Corporate Update

December 12, 2019

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Zynerba Pharmaceuticals (NASDAQ: ZYNE)

A Rare/Near-Rare Neuropsychiatric-focused Pharmaceutical Company

- Deep pipeline focused on high unmet medical needs; translating into multi-billion dollar market opportunity with Zygel™ (CBD transdermal gel)
  - Four clinical shots on goal: FXS, DEE, ASD, 22q
  - Reported compelling safety and efficacy data in BELIEVE 1 DEE open label Phase 2 trial (September 18, 2019)
- 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
Fragile X Syndrome (FXS)*				
	CONNECT-FX			
Developmental and Epileptic Encephalopathies (DEE)				
	BELIEVE 1			
Autism Spectrum Disorder (ASD)				
	BRIGHT			
22q Deletion Syndrome (22q)				
	INSPIRE			
Adult Refractory Focal Epilepsy				
	STAR 2 Open Label Extension			
Other neuropsychiatric conditions				

*Orphan Drug Designation

Zygel (ZYN002) Cannabidiol (CBD) Gel

Differentiated **Transdermal** **Unique MOA** **Neuropsych Indications**

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

Formulation delivers CBD through the epidermis and into the circulatory system

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

Potential utility in rare / near-rare neuropsychiatric conditions

FDA Fast Track and Orphan Drug designations in FXS

Fragile X Syndrome (FXS)

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 the EC system
- ~71K people in U.S.
- No approved drugs indicated for FXS

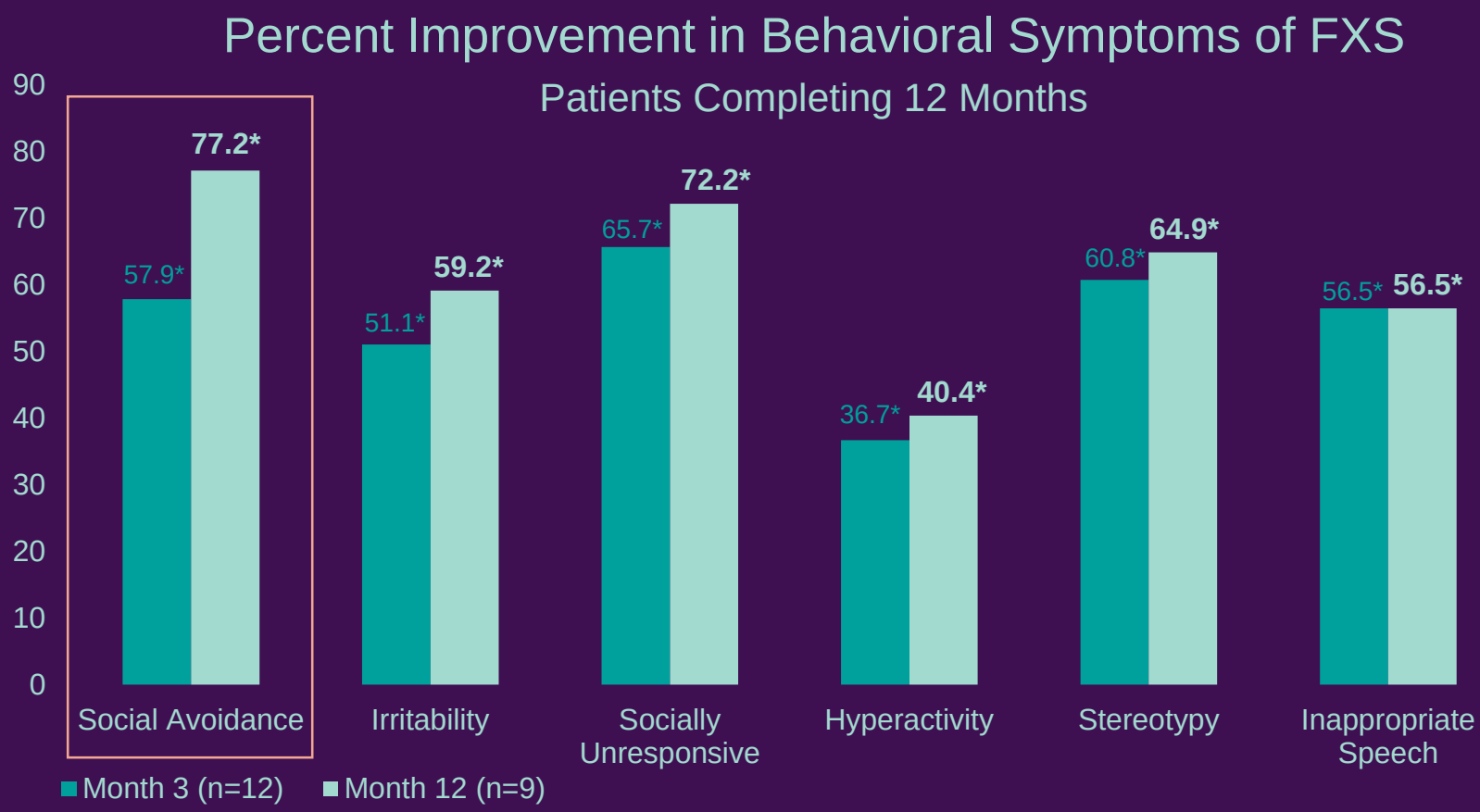
Fragile X Syndrome (FXS)

Clinical Program Update

- Presented new data at SSBP (September 2019)
  - Data further validate the ABC-C_{FXS} to assess core behaviors of FXS
  - ASD, FXS and 22q share a constellation of socio-behavioral symptoms
- US patent for treating FXS with cannabidiol extends IP protection to 2038
- 12-week FAB-C open label Phase 2 data published in the *JND* (August 2, 2019)
  - Statistical improvement from baseline in FXS phenotypic behaviors including social avoidance, anxiety, and irritability
- Presented 12-month FAB-C data at APA (May 2019)
  - Three month improvements sustained through 12 months of treatment

FAB-C Open Label Phase 2

Month 3 and 12: ABC-C_{FXS} Mean Score

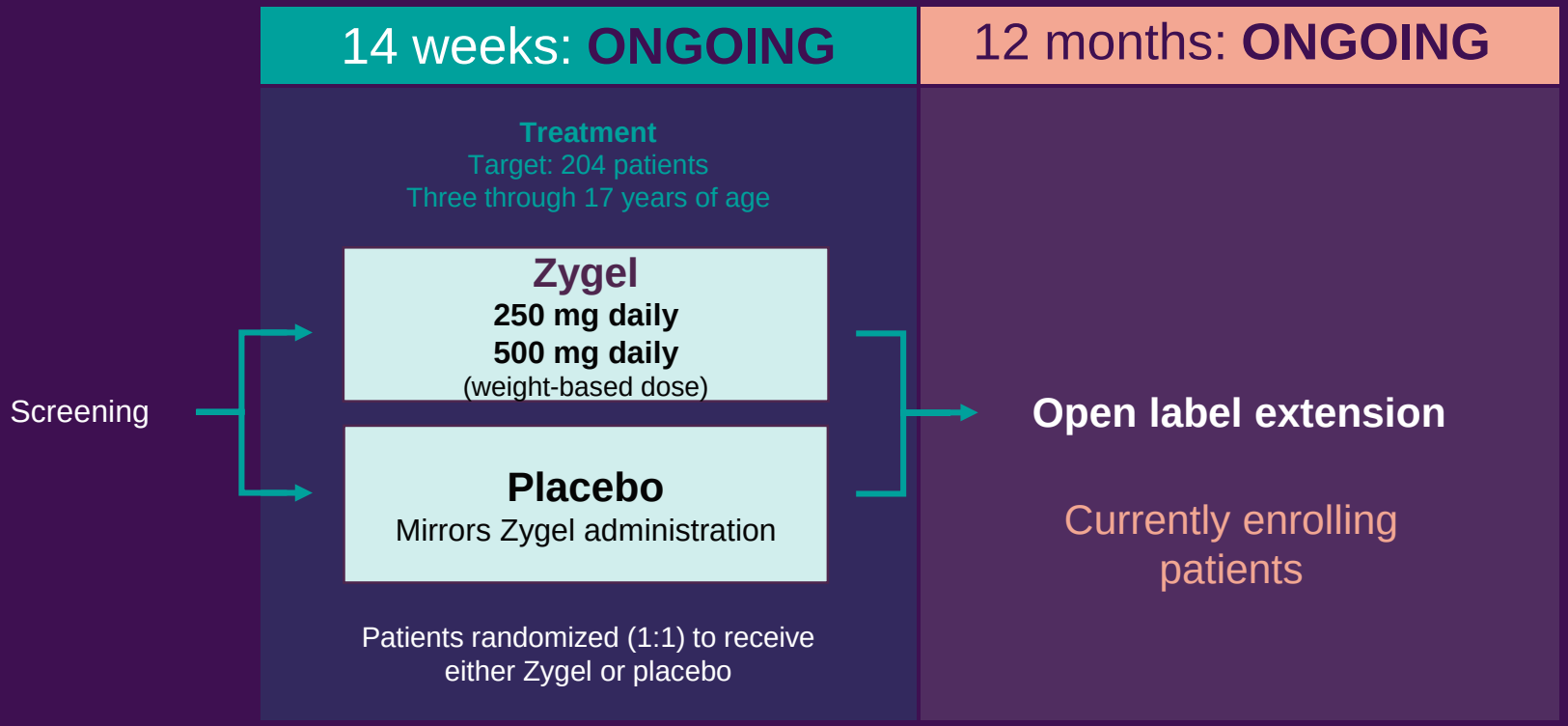


*P ≤ 0.05; statistically significant vs baseline

Data from American Psychiatric Association (APA) meeting, May 2019

CONNECT-FX: A Pivotal Trial In FXS

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

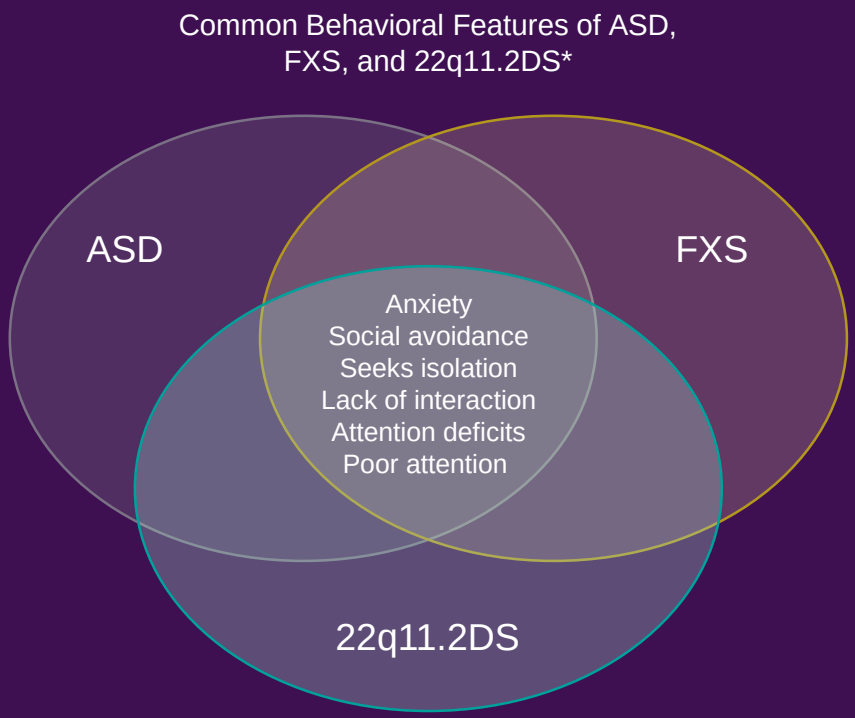


CONNECT-FX: A Pivotal Trial In FXS

- 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 CGI-I (anchored to FXS behaviors) at end of treatment
- Aligned with FDA's 'Voice of the Patient' Guidance
  - Capturing qualitative data on clinical relevance of FXS behaviors
  - New data presented at SSBP (September 2019) further validate core FXS behaviors from the perspective of caregivers
- Top line results expected in 1H2020

Overlap in Behavior May Provide a Read-Through to Zygel Studies

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



**Common Behavioral Features of Autism, Fragile X Syndrome, and 22q11.2 Deletion Syndrome*, SSBP, 2019

Autism Spectrum Disorder (ASD)

ASD Overview

- Near-rare disorder affecting <1MM pediatric and adolescent pts
- DSM-5 diagnosis
  - Autistic disorder, Asperger's syndrome, 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 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 (atypical antipsychotics); neither approved to address social impairment & anxiety

Autism Spectrum Disorder (ASD)

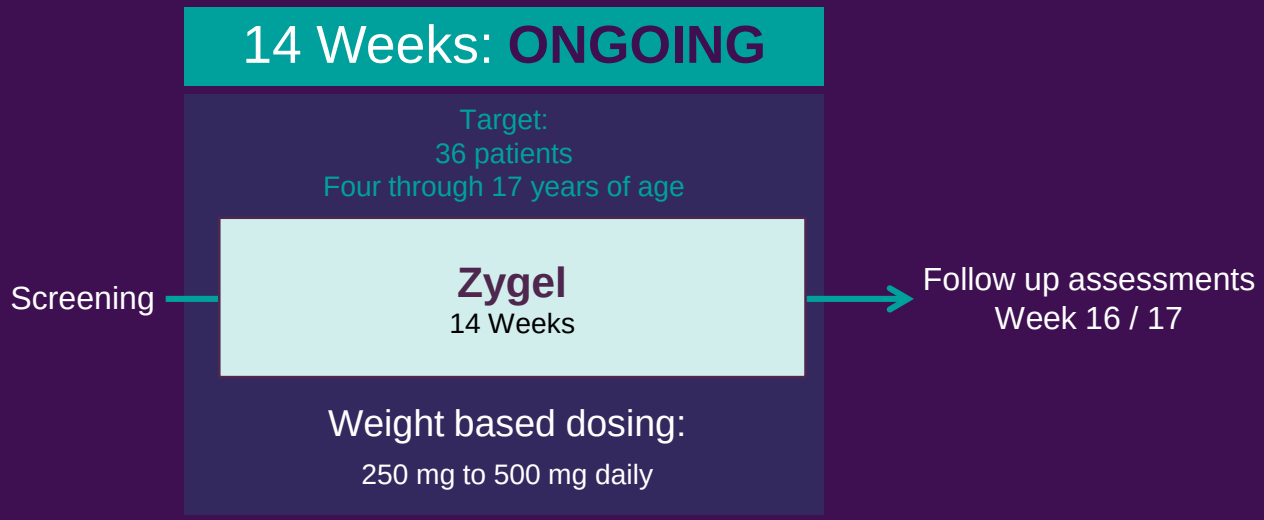
Clinical Program Overview

- Newer studies suggest ASD is linked to disruption in the endocannabinoid system
- 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
- Recent US patent directed towards methods of treating ASD with synthetic CBD extends IP protection to 2038
- BRIGHT Phase 2 study underway in pediatric and adolescent ASD patients
- Top line results expected in 1H2020

BRIGHT Phase 2 Trial in ASD

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

Enrollment ongoing



Efficacy assessments (week 14 vs baseline) include:

- Aberrant Behavior Checklist
- Parent Rated Anxiety Scale – Autism Spectrum Disorder
- Autism Impact Measure
- Clinical Global Impression – Severity and Improvement

22q11.2 Deletion Syndrome (22q)

22q Overview

- Most common 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
  - Associated with increased anxiety, withdrawn behavior and 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. general population

22q11.2 Deletion Syndrome (22q)

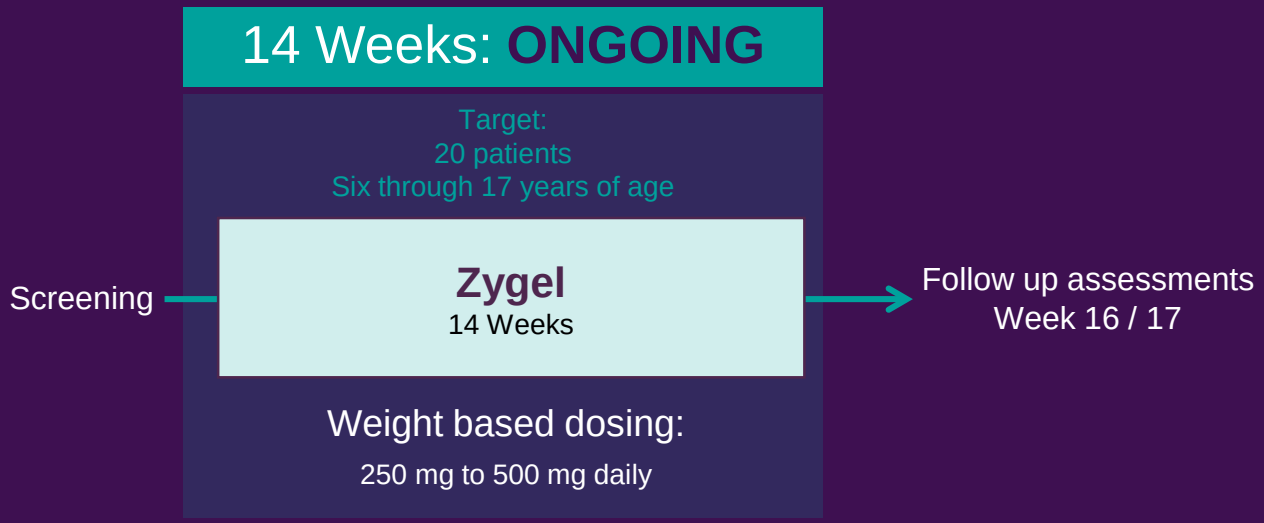
Clinical Program Overview

- CBD may treat neuropsychiatric symptoms in 22q due to activity as:
  - Agonist at serotonin 1A receptors
  - Antagonist at GPR55 receptors
  - Modulator of endocannabinoid system
- Early control of anxiety may delay the development of psychosis
- INSPIRE Phase 2 study underway in pediatric and adolescent patients with 22q
- Top line results expected in 1H2020

INSPIRE Phase 2 Trial in 22q

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

Enrollment ongoing



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

Developmental and Epileptic Encephalopathies (DEE)

DEE Overview

- 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, feeding problems
  - Many wheelchair bound with feeding tubes
- Most common and debilitating seizure types:
  - Focal impaired-awareness seizures (FIAS)
  - Focal to bilateral tonic-clonic and generalized tonic-clonic seizures – commonly known as convulsive seizures (CS)

Developmental and Epileptic Encephalopathies (DEE)

Clinical Program Update

- Positive topline data from six month BELIEVE 1 Phase 2 study announced September 18, 2019
  - 44% median seizure reduction in FIAS and CS by month 2; reductions sustained through month 6 of treatment with Zygel
  - ≥42% of patients with FIAS or CS experienced a ≥50% improvement from month 2 through month 6
  - Qualitative assessments demonstrate improvements in seizure intensity and duration, and improvements in socio-behavioral and cognitive impairments
  - Anticipate meeting with FDA in 1H2020 to discuss the clinical pathway forward

Planned Approach to FDA – All DEE Patients with Consciousness Impairing Seizures

Syndromes and encephalopathies

Dravet	Lennox Gastaut	West	Hypoxic-ischemic enceph.	Early myoclonic epilepsy
Doose	Ohtahara	Landau Kleffner	CDKL5 enceph.	Other Syndromes

Seizure type

Convulsive

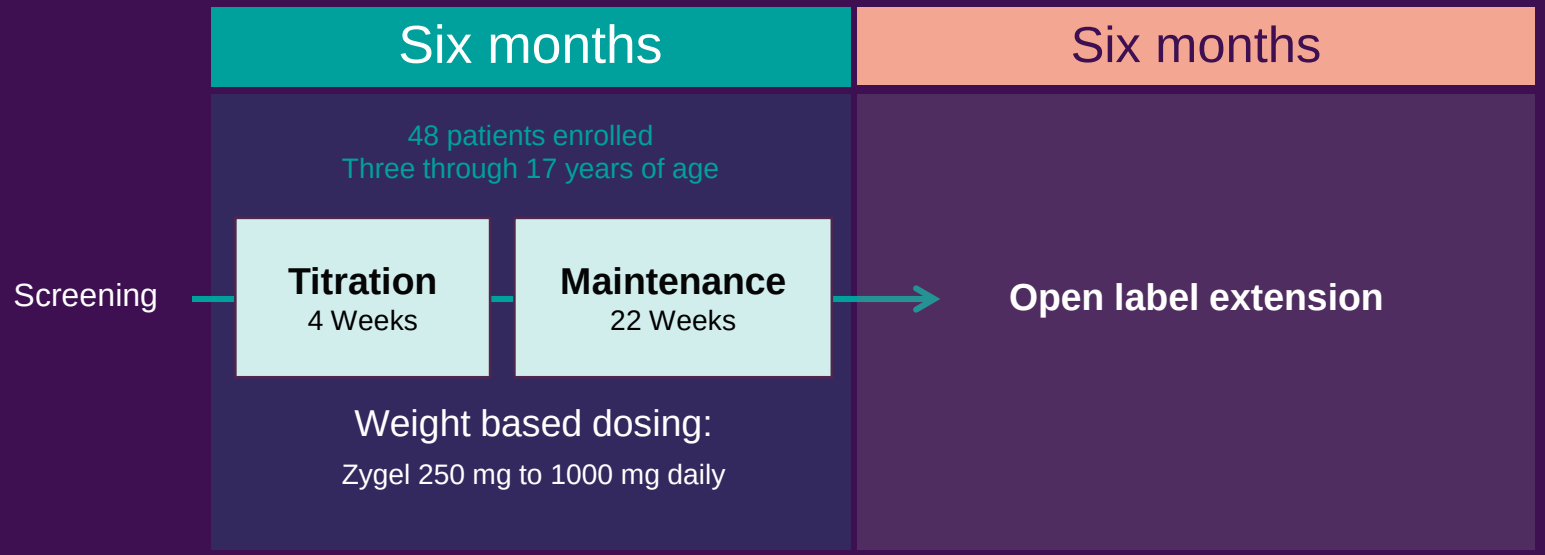
- Focal Impaired Awareness
- Bilateral Tonic Clonic
- Generalized Tonic Clonic

Consciousness impairing seizures

- Focal aware
- Absence
- Other Seizure types

BELIEVE 1 Phase 2 Trial in DEE

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



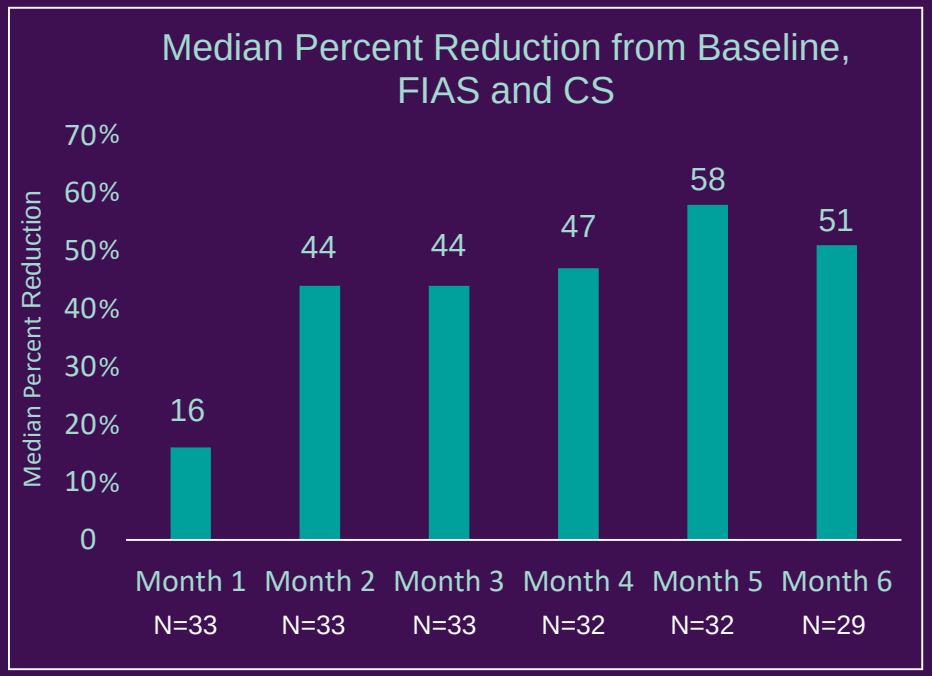
BELIEVE 1 Safety

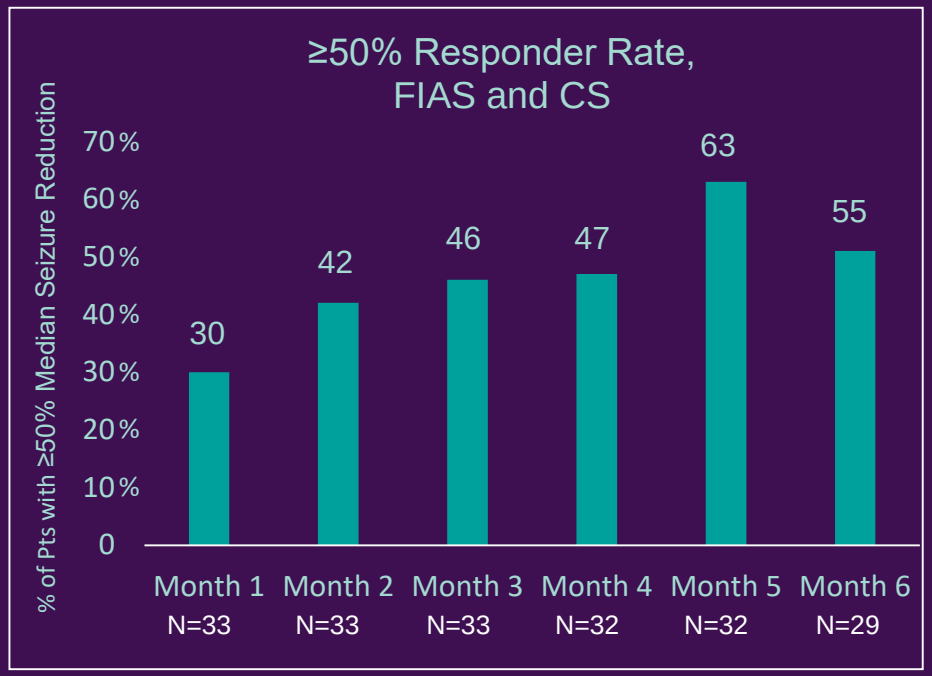
Well Tolerated over Six Month Trial

- DEE is a fragile population; adverse events (AEs) common and expected
- All events whether unrelated or related to study drug were reported as AEs (e.g.: influenza, runny nose, ingrown toenail, scrapes, etc.)
  - 96% of patients experienced an AE
    - Most were mild and transient
    - Only one patient discontinued due to an AE (application site reaction)
- Ten patients experienced a serious adverse event (SAE)
  - Eight were unrelated to study drug
  - Two possibly drug-related (LRTI and status epilepticus)
- No hepatic, gastrointestinal, or lethargy-related SAEs
- Consistent with the safety database for Zygel and compares favorably with reported safety data from oral CBD solution[1, 2, 3, 4]

[1]Devinsky - *Lancet Neurol* 2016
[2]Thiele - *Epilepsia* 2019
[3]Devinsky - *Epilepsy and Behavior* 2018
[4]Epidiolex package insert, June 2018

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





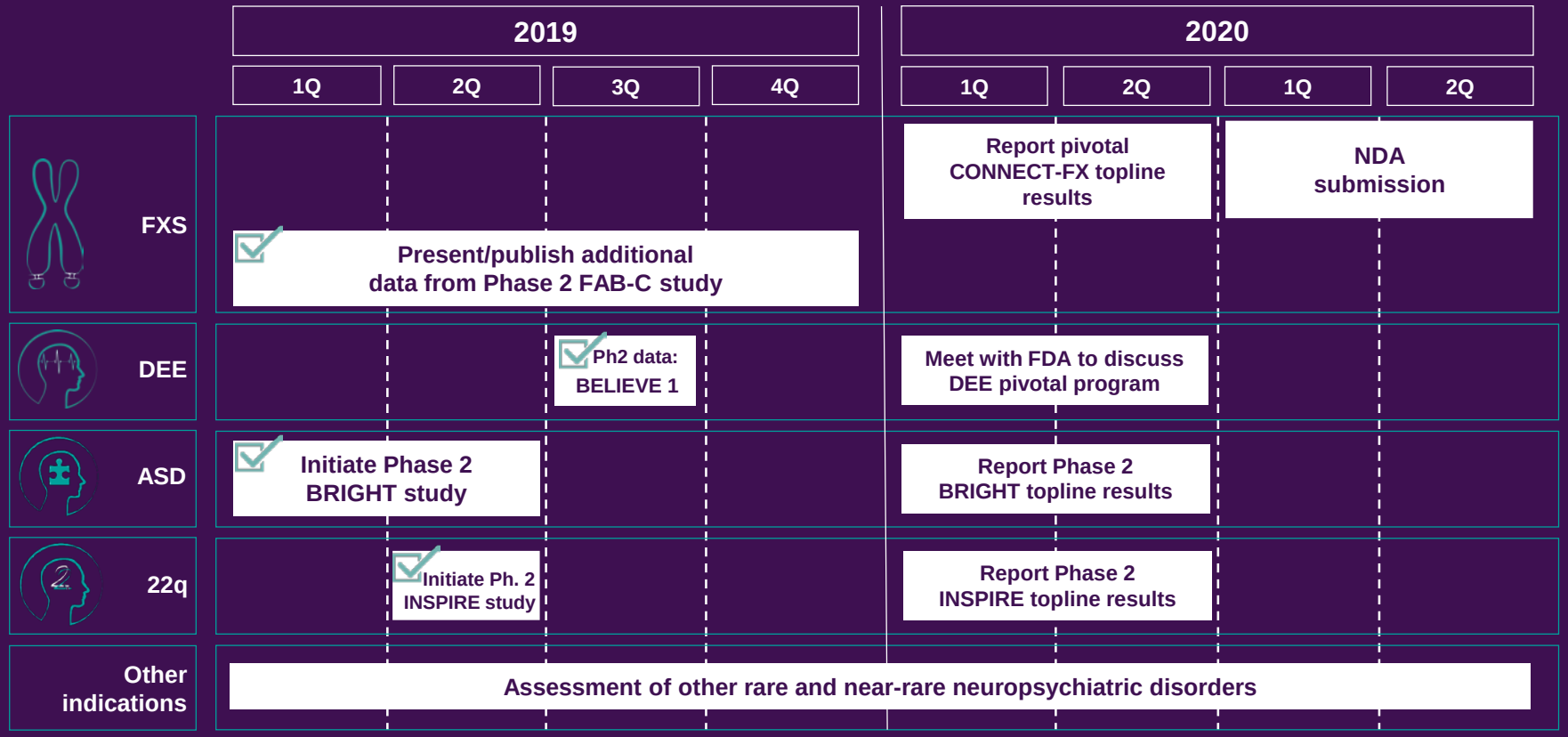
BELIEVE 1: Qualitative Assessments of Behavioral and Cognitive Improvements

- 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

Financial Strength

- Clean balance sheet
  - No debt, 23.2M shares outstanding (as of November 1, 2019)
- Cash and cash equivalent position of $77.5M as of September 30, 2019
- Cash 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 Milestones into 2020



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