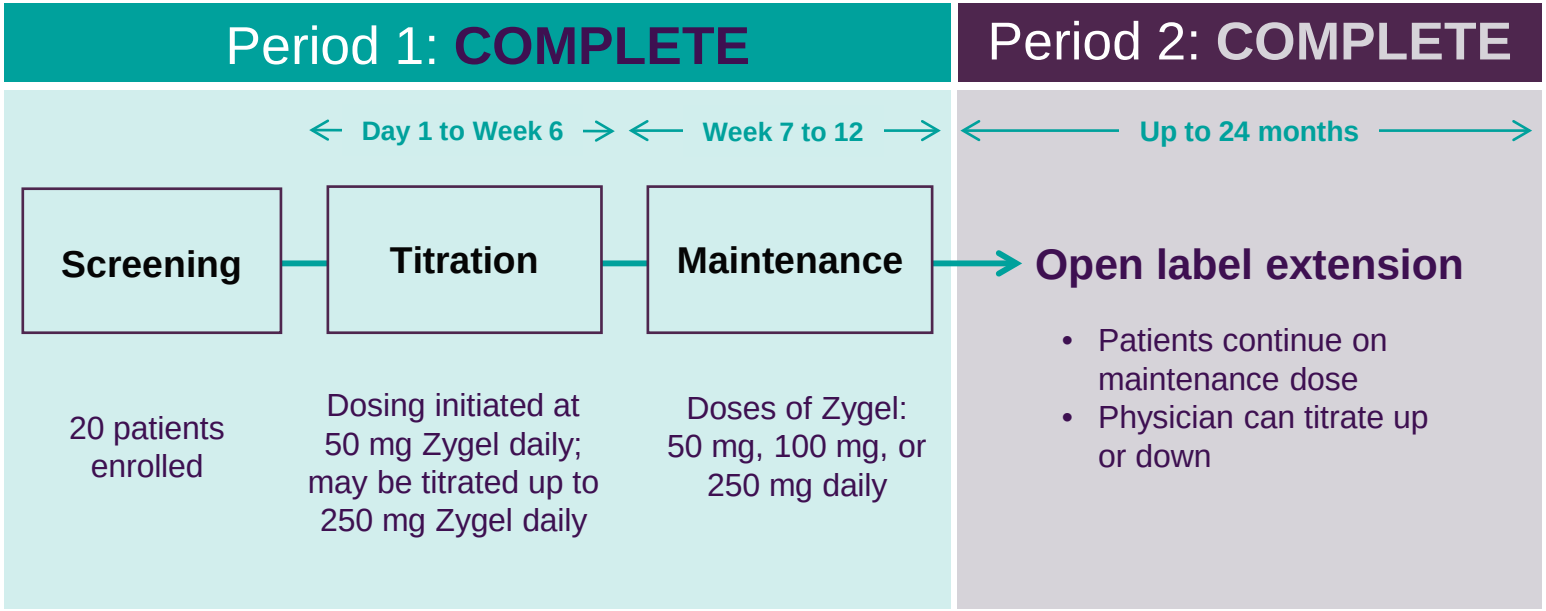
Fragile X Syndrome (FXS)

Fragile X Syndrome (FXS) Overview

- Rare genetic developmental disability
- Leading known cause of both inherited intellectual disability and autism spectrum disorder
- Symptoms linked to deficiencies in the endocannabinoid (EC) system
  - System of neurotransmitters regulating emotional responses, behavioral reactivity to context, social interaction
  - FMR1 mutation causes dysregulation of the EC system
  - Results in core cognitive, social, and behavioral symptoms of FXS
  - CBD may modulate EC system
    - Increases availability of endocannabinoids (anandamide, 2-AG) by inhibiting metabolism
- Affects ~71K people in U.S.
- No approved drugs indicated for FXS

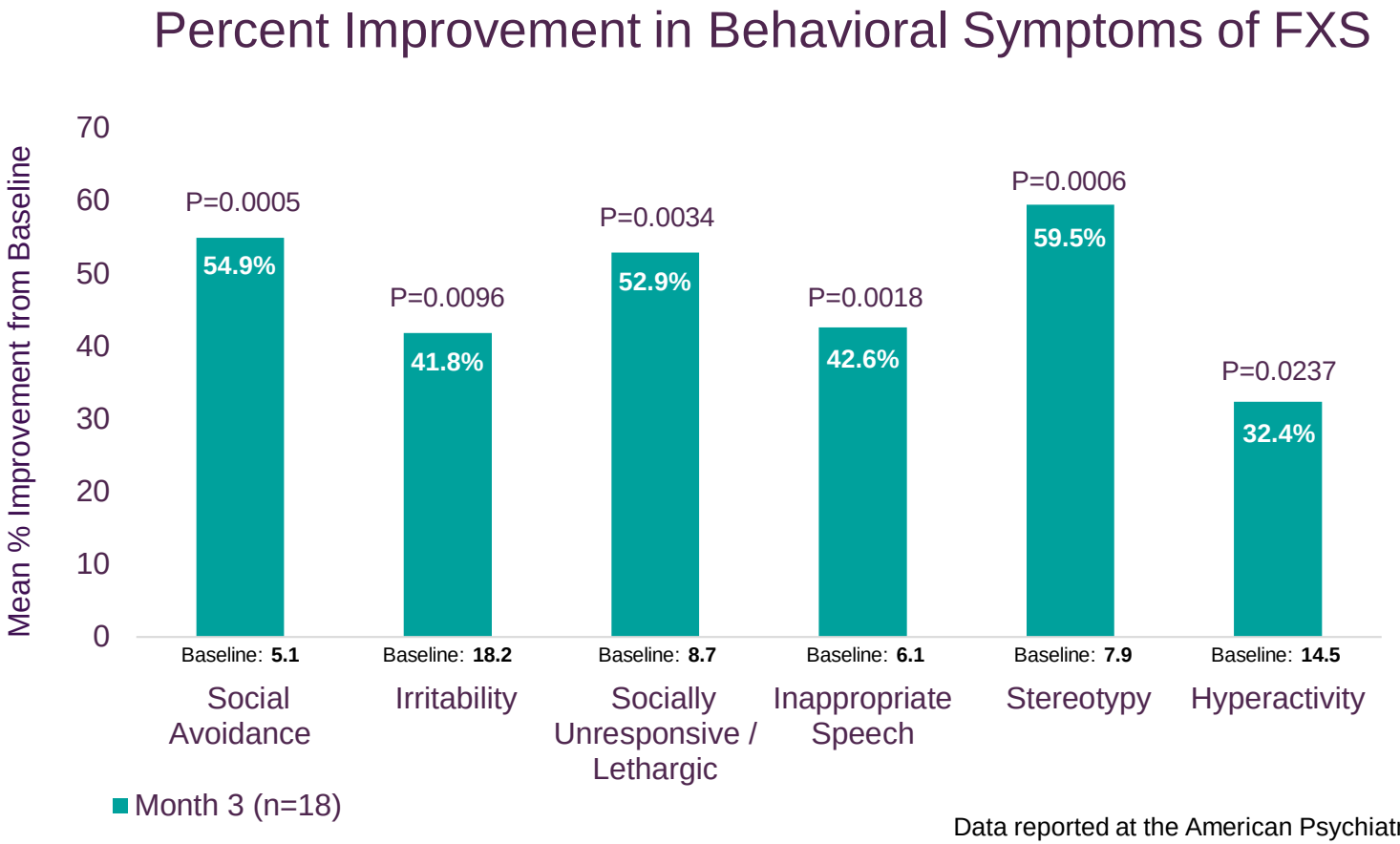
FAB-C Open Label Phase 2 Trial Design

Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD



Data From Three Month FAB-C Phase 2 Trial

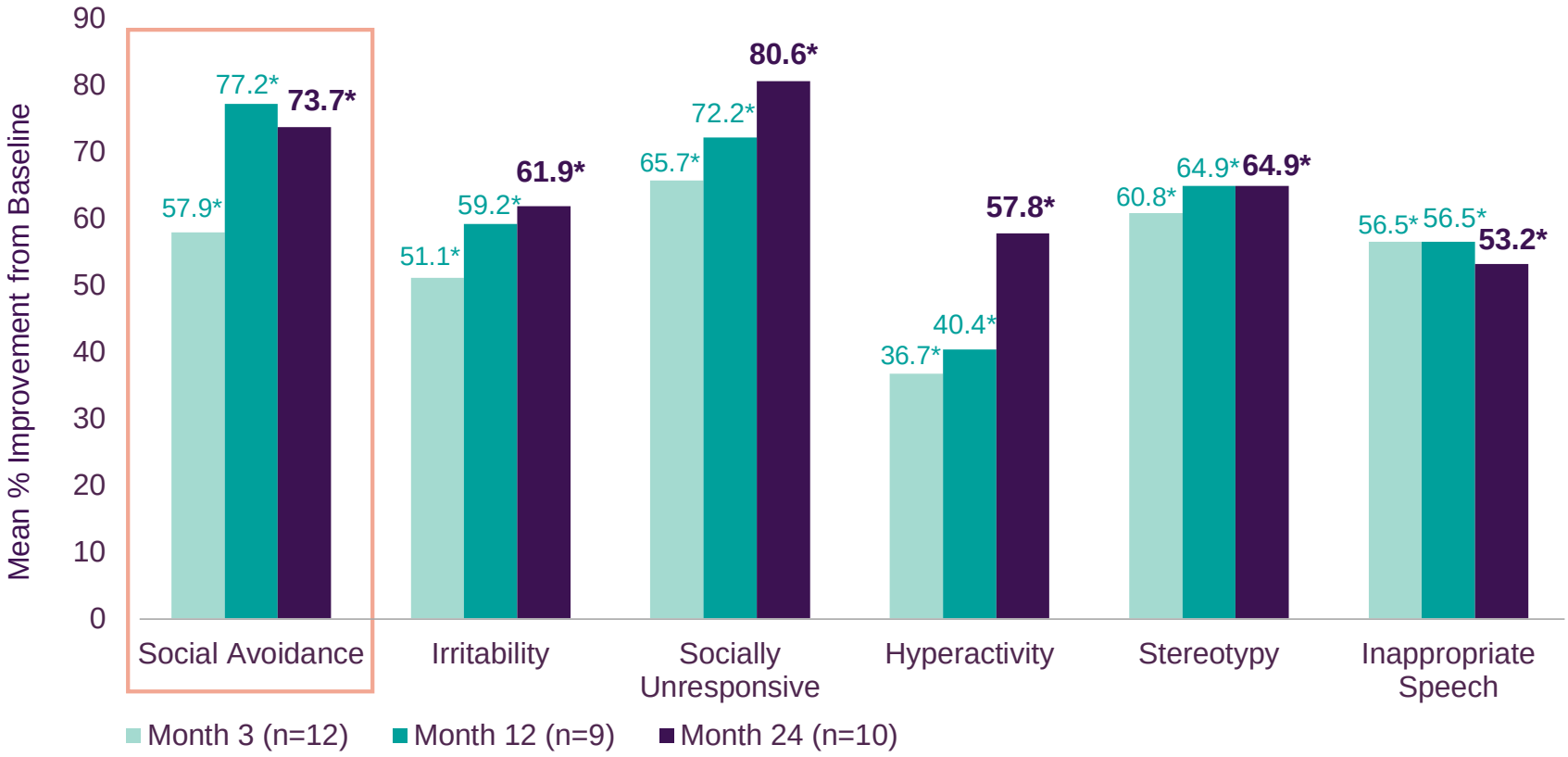
Month Three: ABC-C_{FXS} Mean Score



Data reported at the American Psychiatric Association (APA) meeting, May 2019

Sustained Improvements in FXS Behavioral Symptoms Through Two Years of Treatment

Improvements in Patients Completing 3, 12 and 24 Months



*P ≤ 0.05

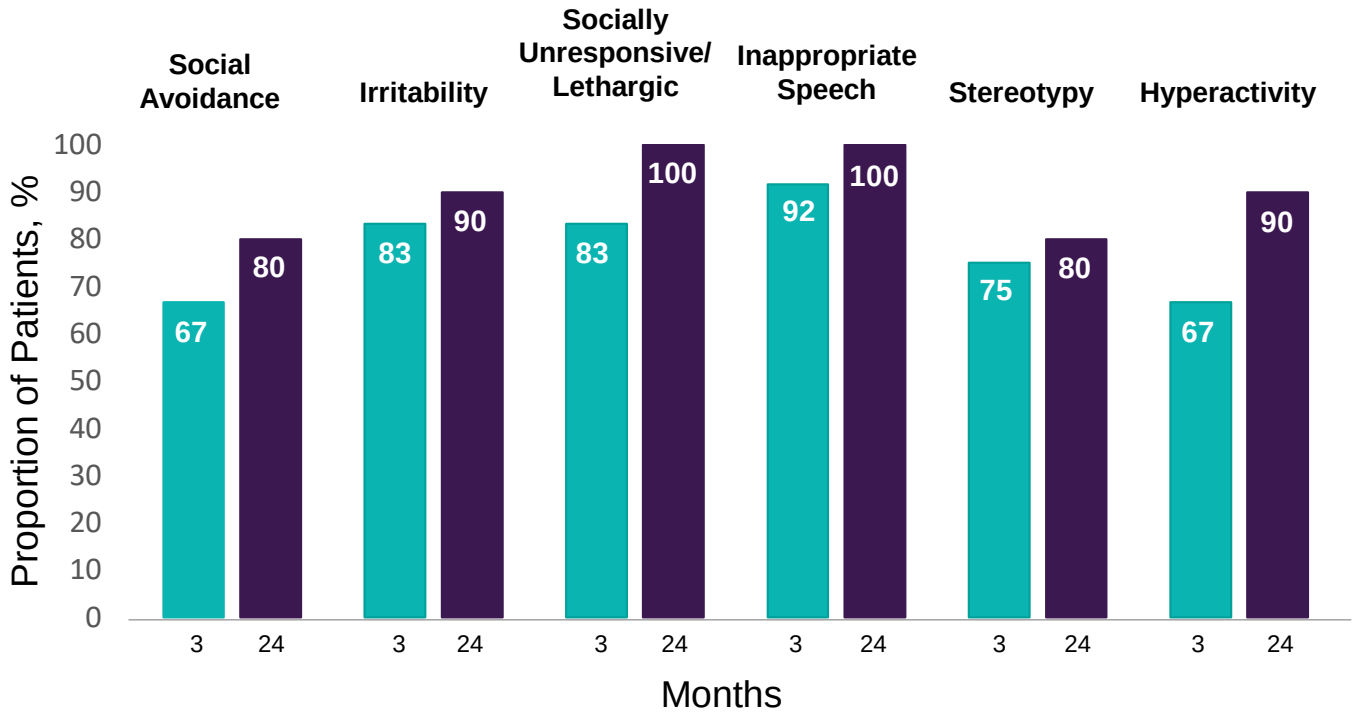
Data reported at the Data reported at the American Psychiatric Association (APA) meeting, May 2019; 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session, May 2020

- Month 3 and 12 include patient completing 12 months
- Month 24 includes patients completing 24 months

FAB-C Open Label Phase 2 Trial

≥25% Responder Analyses for Patients Who Entered Period 2

Proportion of Patients with a ≥25% Improvement from Baseline ABC-C_{FXS} Subscales

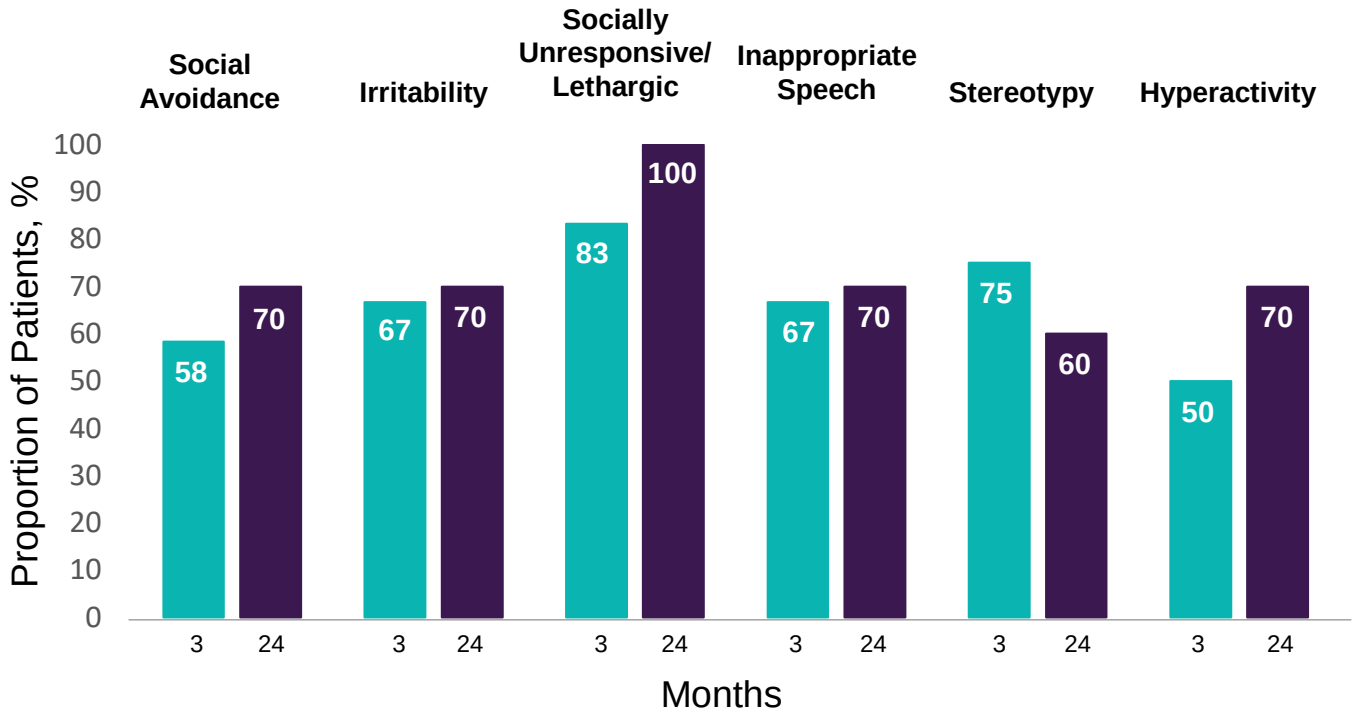


Data reported at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

FAB-C Open Label Phase 2 Trial

≥50% Responder Analyses for Patients Who Entered Period 2

Proportion of Patients with a ≥50% Improvement from Baseline ABC-C_{FXS} Subscales



Data reported at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

FAB-C Open Label Phase 2 Trial

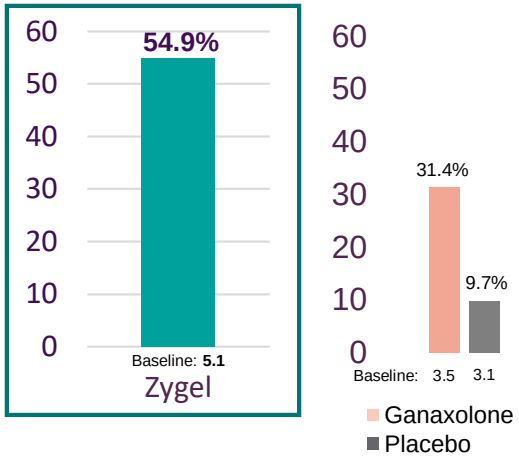
Zygel Safety Summary Through 24 Months

- Well tolerated, consistent with previously reported data
- No drug-related SAEs
- 66 treatment-emergent adverse events (TEAE; all events, whether unrelated or related to study drug) reported in 19 patients
  - All were either mild (85%) or moderate (15%)
  - 91% were determined to be unrelated to treatment
- No treatment-related TEAEs occurred in more than one patient
- No clinically meaningful trends in vital signs, ECG, or clinical safety labs including LFTs; no THC detected in plasma

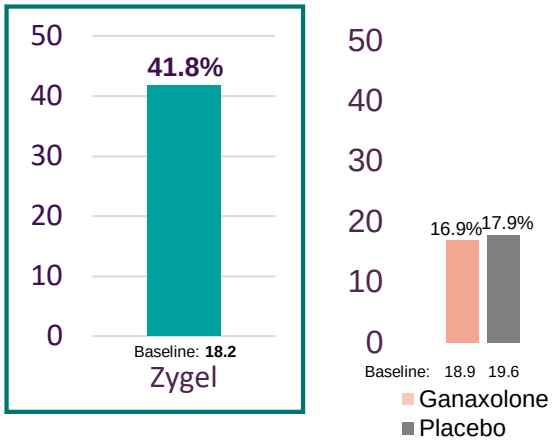
FAB-C ABC-C_{FXS} Subscales

Third Party Data* Suggest PBO Rate of 10 to 18 Percent

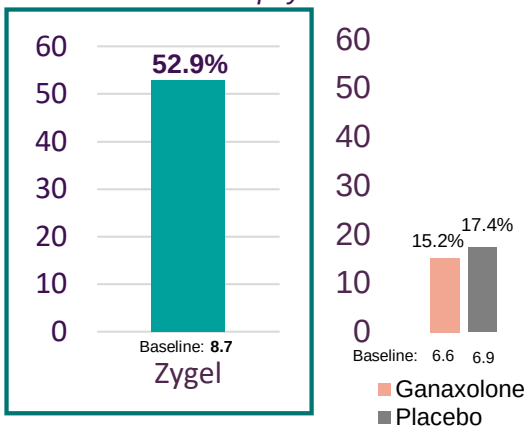
Social Avoidance
Seeks isolation



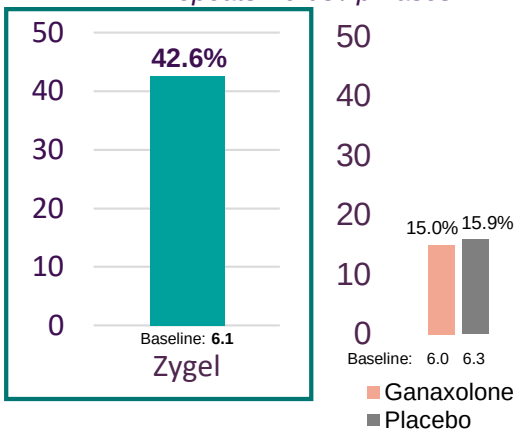
Irritability
Temper tantrums



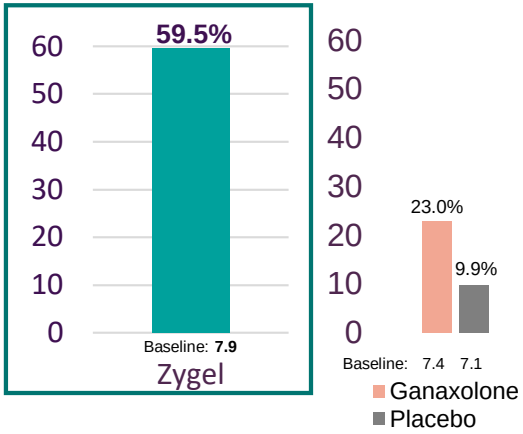
Socially Unresponsive / Lethargic
Does not pay attention



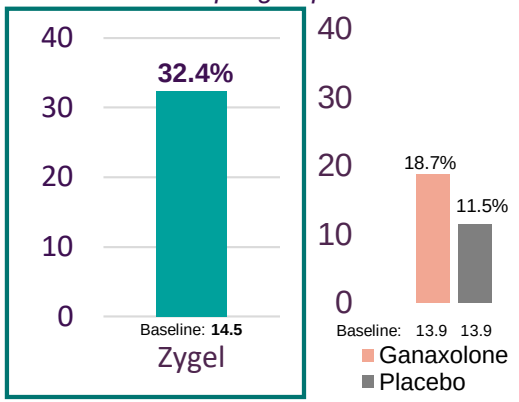
Inappropriate Speech
Repeats words / phrases



Stereotypy
Repetitive movements



Hyperactivity
Disrupts group activities

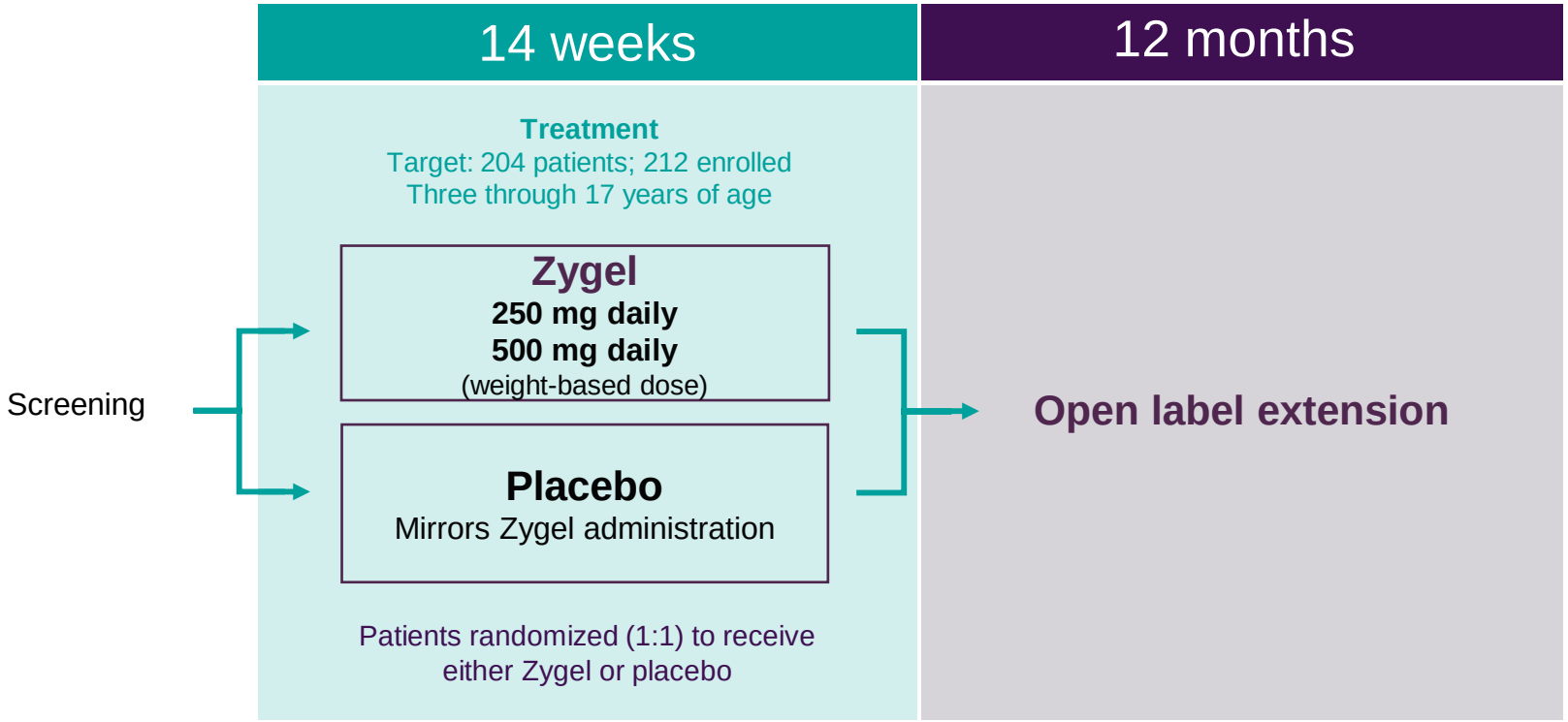


* Ligsay, A., Van Dijck, A., Nguyen, D. V., Lozano, R., Chen, Y., Bickel, E. S., et al. (2017). A randomized double-blind, placebo-controlled trial of ganaxolone in children and adolescents with fragile x syndrome. Journal of Neurodevelopmental Disorders, 9:26.

CONNECT-FX: A Pivotal Trial In FXS

Enrollment Complete; Topline Data Expected in Late 2Q2020

Clinical study Of CaNNabidiol (CBD) in ChildrEn and AdolesCenTs with Fragile X (CONNECT-FX)



CONNECT-FX: A Pivotal Trial In FXS

- Primary endpoint:
  - Change from baseline to end of treatment in ABC-C_{FXS} Social Avoidance subscale
- Key secondary endpoints:
  - Change from baseline to end of the treatment in
    - ABC-C_{FXS} Irritability subscale score
    - ABC-C_{FXS} Socially Unresponsive/Lethargic subscale score
  - Improvement in Clinical Global Impression (CGI-I) at end of treatment, anchored to FXS behaviors
- Aligned with FDA's 'Voice of the Patient' Guidance
  - Capturing qualitative data on clinical relevance of FXS behaviors
  - New data presented at ISCTM (February 2020) and ASENT (March 2020) further validate core FXS behaviors from the perspective of caregivers
- Top line results expected in late June 2020

CONNECT-FX Demographics

Patients	n
Randomization: Enrollment complete	212
Number of male patients	159 (75%)
Mean age at randomization in study	9.7 years
Completed 14-week Tx period (as of 5/8/2020)	188
Percent of completed patients enrolling in CONNECT-FX OLE	96%

Baseline Behavior Severity: CONNECT-FX vs Ph2 FAB-C

Prospective inclusion criteria expected to provide a more severely impacted population which we believe should enhance ability to demonstrate a strong signal of activity and minimize response variability

ABC-C_{FXS} Subscale	CONNECT-FX baseline score	Phase 2 FAB-C baseline score
Social Avoidance (12 point scale)	**7.2**	5.1
Irritability (54 point scale)	**28.1**	18.2
Socially Unresponsive / Lethargic (39 point scale)	**13.2**	8.7
Hyperactivity (30 point scale)	**18.4**	14.5
Stereotypy (18 point scale)	**9.4**	7.9
Inappropriate Speech (12 point scale)	**6.9**	6.1

Note: Higher baseline scores denote more severe behaviors

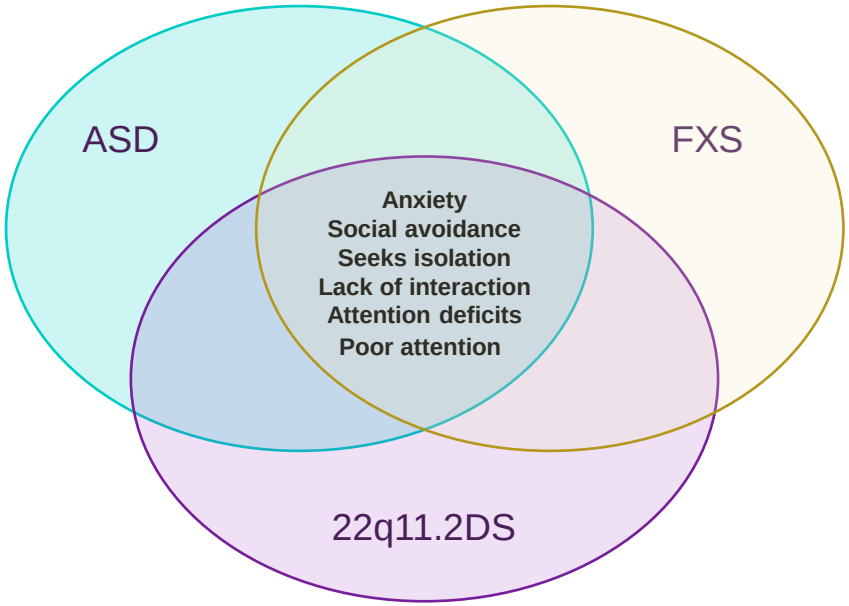
CONNECT-FX

- With positive results in pivotal trial, Zynerba intends to request a meeting with the FDA to:
  - Determine acceptability of data as basis for NDA filing by YE 2020
  - Seek advice on marketing authorization preparation
- Potential approval by mid-year 2021
- Zynerba believes the indication may be the treatment of behavioral symptoms associated with FXS

Improvements in Behavior May Provide a Read-Through to Other Zygel Studies

- Presented data at SSBP* showing constellation of shared socio-behavioral symptoms in ASD, FXS, and 22q11.2DS
- These include anxiety leading to:
  - Isolation and social avoidant behaviors
  - Irritability
  - Attention deficits
  - Poor communication

Common behavioral Features of ASD, FXS, and 22q11.2DS*



Common Behavioral Features of Autism, Fragile X Syndrome, and 22q11.2 Deletion Syndrome, Society for the Study of Behavioural Phenotypes (SSBP), 2019

Autism Spectrum Disorder (ASD)
in children and adolescents

ASD in Pediatrics Overview

- Near-rare disorder affecting ~1MM pediatric and adolescent pts
- DSM-5 diagnosis
- Symptoms include
  - Irritability
  - Anxiety
  - Restricted, repetitive patterns of behavior
  - Impairments in social communication
  - Deficits in verbal and non-verbal communication
  - Deficits in developing, understanding and maintaining relationships
- Most diagnosed after age 4; can be diagnosed as early as age 2
- Significant unmet medical need
  - Accelerating rate of diagnosis but only two FDA approved products
    - Both atypical antipsychotics have significant side effect profile
    - Neither approved to address the key symptoms of social impairment and anxiety

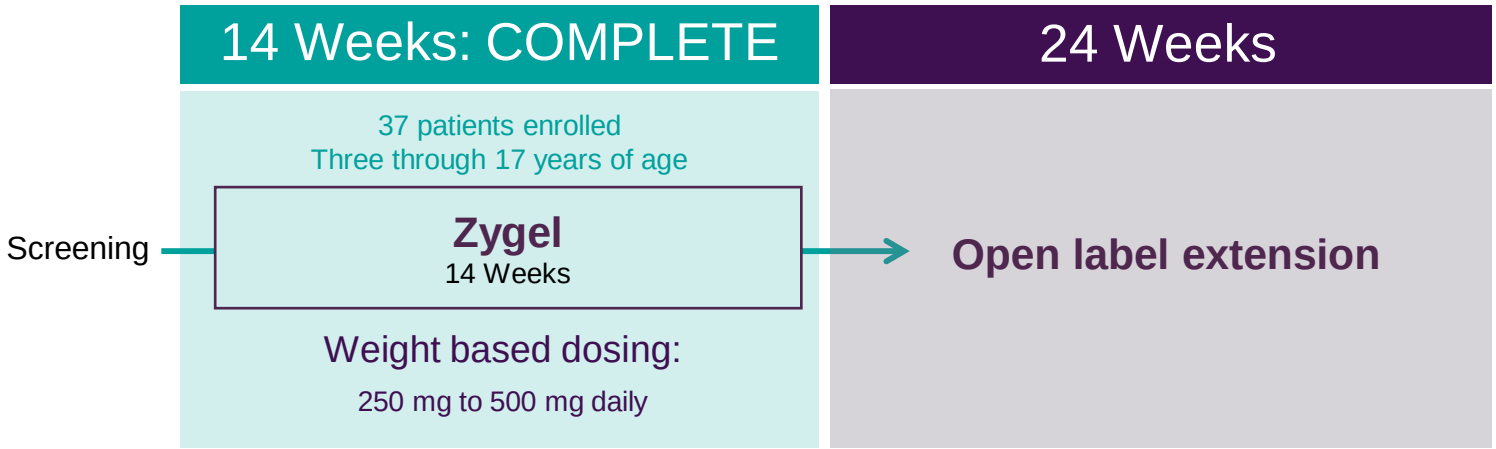
Developing Zygel in ASD

- Newer studies suggest ASD is linked to disruption in the EC system
  - Altered anandamide signaling may contribute to ASD-related social and communication impairments
  - EC system modulates many cellular functions and molecular pathways altered in ASD: imbalanced GABAergic, glutamatergic transmission, oxidative stress, immune dysregulation and altered energy metabolism
- Children dosed with CBD displayed clinical and anecdotal data improvement in social avoidance and anxiety
  - CBD may modulate the EC system and improve certain autism-related behaviors
- Two recent US patents directed to methods of treating ASD by transdermally administering synthetic or purified cannabidiol, respectively, provide IP protection to 2038

BRIGHT Phase 2 Trial in ASD

Positive Topline Data Reported on May 27, 2020

Open-LaBel TolERabIlity and Efficacy Study of ZYN002 Administered as a Transdermal Gel to CHildren and AdolescenTs with Autism Spectrum Disorder



Efficacy assessments (primary efficacy assessment = week 14 vs baseline) :

- Aberrant Behavior Checklist (ABC-C)
- Parent Rated Anxiety Scale – Autism Spectrum Disorder (PRAS-ASD)
- Autism Parenting Stress Index
- Autism Impact Measure (AIM)
- Clinical Global Impression – Improvement (CGI-I) and Severity (CGI-S)
- Qualitative Caregiver Reported Behavioral Problems Survey

BRIGHT Trial Patient Populations

Baseline Patient Population: BRIGHT	
Patients enrolled	N = 37
Included in safety analysis	37
Included in efficacy analyses	36*
Discontinuations	9
Patients completing 14-week trial	28

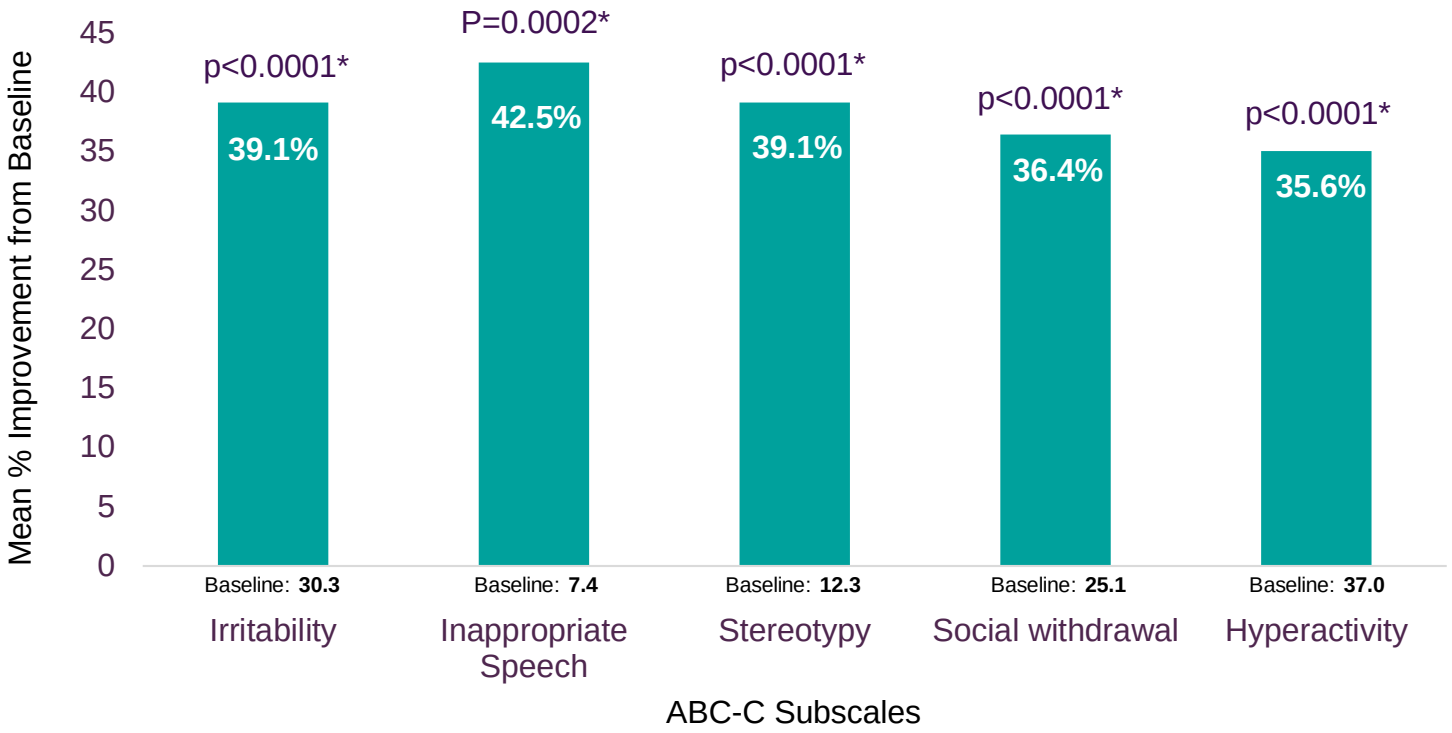
* One patient was lost to follow up and did not have post-dosing efficacy assessments

BRIGHT Trial Patient Demographics

Baseline Patient Demographics	
Patients enrolled, n	37
Age, years	
Mean (range)	9.2 (3-16)
Sex, n (%)	
Male	34 (91.9)
Female	3 (8.1)
Race, %	
White	70.3
Asian	8.1
Native Hawaiian or other Pacific Island	2.7
Other	18.9
Time to diagnosis, years	5.4
Underlying medication, %	
Subjects entering with ≥1 underlying medication	92
Subjects entering with ≥1 underlying psychotropic medication (includes anti-depressants, anxiolytics and antipsychotics)	65

Percent Improvement in ABC-C Subscale Scores at Week 14 vs. Baseline

Statistical Significance Achieved in All Subscales



* Statistically significant

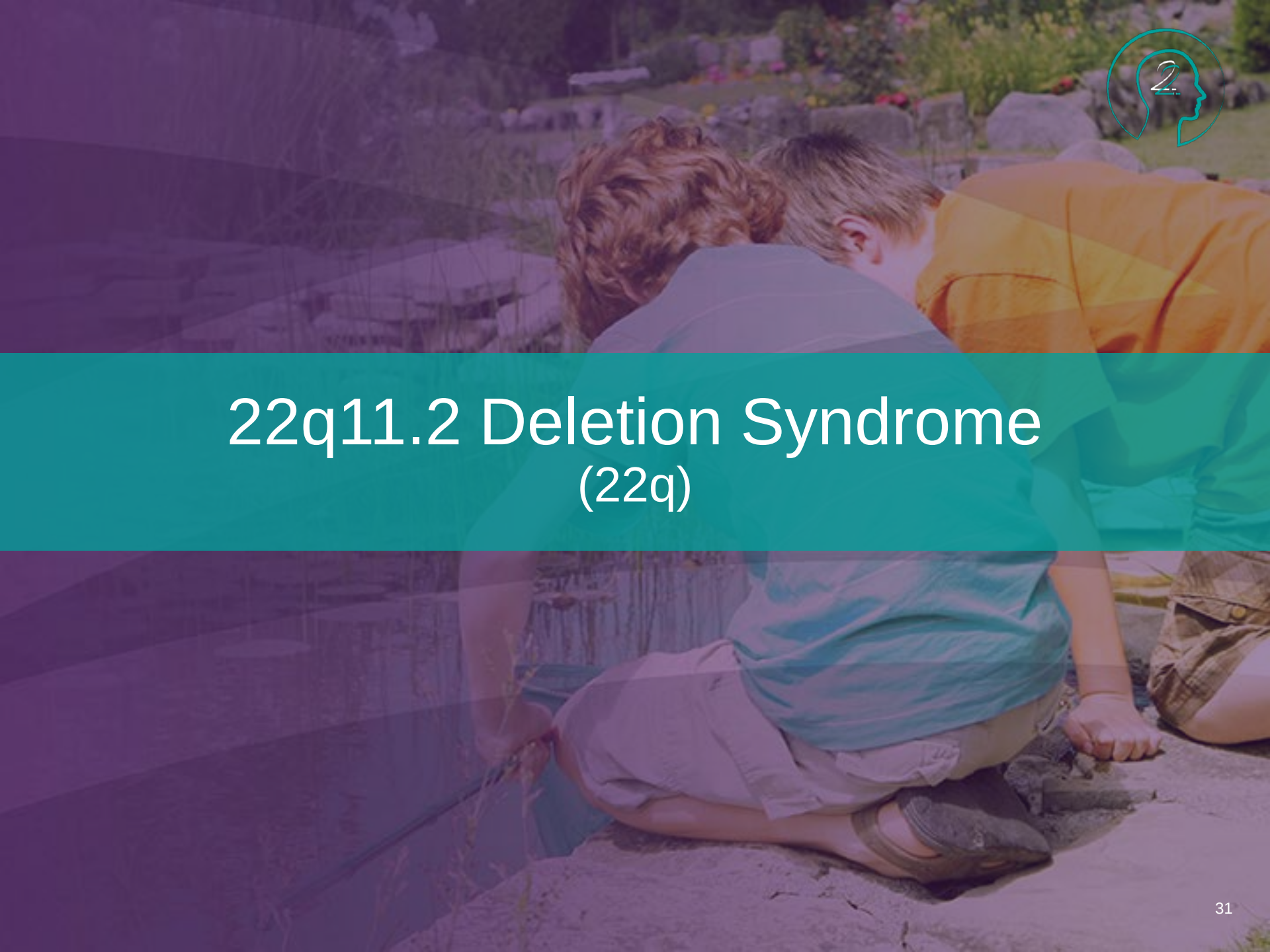
ABC-C Responses Supported by Other Efficacy Assessments

Results of other efficacy assessments support the results demonstrated in the ABC-C, including:

- Parent Rated Anxiety Scale - Autism Spectrum Disorder (PRAS-ASD):
  - Mean improvement of 46% at week 14 from baseline ($p<0.0001$)
- Clinical Global Impression - Improvement (CGI-I)
  - 57% of patients were rated by clinician as Very Much or Much Improved at week 14
- Zynerba intends to present additional data at future medical meetings

Strong Safety and Tolerability Profile in BRIGHT Trial in ASD

- Well tolerated; consistent with previously released data
- Fewer than half of patients experienced an AE; most were mild and transient
- Only 14% of patients experienced a treatment-related AE
  - All application site-related
- No severe or serious adverse events reported during the study.



22q11.2 Deletion Syndrome
(22q)

22q Overview

- Most common contiguous gene deletion syndrome
- Rare disorder: ~81K patients in US
- Midline condition with abnormalities affecting palate, face, heart and other organs; surgically corrected in infancy
- Neuropsychiatric illnesses (anxiety disorders, ASD) and learning disabilities common and impactful
  - 22q associated with increased anxiety, withdrawn behavior and social interaction problems
  - Early onset of neuropsychiatric symptoms disrupts development and QOL, and heightens risk of later psychotic disorders
    - 25-fold increased risk of developing schizophrenia vs. 1% lifetime risk in general population

22q Patient Management

- Two primary stages of 22q patient management:
  - During infancy, doctors address acute physical concerns, such as anomalies of heart and palate, with surgery
  - Once the physical concerns are stabilized, focus shifts to managing neuropsychiatric symptoms, such as anxiety and autistic behaviors
- No approved drugs indicated for 22q

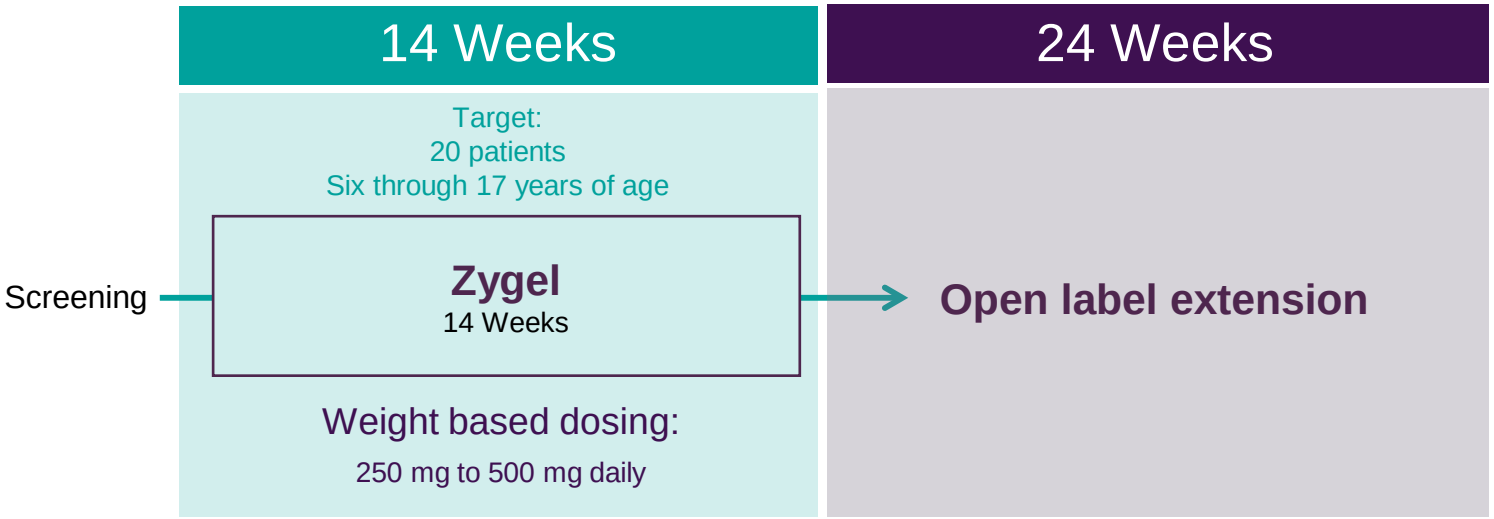
Developing Zygel in 22q

- CBD may treat neuropsychiatric symptoms in 22q due to activity as:
  - Modulator of endocannabinoid system
  - Agonist at serotonin$_{1A}$ receptors
  - Antagonist at GPR55 receptors
- Early control of anxiety may delay the development of psychosis
- Phase 2 study underway in pediatric and adolescent patients with 22q
- Top line results expected in 3Q2020

INSPIRE Phase 2 Trial in 22q

Enrollment Ongoing; Topline Data Expected in 3Q2020

Assessing the Impact of Zygel (Transdermal CBD Gel) on Pediatric Behavioral and Emotional Symptoms of 22q11.2 Deletion Syndrome



Efficacy assessments (week 14 vs baseline) include:

- Aberrant Behavior Checklist-Community (ABC-C)
- Anxiety, Depression and Mood Scale (ADAMS)
- Qualitative Caregiver Reported Behavioral Problem Survey
- Clinical Global Impression – Severity and Improvement

DEE
Developmental and Epileptic Encephalopathies

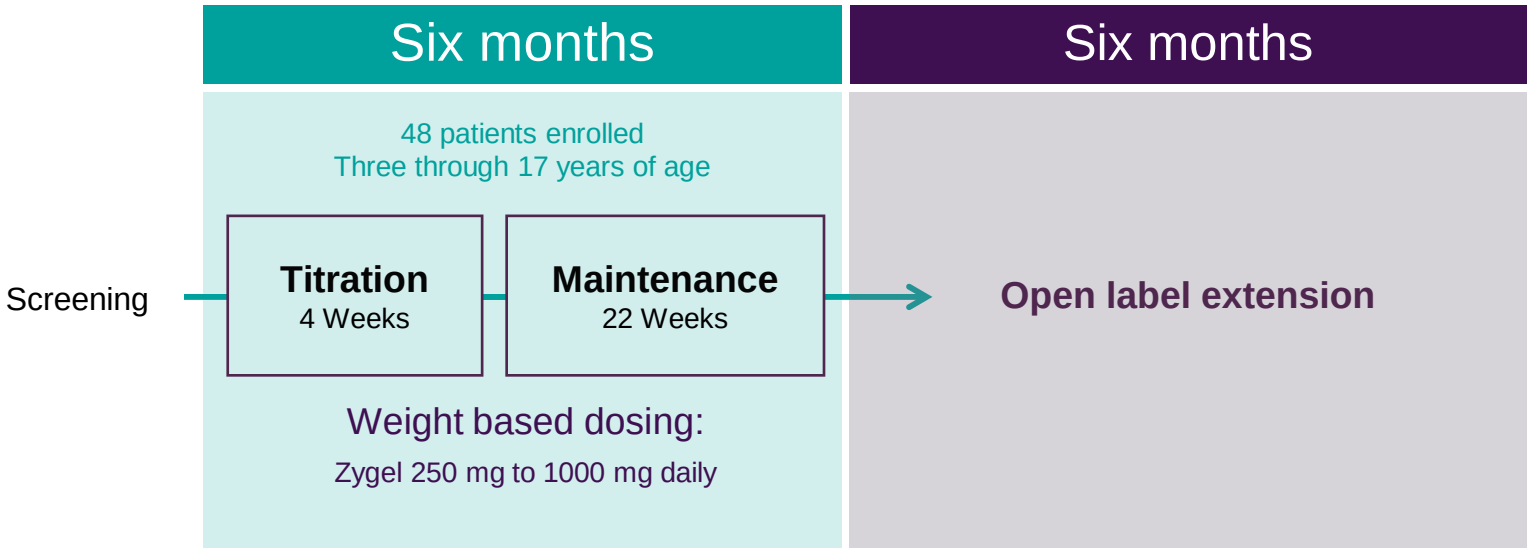
DEE Patients are Medically Fragile

- Group of rare / ultra rare childhood-onset epilepsies with impaired or regressed developmental progress
- Cognitive impairment, psychiatric problems, and behavioral disturbances are phenotypic
- Medically fragile population
  - Comorbidities include cerebral palsy, chronic respiratory infections, gait disturbances, movement disorders, scoliosis, and feeding problems
  - Many wheelchair bound with feeding tubes
- Most common and debilitating seizure types in DEEs are:
  - Focal impaired-awareness seizures (FIAS) – formerly known as complex partial
  - Focal to bilateral tonic-clonic and generalized tonic-clonic seizures – commonly known as convulsive seizures (CS)

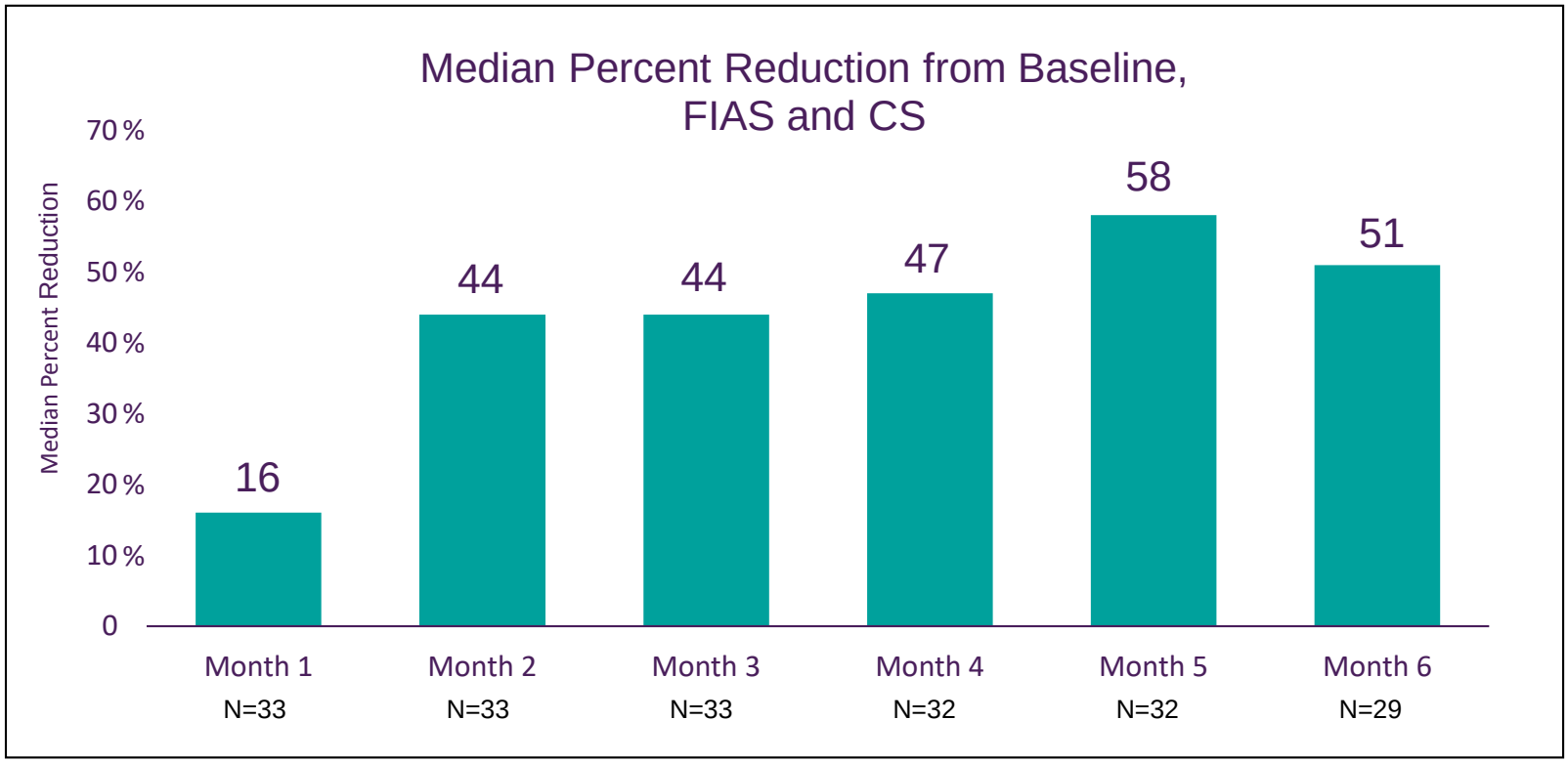
BELIEVE Phase 2 Trial in DEE

Completed; Reported Positive Topline Results on 9/18/19

Open LaBel Study to Assess the Safety and Efficacy of ZYN002 Administered as a TransdermaL Gel to ChIldren and AdolEscents with DeVelopmental and Epileptic Encephalopathy

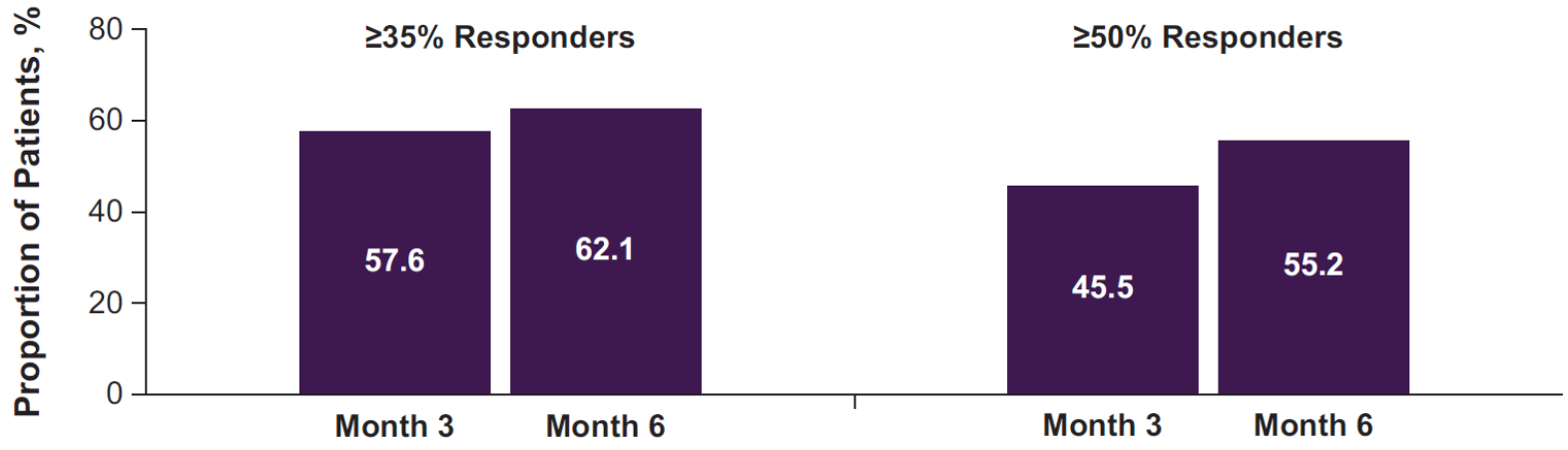


BELIEVE: Clinically Meaningful Seizure Reductions from Baseline and Sustained through Six Months in DEE



BELIEVE: Percentage of Patients with ≥35% and ≥50% Reduction in FIAS and TCS

≥35% and ≥50% Reduction in FIAS and TCS by Time Point, mITT Population With FIAS and/or TCS at Baseline (n = 33)



FIAS, focal impaired awareness seizures; mITT, modified intent-to-treat; TCS, tonic-clonic seizures.
Month = SF28

Data reported at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

BELIEVE Safety

Well Tolerated in this Six Month Trial: No Safety Signal Identified

- All events in six month period, whether unrelated or related to study, drug reported as adverse events (AEs) (e.g.: influenza, runny nose, ingrown toenail, scrapes, etc.)
- As a result and as anticipated, most patients experienced an AE
  - Most were mild and transient
  - Only one patient discontinued due to an AE (application site reaction)
- Most common treatment-related adverse events occurred in only four patients each:
  - application site dryness, application site pain, and somnolence (all four patients exhibiting somnolence were taking concomitant clobazam)
- Low rate of serious adverse events (SAE)
  - Only two SAEs deemed possibly drug-related (LRTI and status epilepticus)
  - No drug-related hepatic, gastrointestinal, or lethargy-related SAEs
- Tolerability profile consistent with the safety database for Zygel

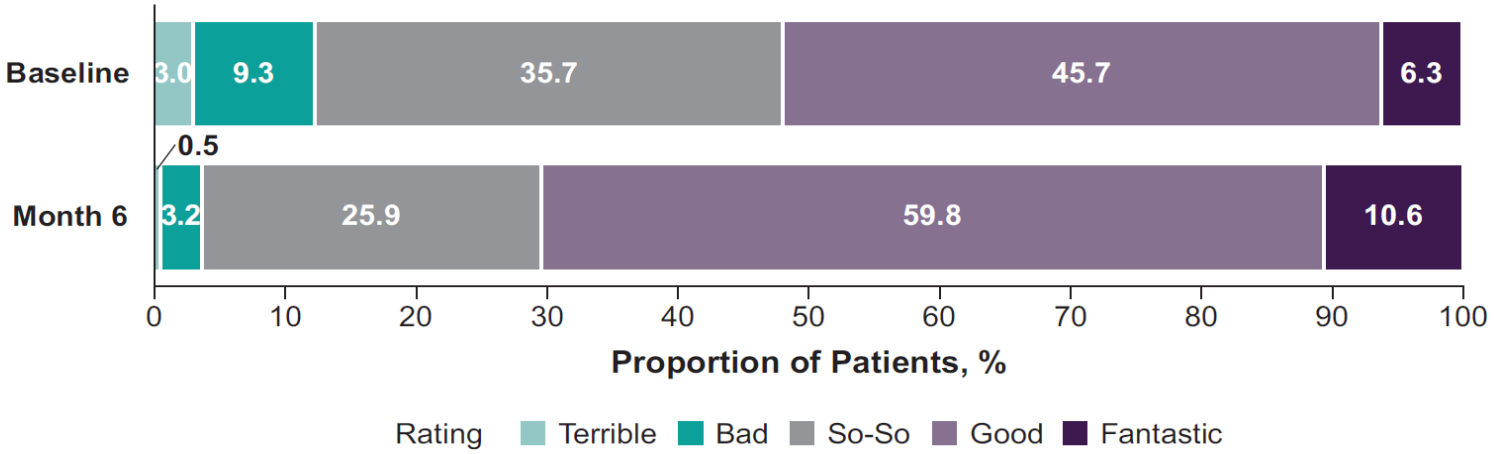
BELIEVE: Qualitative Assessments of Behavioral and Cognitive Improvements

- Epilepsy and Learning Disabilities Quality of Life (ELDQOL) scale
  - Statistically significant reductions from baseline in subscale scores for seizure severity, behavior, and mood observed at month 6 ($p<0.01$)
- Qualitative caregiver feedback on improvements included:
  - Any improvement: 84% (n = 36)
  - Improved vitality: 58% (n = 25)
  - Improvement in seizures: 51% (n = 22)
  - Improved cognition/concentration: 47% (n = 20)
  - Improved socially avoidant behaviors: 44% (n = 19)
  - Improvement in irritability: 33% (n = 14)
  - School improvement: 28% (n = 12)
  - Medical improvement: 14% (n = 6)

Data reported at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

BELIEVE: Qualitative Assessments of Behavioral and Cognitive Improvements

- Good Day/Bad Day comparing baseline to month six:
  - “Good day” and “fantastic day” reports increased from 52% to 70%
  - “Terrible day” and “bad day” reports decreased from 12% to 4%



Data reported at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

Compelling Results Suggest a Pathway to Pivotal Trials

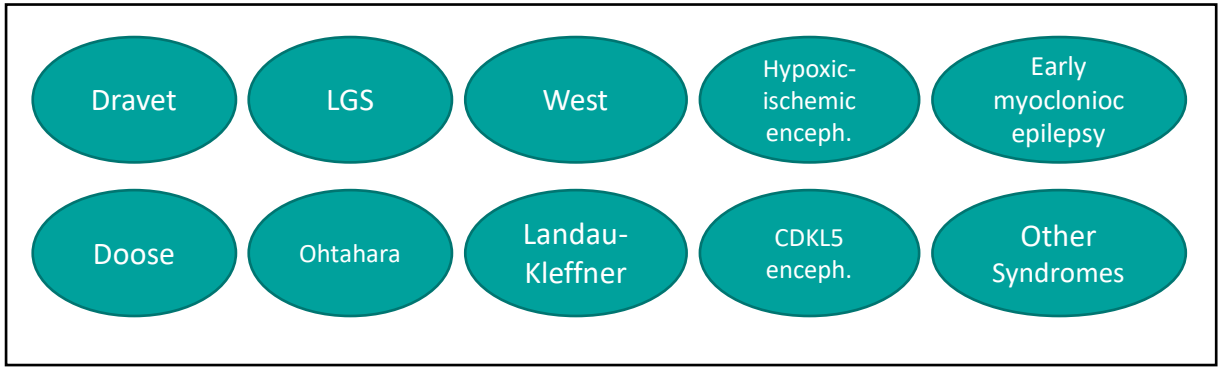
Results of FDA Discussions Regarding Clinical Path Forward Now Expected in 3Q2020

- Zynerba engaging with FDA on next clinical steps
- Efficacy results:
  - Clinically meaningful reductions in seizures beginning in month two and sustained through six months
  - Suggest improvements on important behavioral symptoms
- Safety results:
  - Zygel was well tolerated
  - Consistent with previously reported Zygel studies
- Zynerba approach to FDA approval will likely focus on most common and disabling seizure types in DEE, rather than patient syndromes

Planned Approach to FDA

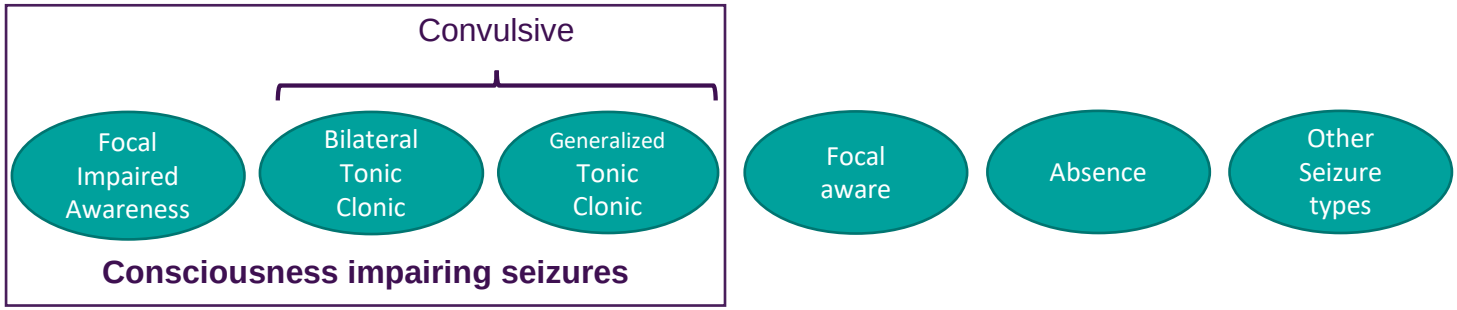
All DEE Patients with Consciousness Impairing Seizures

Syndromes and encephalopathies



Zynerba Planned Approach

Seizure type



Financial Strength

- Clean balance sheet
  - No debt, 25.0M shares outstanding (as of May 7, 2020)
- Cash and cash equivalent position of $60.6M as of March 31, 2020
- Cash runway expected to be sufficient to fund operations and capital requirements into the second half of 2021
  - Beyond the expected NDA submission and potential approval in FXS

Expected Clinical Milestones in 2020

	1Q 2020	2Q 2020	3Q 2020	4Q 2020
FXS		Report pivotal CONNECT-FX topline results		NDA submission
DEE			Results of FDA discussions on clinical path	
ASD		Report Ph. 2 BRIGHT topline results	Meet with FDA to discuss clinical path forward	
22q			Report Ph. 2 INSPIRE topline results	

Corporate Overview

June 2, 2020