Corporate Overview

March 10, 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
  - Enrollment complete in pivotal CONNECT-FX FXS trial and in Phase 2 BRIGHT ASD study
    - Topline data expected from both trials in 2Q2020
- 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

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 2Q2020
Developmental and Epileptic Encephalopathies (DEE)					
BELIEVE 1: Complete					Meet with FDA in 1H2020 to discuss clinical path forward
Autism Spectrum Disorder (ASD)					
BRIGHT: Enrollment complete					Topline Phase 2 data in 2Q2020
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

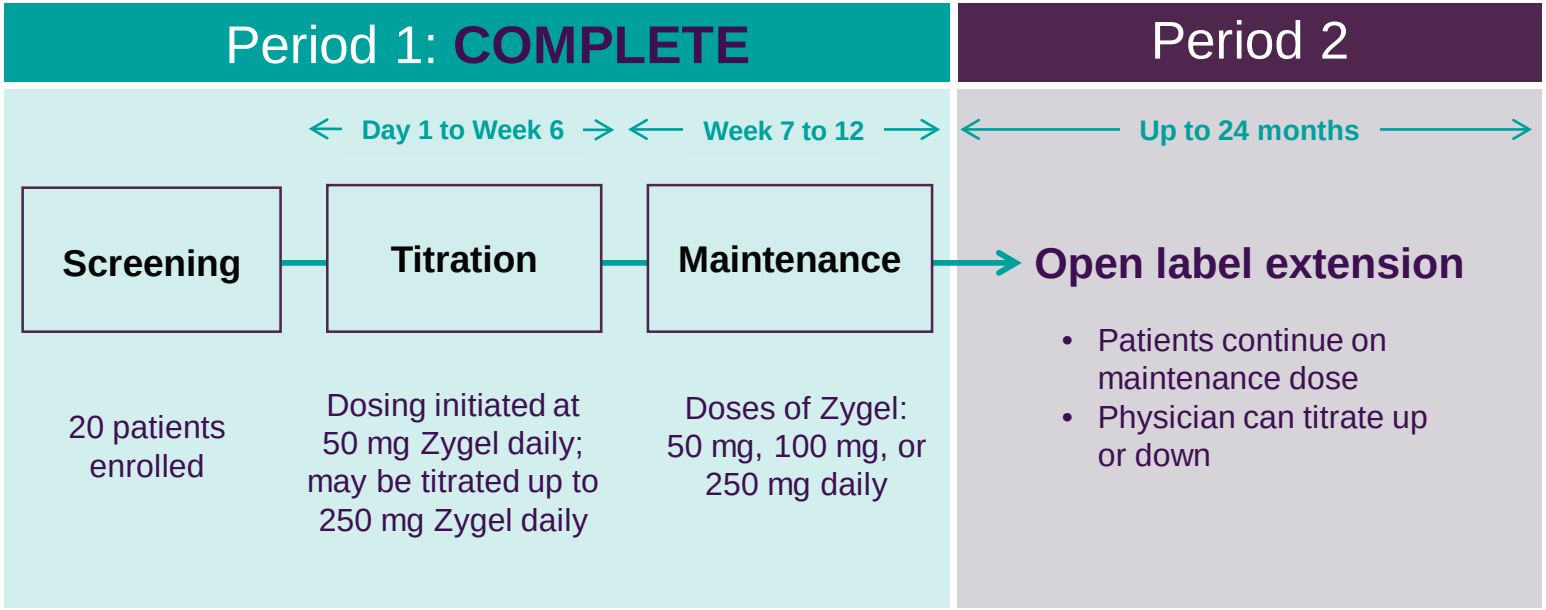
Fragile X Syndrome (FXS)

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

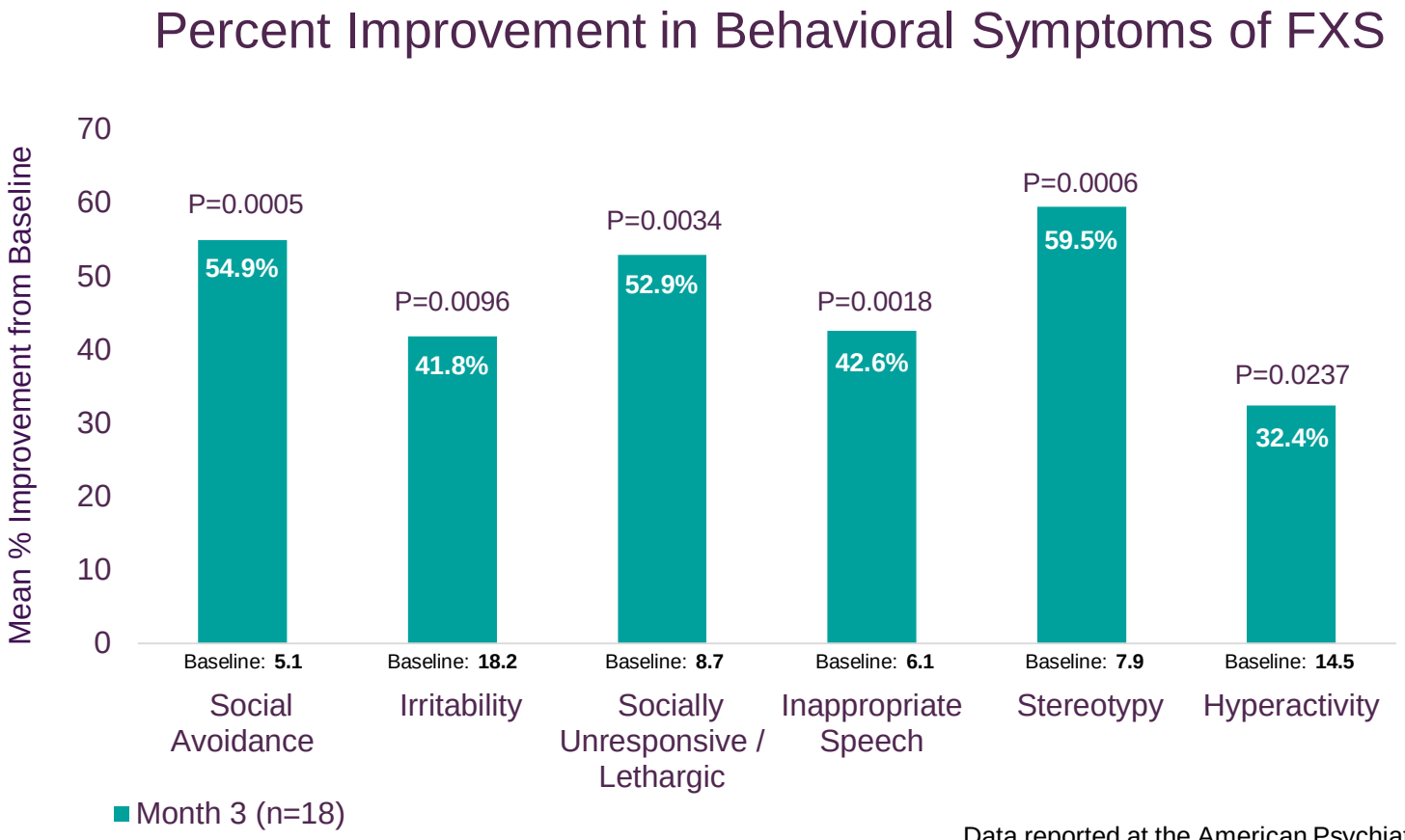
FAB-C Open Label Phase 2 Trial Design

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

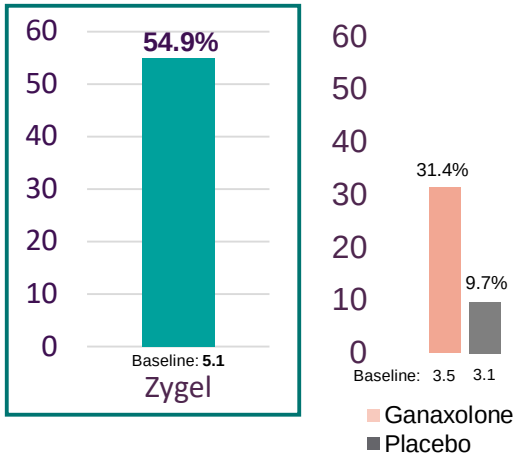


Data reported at the American Psychiatric Association (APA) meeting, May 2019

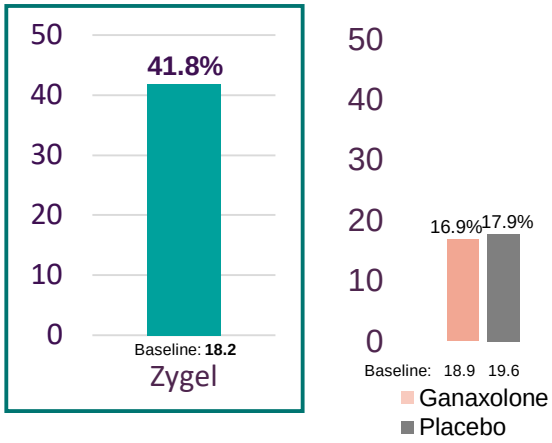
FAB-C ABC-C_{FXS} Subscales

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

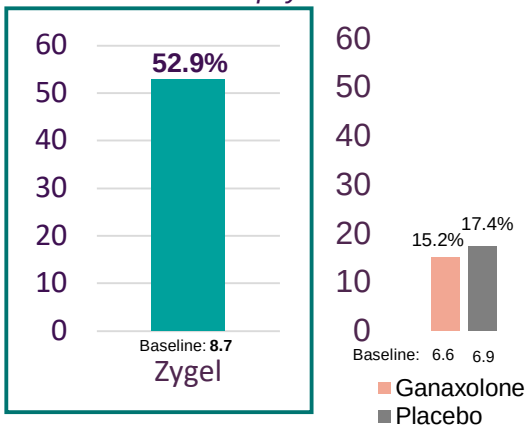
Social Avoidance
Seeks isolation



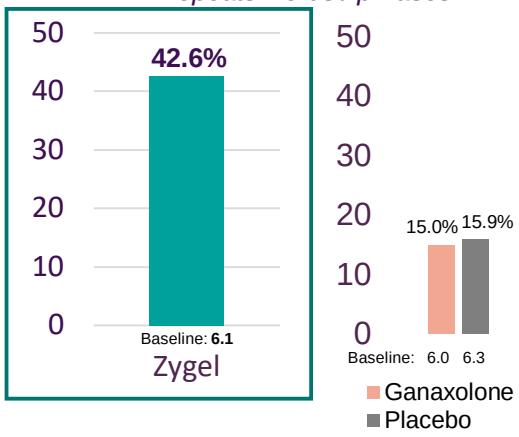
Irritability
Temper tantrums



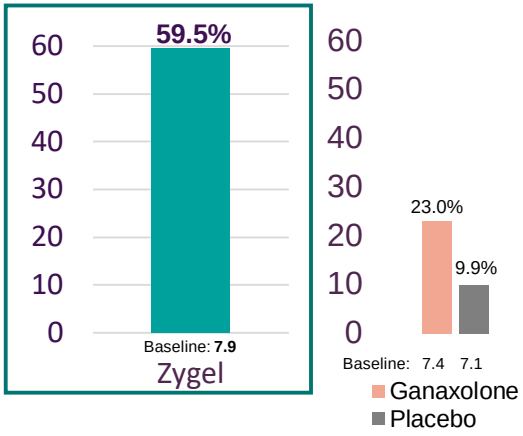
Socially Unresponsive / Lethargic
Does not pay attention



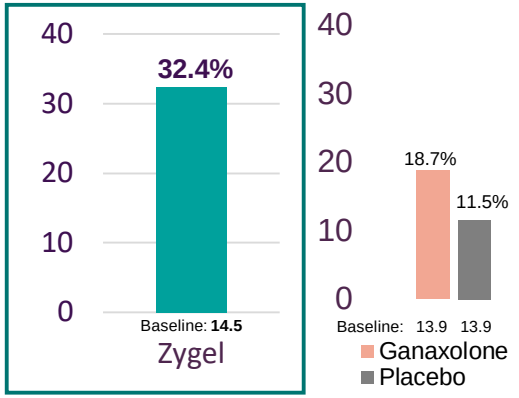
Inappropriate Speech
Repeats words / phrases



Stereotypy
Repetitive movements



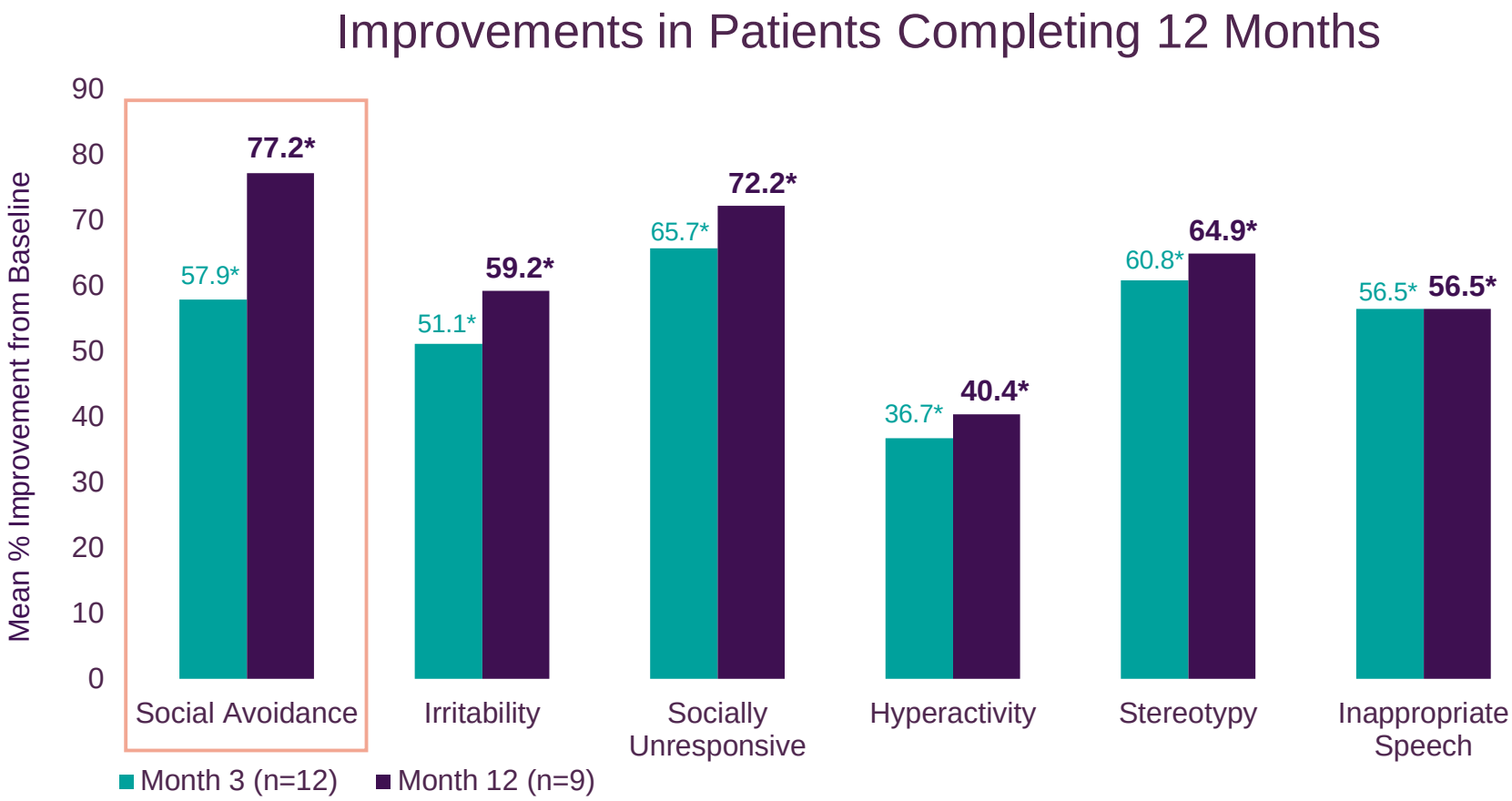
Hyperactivity
Disrupts group activities



* 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.

Three Month FAB-C Data vs. 12 Months of Treatment

Sustained Improvements in FXS Behavioral Symptoms Through 12 Months of Treatment



*P ≤ 0.05

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

FAB-C Open Label Phase 2 Trial

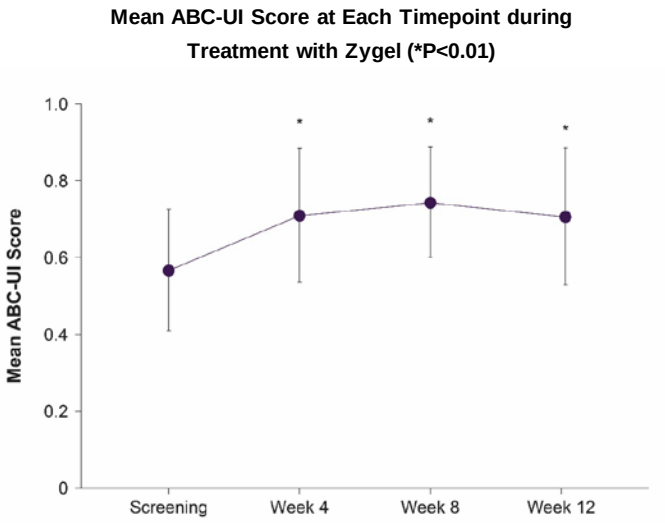
Zygel Safety Summary Through 12 Months

- Well tolerated, consistent with previously reported data; no SAEs
- No clinically meaningful trends in vital signs, ECG, or clinical safety labs including LFTs; no THC detected in plasma
- Discontinuations
  - Two siblings discontinued in Period 1
    - One for worsening of pre-existing eczema (not considered Tx-related)
    - One due to administrative reasons
  - Three patients discontinued in Period 2 (administrative reasons; non-compliance)
- Little to no redness at application site
  - One patient developed moderate application site rash (resolved, did not recur); remains in the study
- TEAEs mild or moderate
  - Most common: Gastroenteritis (14%), URTI (12%)
  - All resolved during study period

FAB-C Open Label Phase 2 Trial

Estimating the Health State Utility (HUI) Score for FXS and Potential Benefit of Treatment with Zygel

- An HUI specific to FXS - the ABC-UI - was derived from the ABC-C_{FXS} to measure the health-related quality of life (HRQoL) benefit of treatments for FXS[1]
  - HUI, measured on a scale of 0 to 1, are used in clinical and economic analyses of therapies with potential impact on HRQoL
- Analysis evaluated the potential benefit of Zygel on the ABC-UI in FXS through post hoc analysis of data from FAB-C
- Patient-level data from FAB-C were mapped to the ABC-UI algorithm to generate a utility index score for each patient
  - Mean ABC-UI for FXS patients estimated to be 0.57 at baseline
    - Reflects important impact of FXS on HRQoL despite children and adolescents being maintained on standard of care for FXS
    - Suggests impact similar or worse than other debilitating pediatric conditions
- Compared to baseline, patients receiving Zygel experienced significant ($P < 0.01$) and sustained improvement in their mean ABC-UI from week 4 to 12



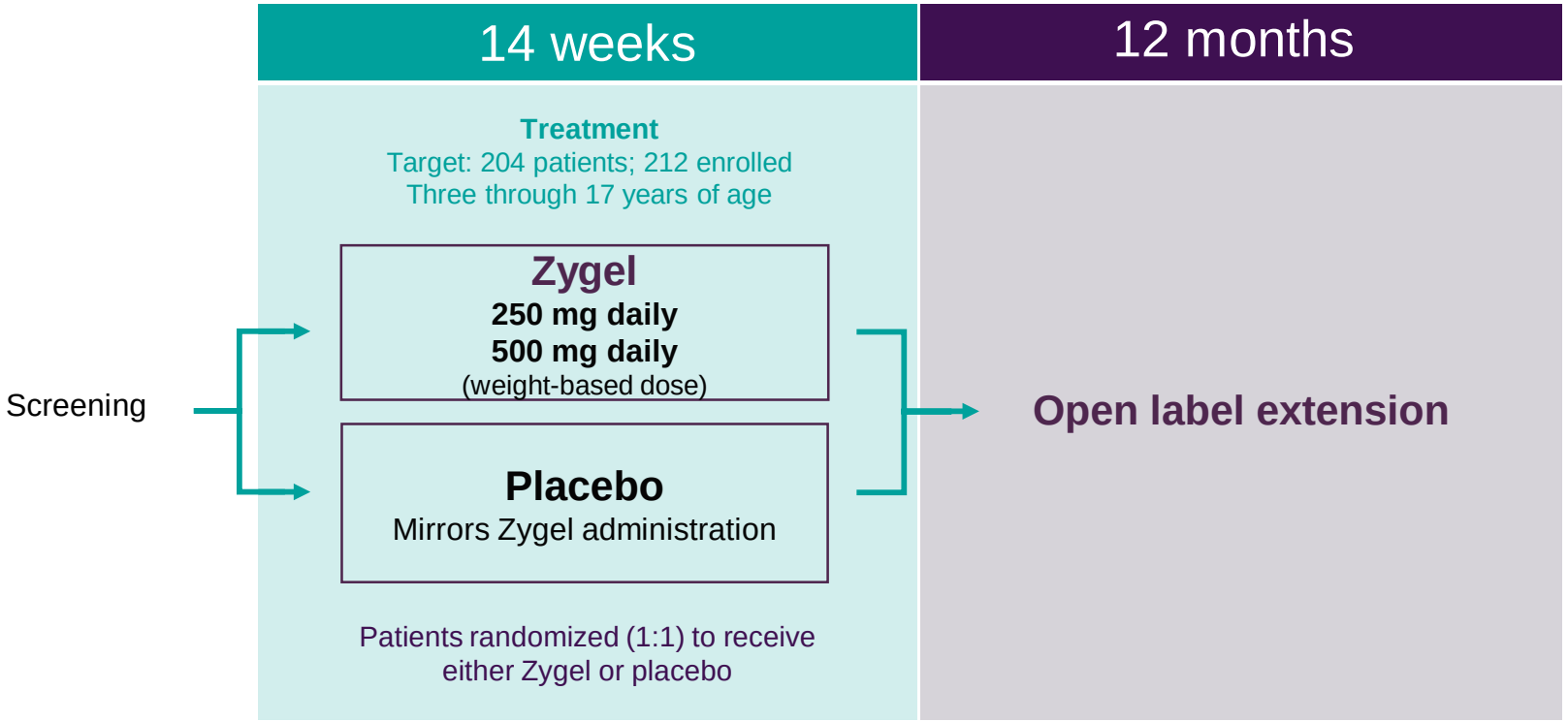
Data reported at the American Society for Experimental Neurotherapeutics (ASENT) 2020 Meeting

[1]Kerr C et al. *Qual Life Res*.2015;24(2):305-314

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 2Q2020

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 3/9/2020)	163
Percent of completed patients enrolling in CONNECT-FX OLE	97%

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

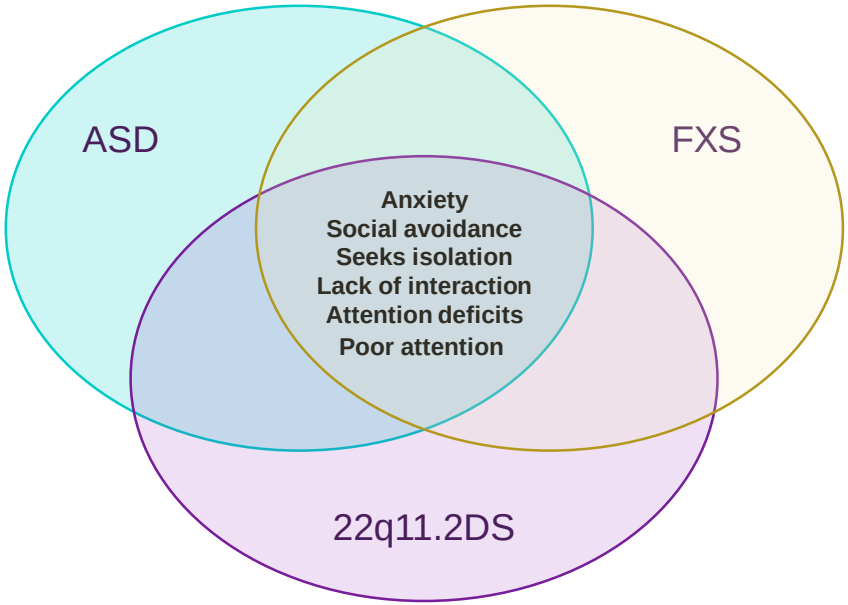
CONNECT-FX

- 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 pediatric patients

ASD in Pediatrics Overview

- Near-rare disorder affecting ~1MM pediatric and adolescent pts
- DSM-5 diagnosis
  - Includes Autistic disorder, Asperger's syndrome, and Pervasive Development Disorder-not otherwise specified (PDD-NOS)
- Symptoms include
  - 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

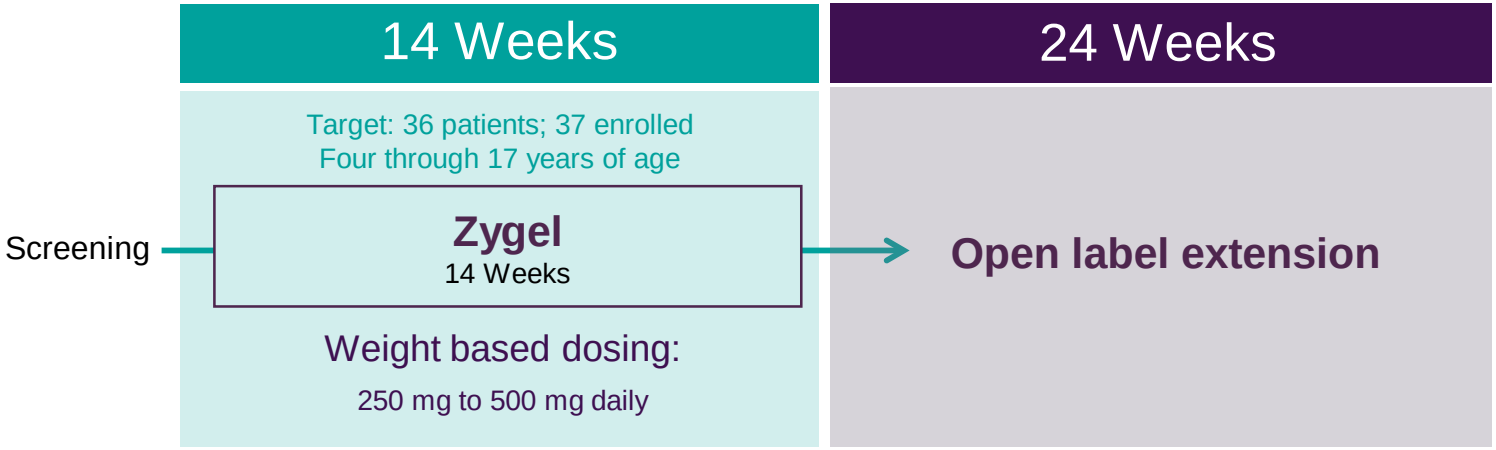
Developing Zygel in ASD

- 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
- Clinical and anecdotal data show improvement in social avoidance and anxiety in children with CBD
  - 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
- Enrollment complete in Phase 2 study in pediatric and adolescent patients with ASD
- Top line results expected in 2Q2020

BRIGHT Phase 2 Trial in ASD

Enrollment Complete; Topline Data Expected in 2Q2020

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 – Severity (CGI-S) and Improvement (CGI-I)
- Qualitative Caregiver Reported Behavioral Problems Survey
- Autism Diagnostic Observation Schedule® (ADOS-2): *Baseline only*
- Children's Sleep Habits Questionnaire (CSHQ): *Baseline and EOS (week 38) only*

BRIGHT Trial Patient Demographics

Baseline Patient Demographics	
Demographic	BRIGHT Patients N = 37
Age, years Mean (range)	 9.2 (3-16)
Sex, n (%) Male Female	 34 (91.9) 3 (8.1)
Race, % White Aboriginal Asian Other	 75.7 5.4 8.1 10.8

BRIGHT Disease Characteristics Confirm a Moderate-to-Severe Population

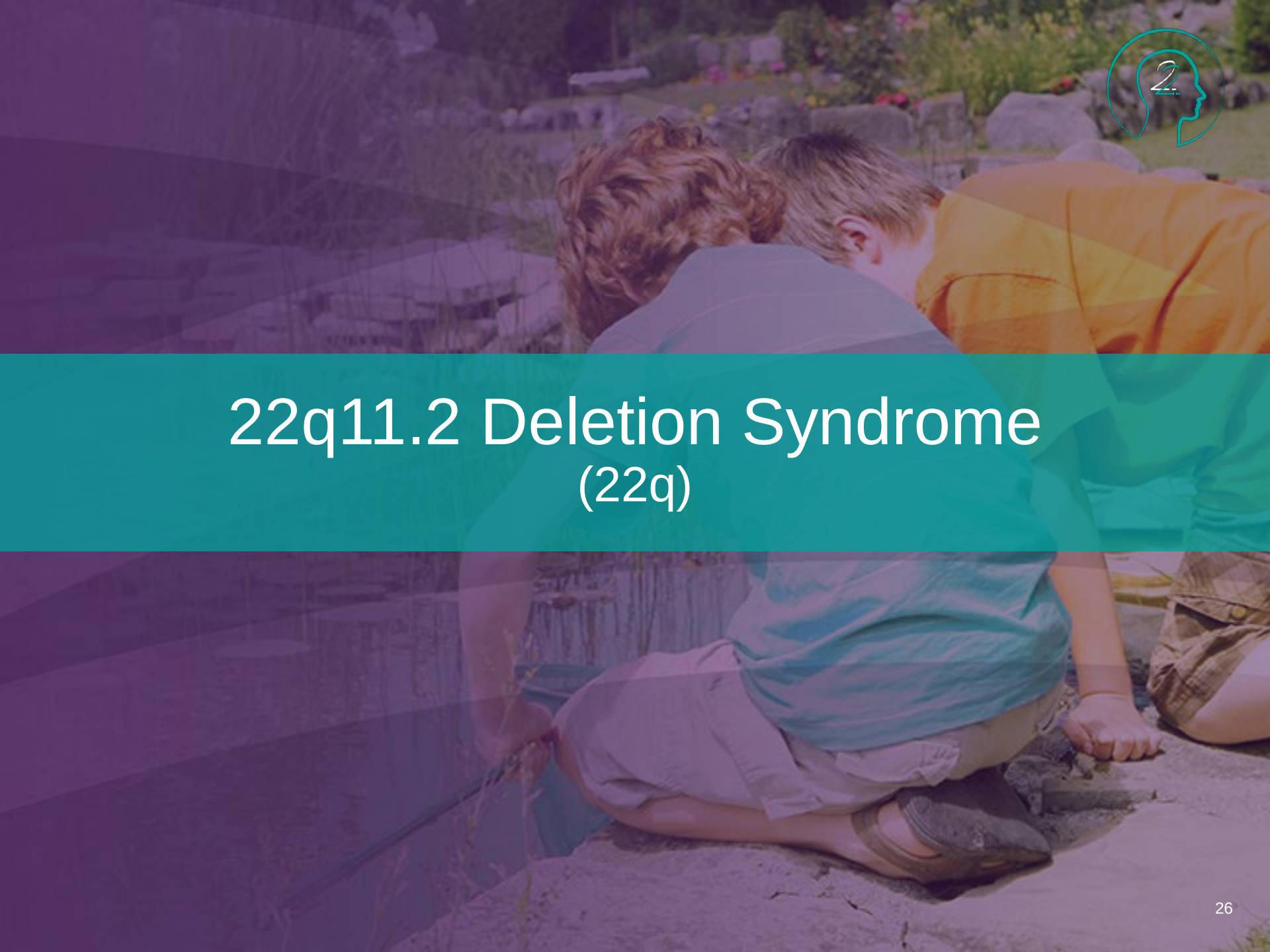
Baseline Disease Characteristics	
ABC-C Irritability Subscale score (0-45)	
n	37
Mean (range)	30.0 (18-43)
ADOS®-2 comparison score	
n	36
Mean (range)	7.5 (4-10)
<5 (mild ASD), n (%)	2 (5.6)
5-7 (moderate ASD), n (%)	19 (52.8)
8-10 (severe ASD), n (%)	15 (41.7)
DSM-5 severity level	
Level 1 (mild), n (%)	3 (8.1)
Level 2 (moderate), n (%)	15 (40.5)
Level 3 (severe), n (%)	19 (51.4)
PRAS-ASD score (0-75; >52 suggests possible clinical anxiety)	
n	37
Mean (range)	40.9 (21-68)
>52, n (%)	9 (24.3)

ABC-C Irritability subscale: Score of 30 provides confirmation of severity

ADOS-2: 94% of patients have moderate to severe symptoms of ASD at baseline

DSM-5: 92% of patients have moderate to severe symptoms of ASD at baseline

PRAS-ASD: 24% of the enrolled patients had scores >52, indicating possible clinical anxiety



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

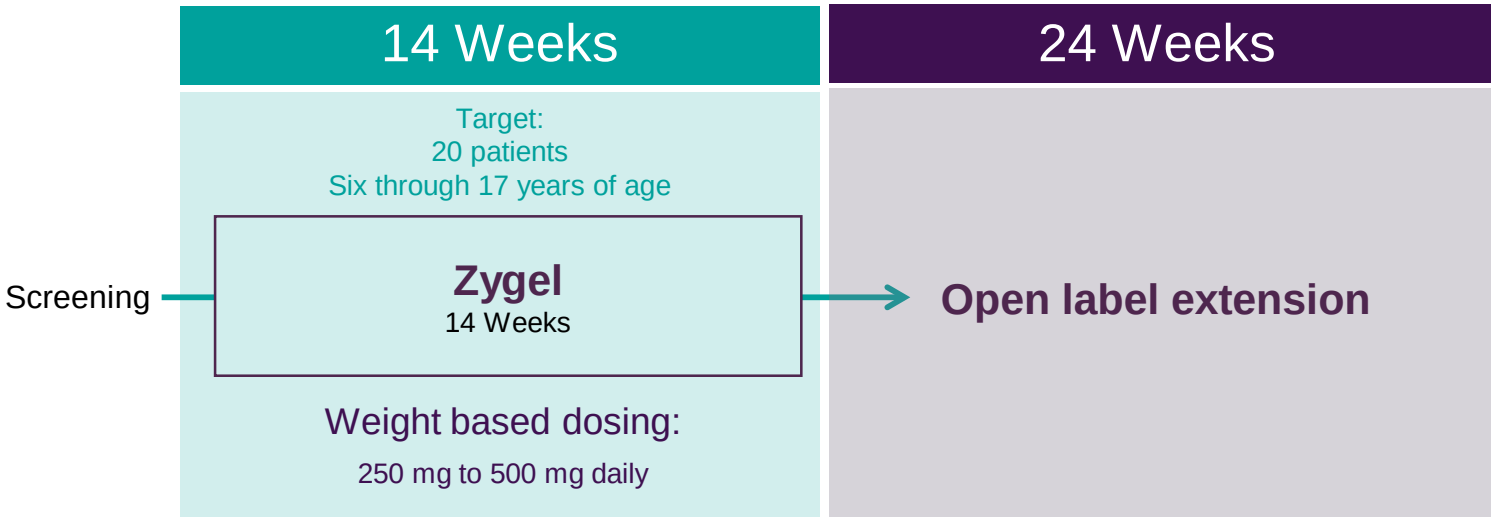
Developing Zygel in 22q

- 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 now 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

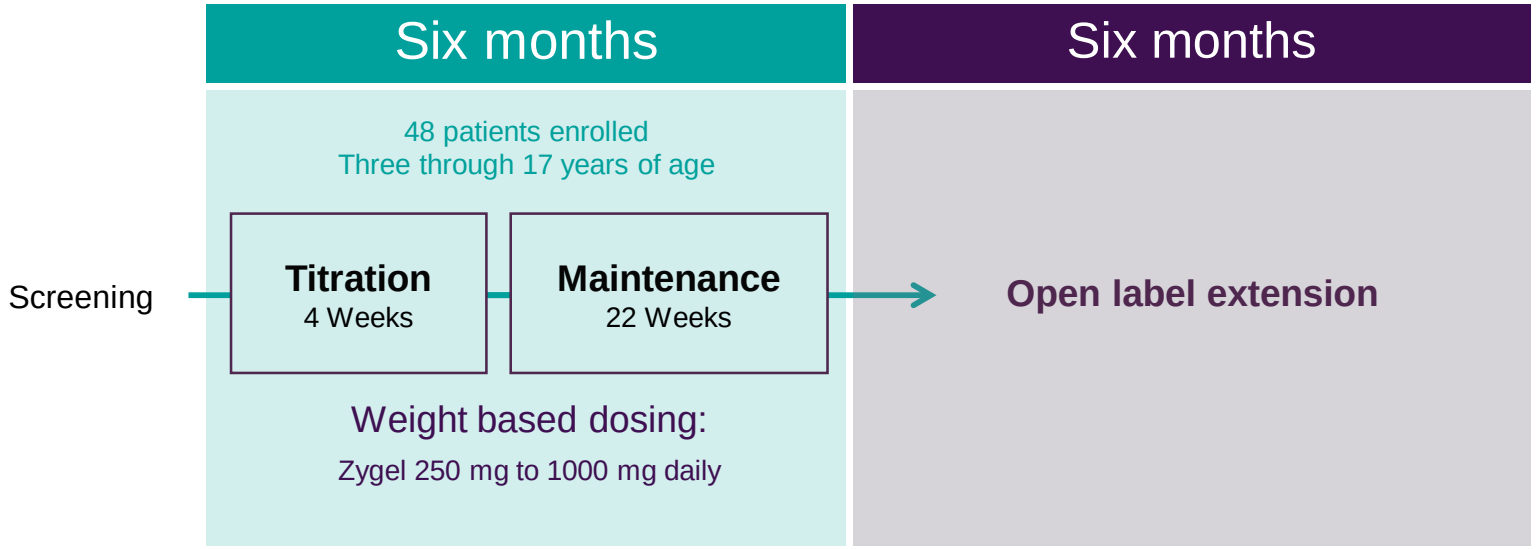
DEE Patients are Medically Fragile

- 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)

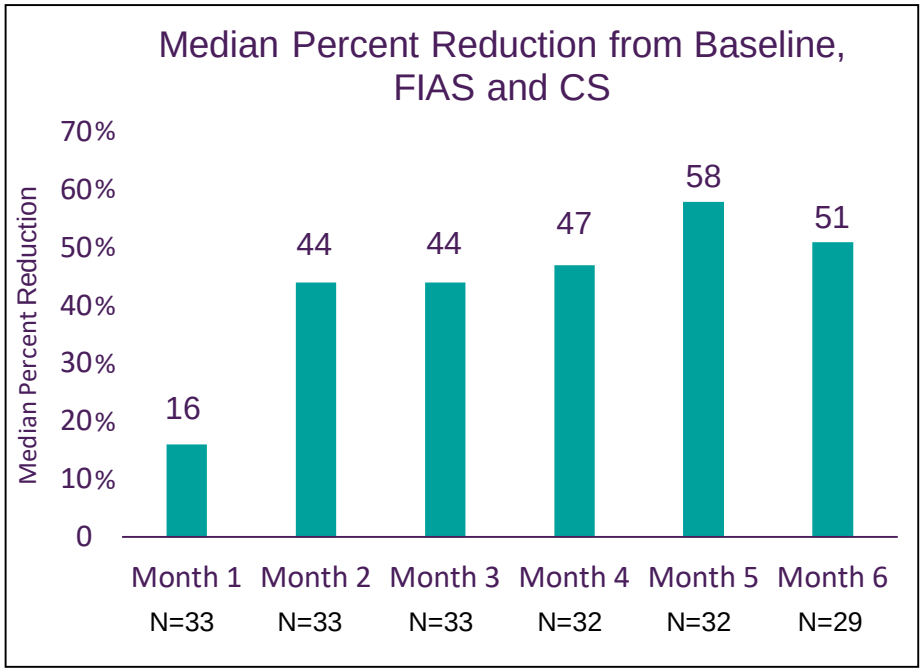
BELIEVE 1 Phase 2 Trial in DEE

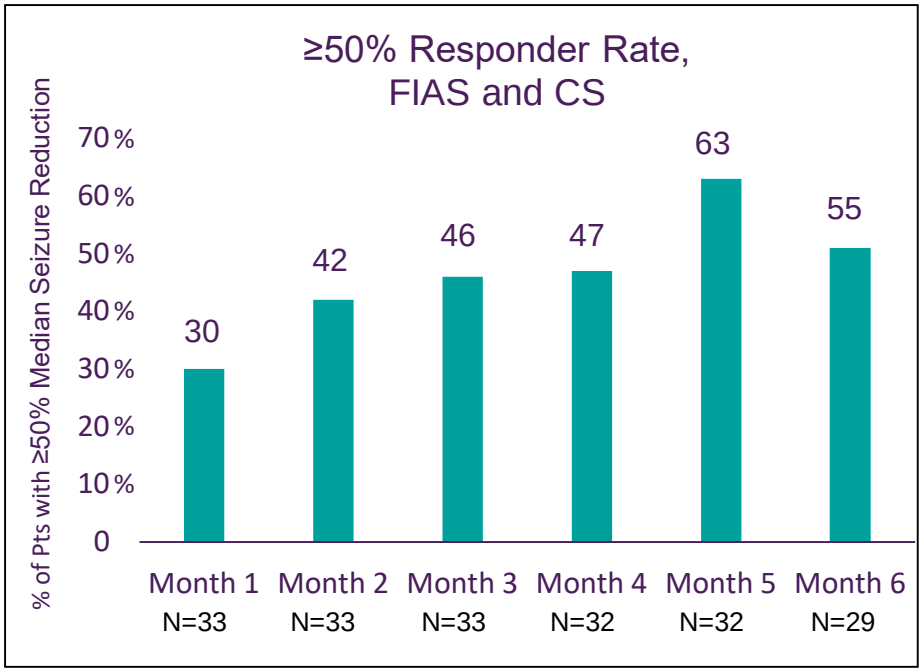
Completed; Reported Positive Topline Results on 9/18/19

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





BELIEVE 1 Safety

Well Tolerated in this Six Month Trial

- All events in six month period, whether unrelated or related to study, drug are reported as adverse events (AEs) (e.g.: influenza, runny nose, ingrown toenail, scrapes, etc.)
- AEs common in this medically fragile population, and expected in a six-month trial
  - As a result, most patients experienced an AE
    - Most were mild and transient
    - Only one patient discontinued due to an AE (application site reaction)
  - 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
  - May compare favorably to tolerability profiles of reported safety data from oral CBD solution[1] and other currently available AEDs[2]

[1]Devinsky - *Lancet Neurol* 2016

[2]Moavero – *Expert Opin Drug Saf*, 2018

BELIEVE 1: Qualitative Assessments of Behavioral and Cognitive Improvements

- Parents and caregivers provided qualitative assessment on their child's overall experiences with Zygel
- Improvements were seen in seizure intensity and duration, and socio-behavioral and cognitive impairments
- Improvements in >25% of children:
  - 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
- Improvements in socio-behavioral and cognitive impairments provide additional confidence in design of FXS, ASD and 22q11.2DS (22q) studies

Compelling Results Suggest a Pathway to Pivotal Trials

Anticipate Meeting with FDA in 1H2020

- 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
  - May compare favorably to tolerability profiles of reported safety data from oral CBD solution[1] and other currently available AEDs[2]
- Zynerba approach to FDA approval will likely focus on most common and disabling seizure types in DEE, rather than patient syndromes

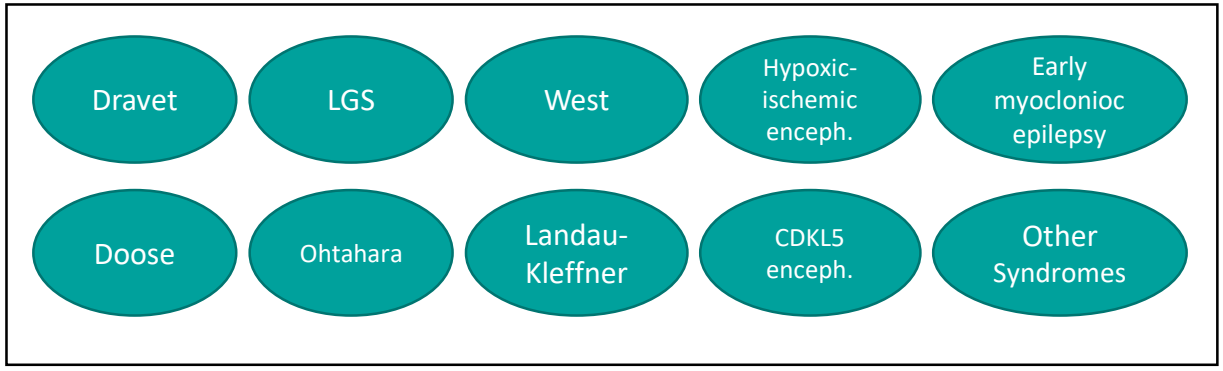
[1]Devinsky - *Lancet Neurol* 2016

[2]Moavero – *Expert Opin Drug Saf*, 2018

Planned Approach to FDA

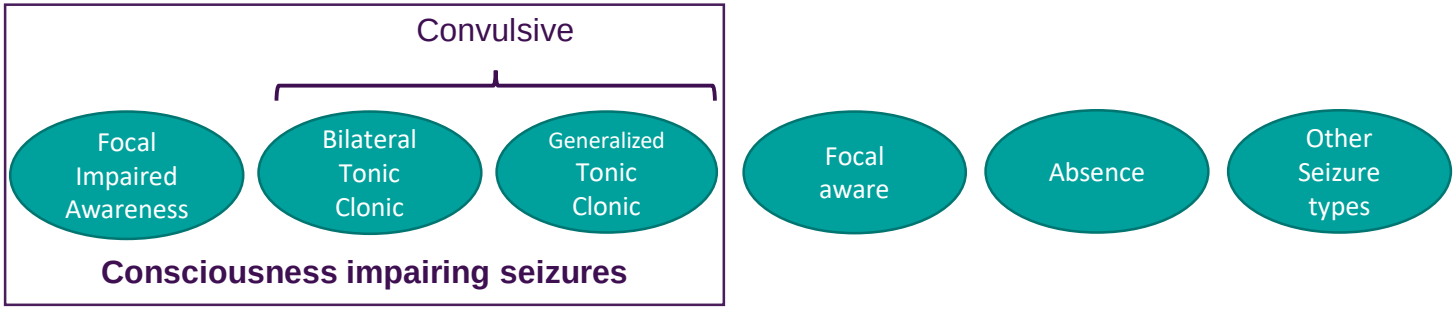
All DEE Patients with Consciousness Impairing Seizures

Syndromes and encephalopathies



Zynerba Planned Approach

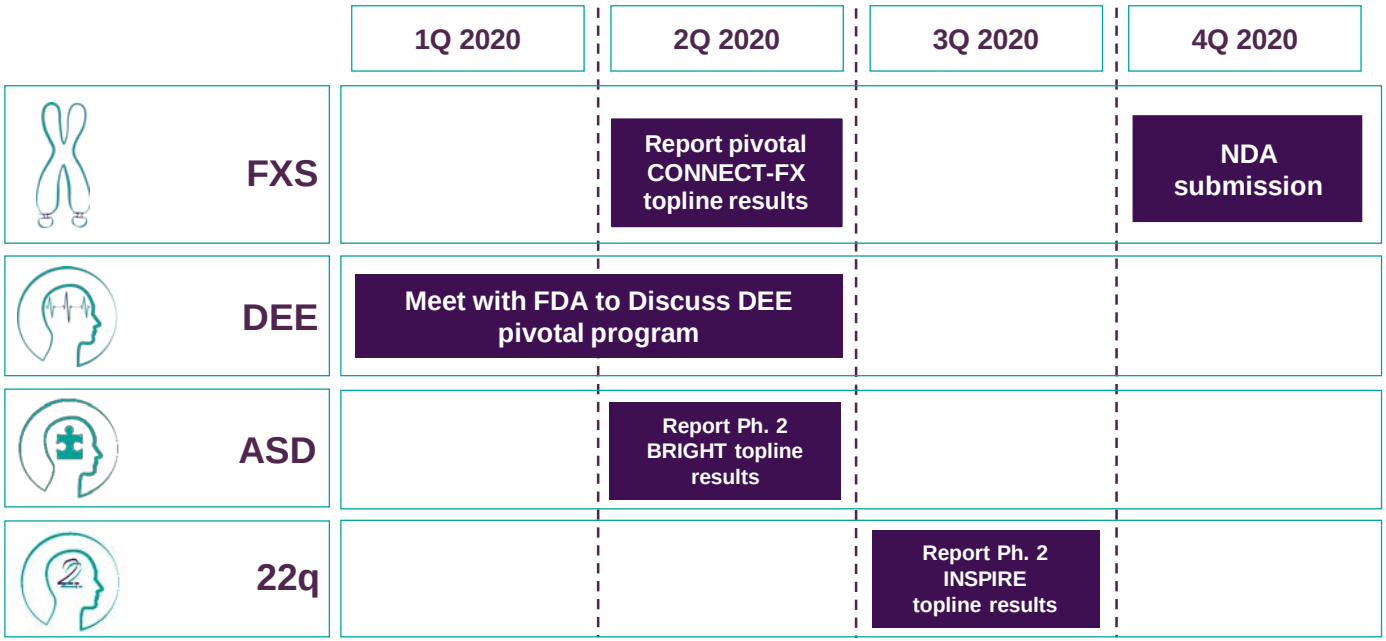
Seizure type



Financial Strength

- Clean balance sheet
  - No debt, 23.6M shares outstanding (as of March 4, 2020)
- Cash and cash equivalent position of $70.1M as of December 31, 2019
- 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



Corporate Overview

March 10, 2020