Corporate Overview

November 2019

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 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 (9/18/19)
- 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			
	FAB-C Open Label Extension			
Developmental and Epileptic Encephalopathies (DEE)				
	BELIEVE 1: Complete			
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

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

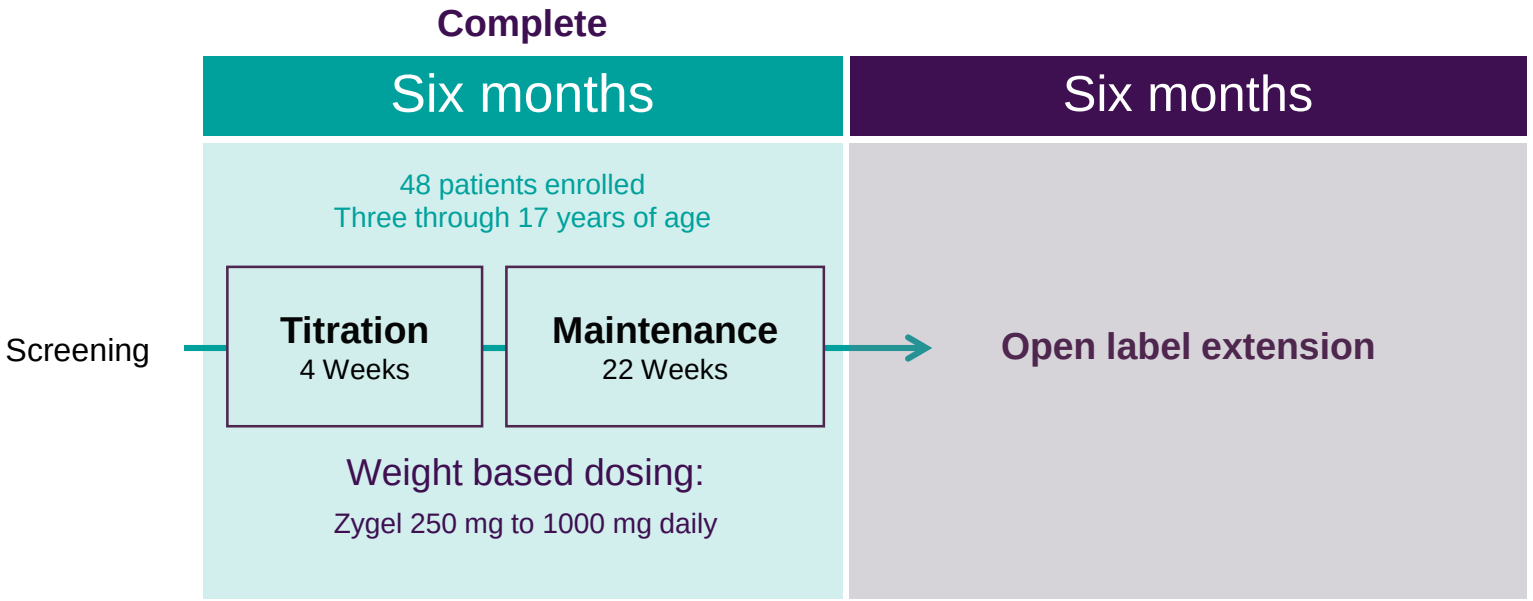
Potential utility in rare / near-rare neuropsychiatric conditions

FDA Fast Track and Orphan Drug designations in FXS

DEE
Developmental and Epileptic Encephalopathies

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



Compelling Results from the BELIEVE 1 Trial Appear to have been Misinterpreted

- DEE is a medically fragile population and adverse events are common and expected
- 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
- Efficacy results:
  - Clinically meaningful reductions in seizures beginning in month two and sustained through six months
  - Suggest improvements on important behavioral symptoms

[1]Devinsky - *Lancet Neurol* 2016

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

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 Safety

Well Tolerated over Six Month Trial

- DEE is a fragile population; adverse events (AEs) common and expected
- 96% of patients experienced an AE
  - All events whether unrelated or related to study drug were reported as AEs (e.g.: influenza, runny nose, ingrown toenail, scrapes, etc.)
  - 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
  - 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

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

Syndromes and encephalopathies

Dravet | LGS | West | Hypoxic-ischemic enceph. | Early myoclonioc epilepsy

Doose | Ohtahara | Landau-Kleffner | CDKL5 enceph. | Other Syndromes

Seizure type

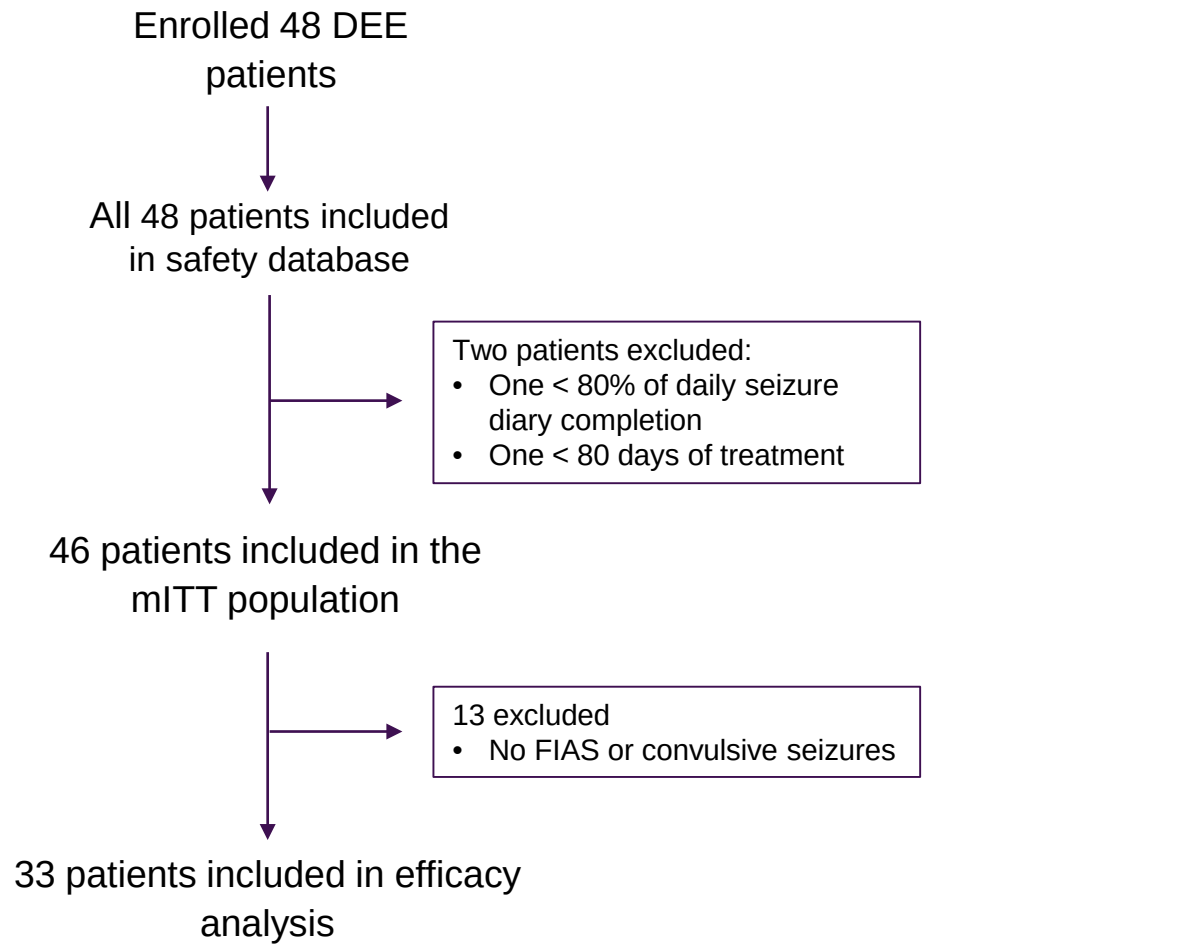
Convulsive

Focal Impaired Awareness | Bilateral Tonic Clonic | Generalized Tonic Clonic

Consciousness impairing seizures

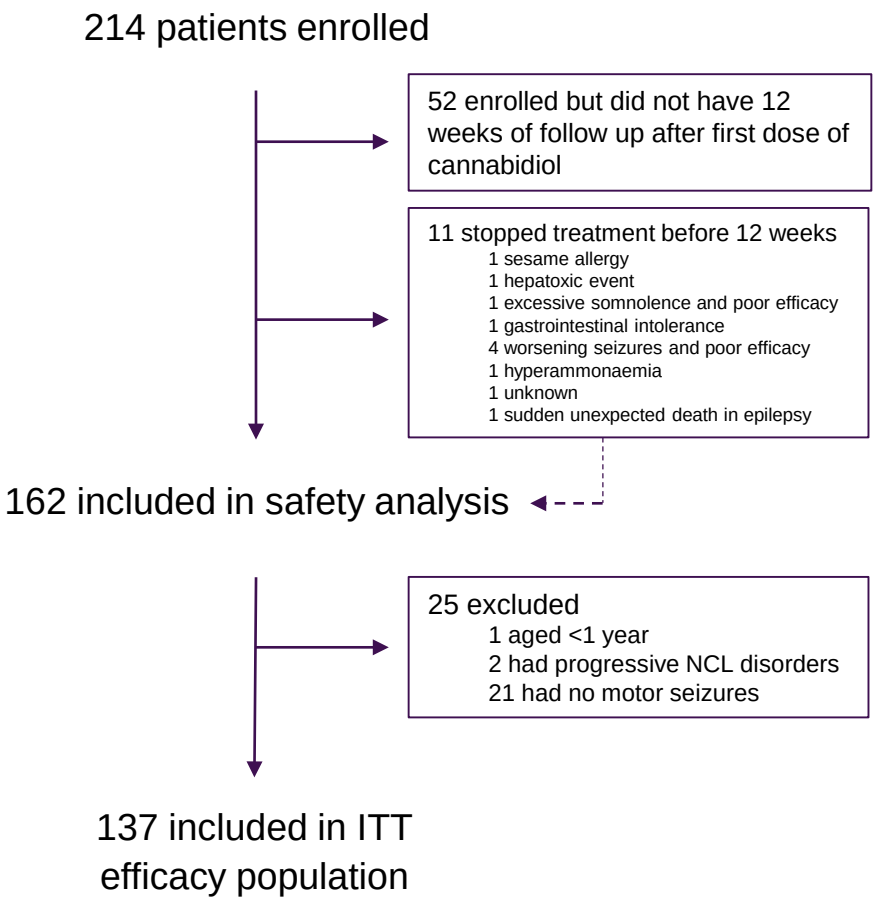
Focal aware | Absence | Other Seizure types

BELIEVE 1 Patient Disposition



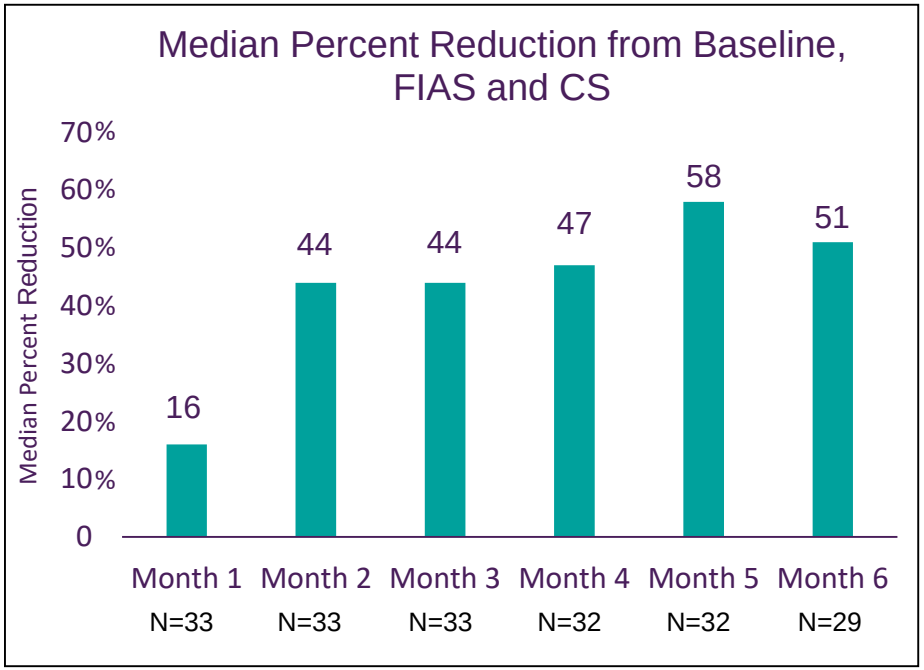
Oral CBD Solution Open Label Patient Disposition

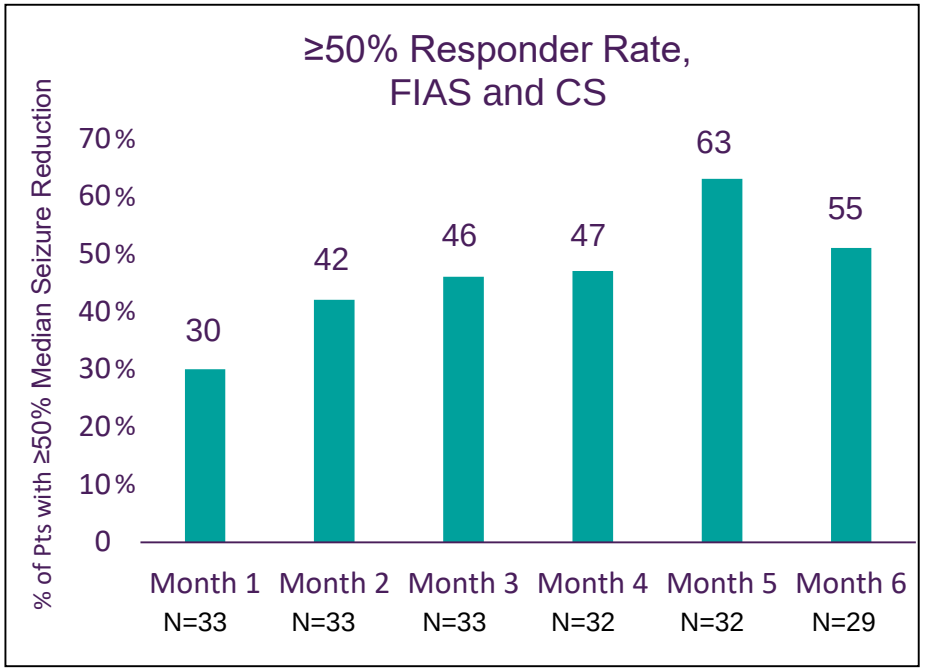
Devinsky, *Lancet Neurol* 2016



Note: Head to head clinical trials with Zygel and Epidiolex® were not undertaken and information in this slide is sourced from publicly available data.

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



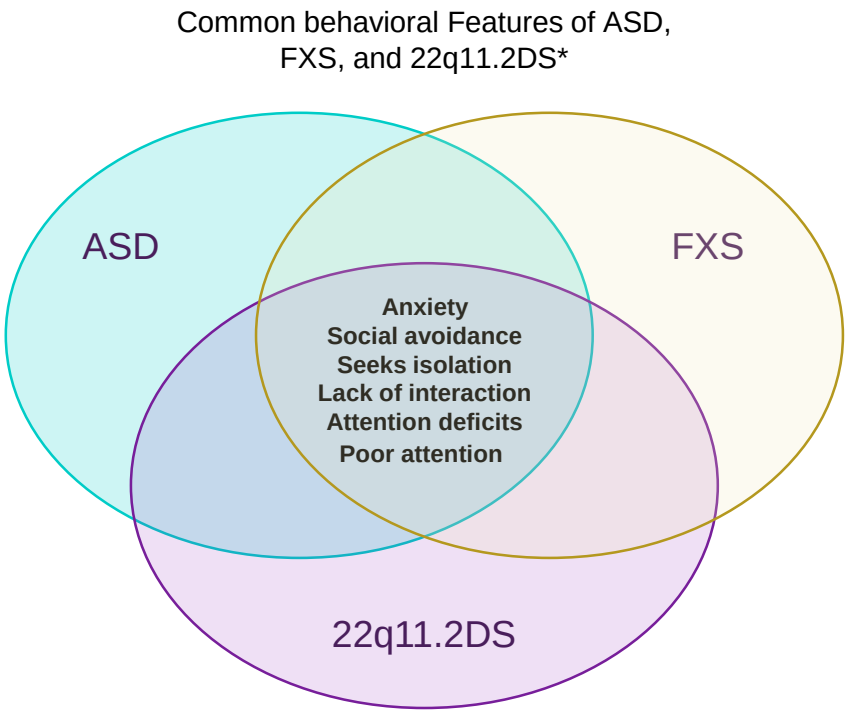


BELIEVE 1: Qualitative Assessments of Behavioral and Cognitive Improvements

- 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

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
- Qualitative data from BELIEVE 1 suggest improvements in overlapping behaviors in ASD, FXS, and 22q



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

Compelling Results Suggest a Pathway to Pivotal Trials – Anticipate Meeting with FDA in 1H2020

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

Fragile X Syndrome (FXS)

Fragile X Syndrome (FXS) Overview

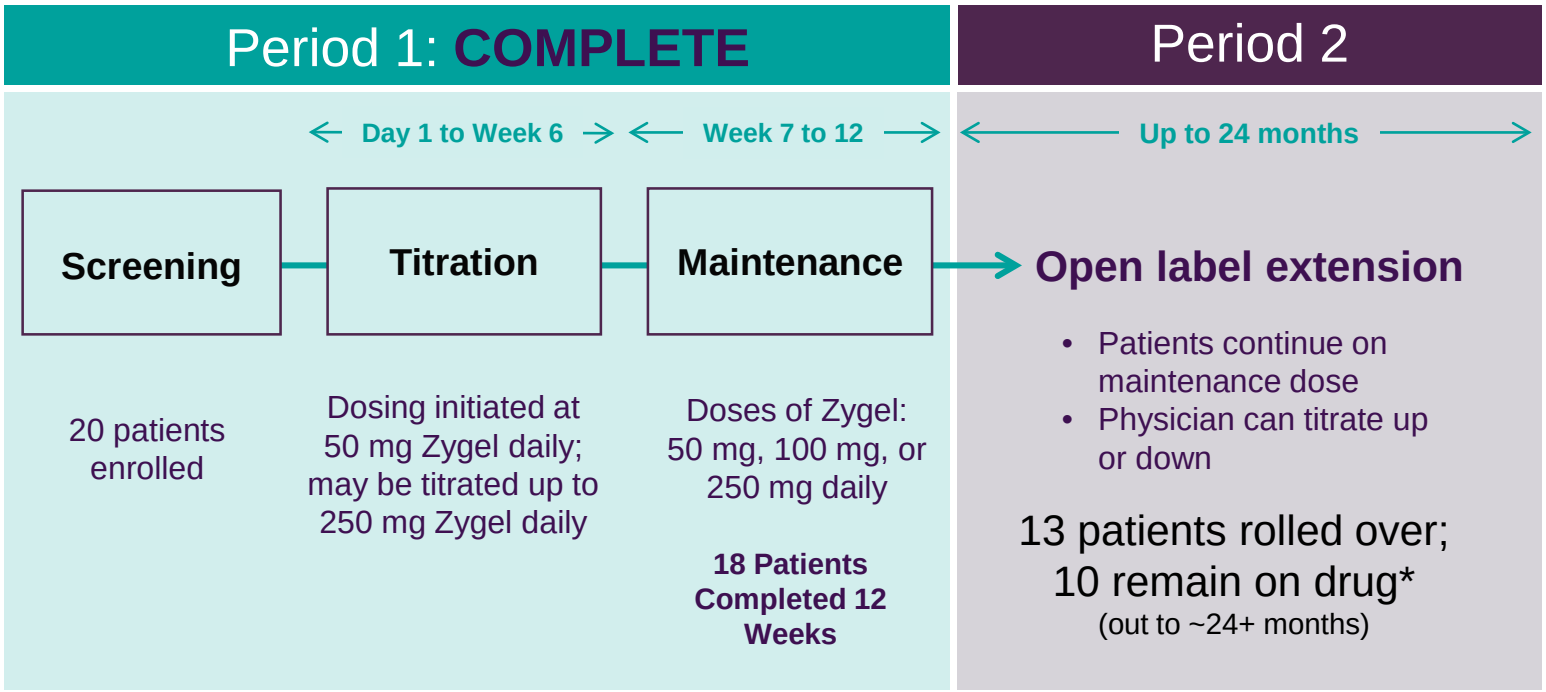
- Rare genetic developmental disability
- Leading known cause of both inherited intellectual disability and autism spectrum disorder
- Symptoms linked to deficiencies in the endocannabinoid (EC) system
  - System of neurotransmitters regulating emotional responses, behavioral reactivity to context, social 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

Recent Development Progress in FXS

- 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
- Recently issued US patent directed to methods of treating FXS with cannabidiol extends IP protection to 2038
- 12-week FAB-C open label Phase 2 data published in the *Journal of Neurodevelopmental Disorders* (August 2, 2019)
  - Statistical improvement from baseline in FXS phenotypic behaviors including social avoidance, anxiety, and irritability
- Presented 12-month FAB-C open label Phase 2 data at American Psychiatric Association meeting (APA; May 2019)
  - Statistical improvement from baseline in FXS phenotypic behaviors including social avoidance, anxiety, and irritability
  - Three month improvements sustained through 12 months of treatment
  - Excellent tolerability profile

FAB-C Open Label Phase 2 Trial Design

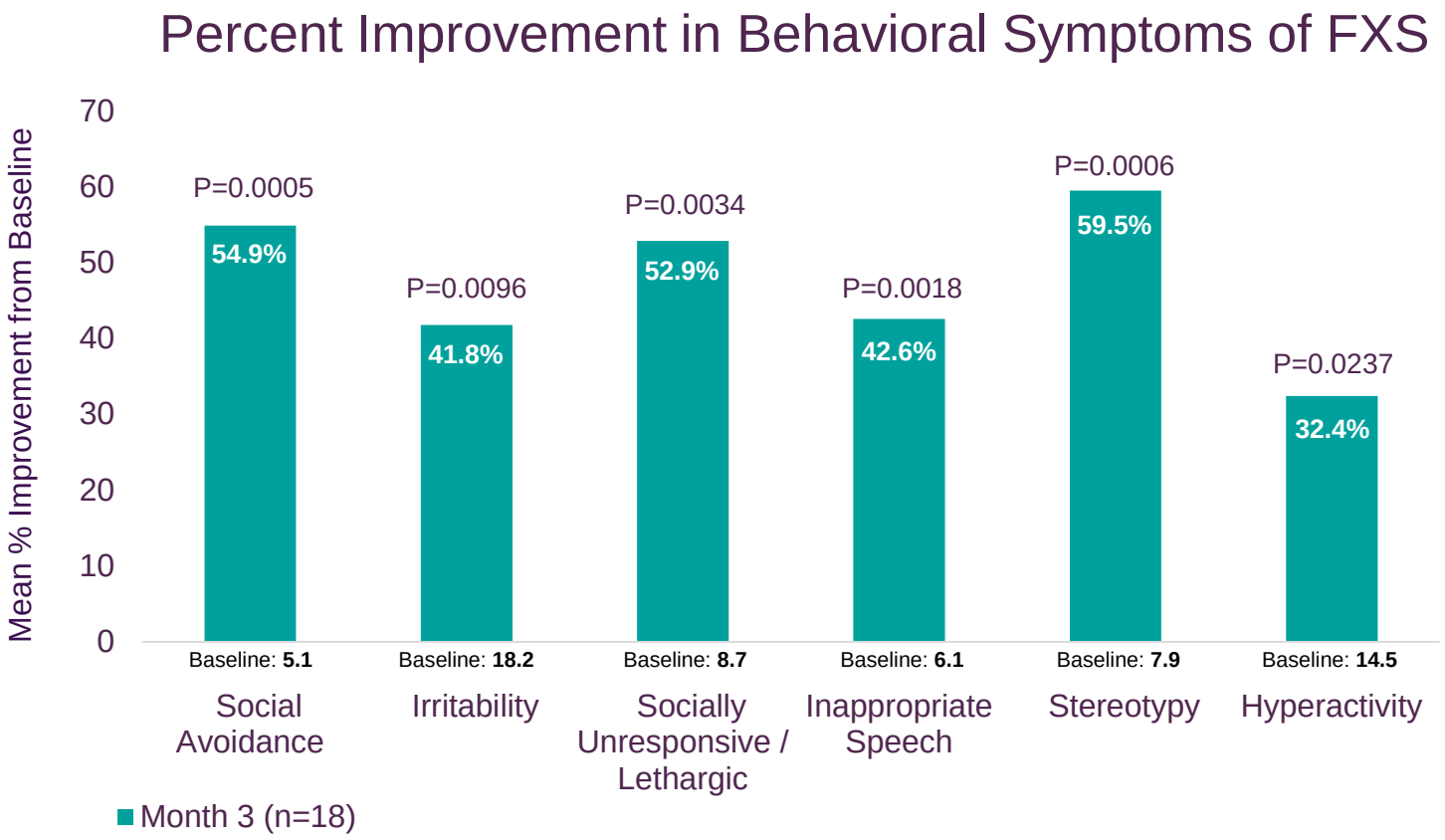
Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD



*As of September 3, 2019

FAB-C Open Label Phase 2

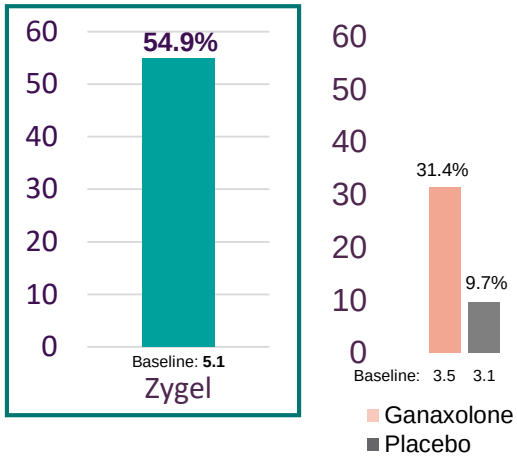
Month Three: ABC-C_{FXS} Mean Score



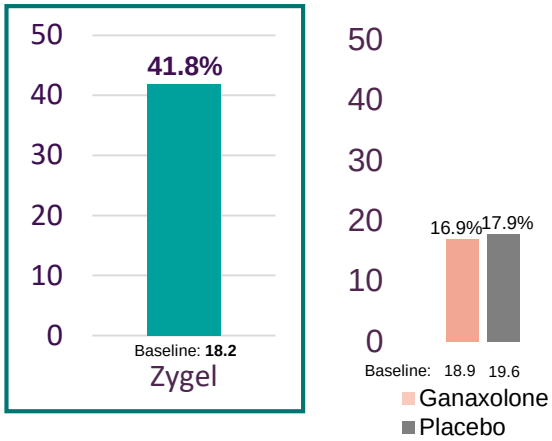
FAB-C ABC-C_{FXS} Subscales

Month Three: Percent Improvement vs. 3rd Party Data*

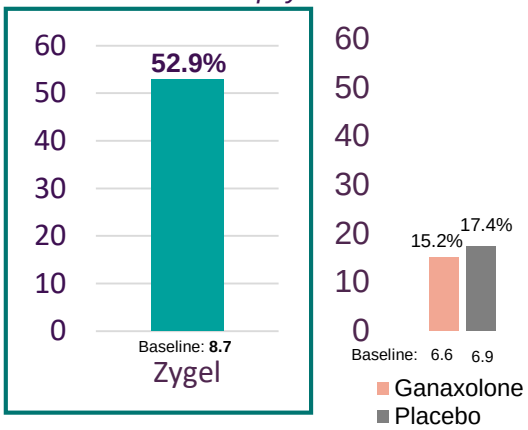
Social Avoidance
Seeks isolation



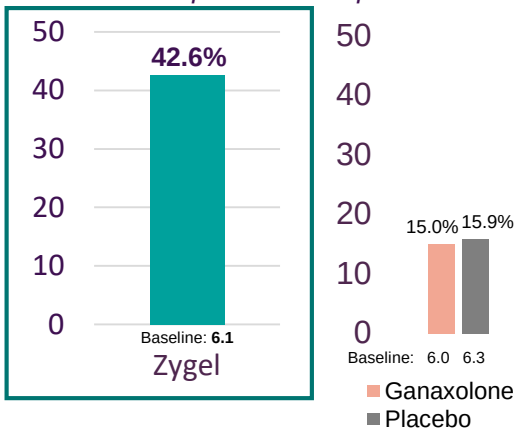
Irritability
Temper tantrums



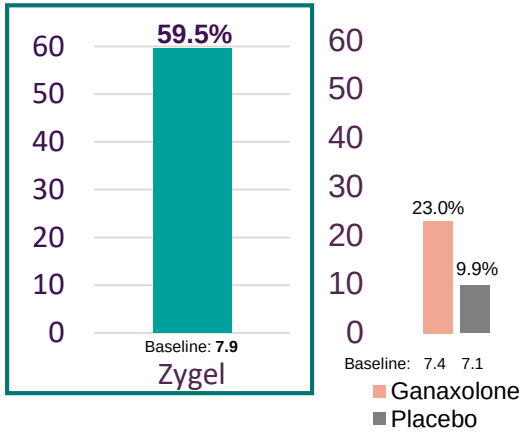
Socially Unresponsive / Lethargic
Does not pay attention



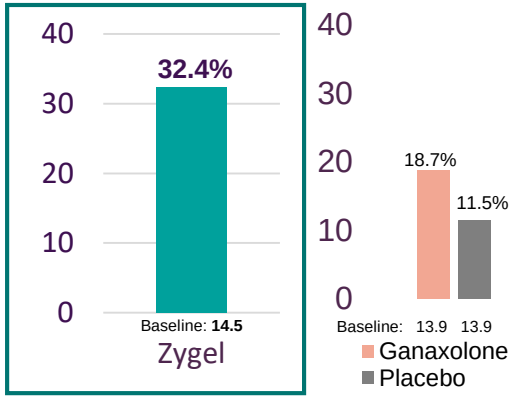
Inappropriate Speech
Repeats words / phrases



Stereotypy
Repetitive movements



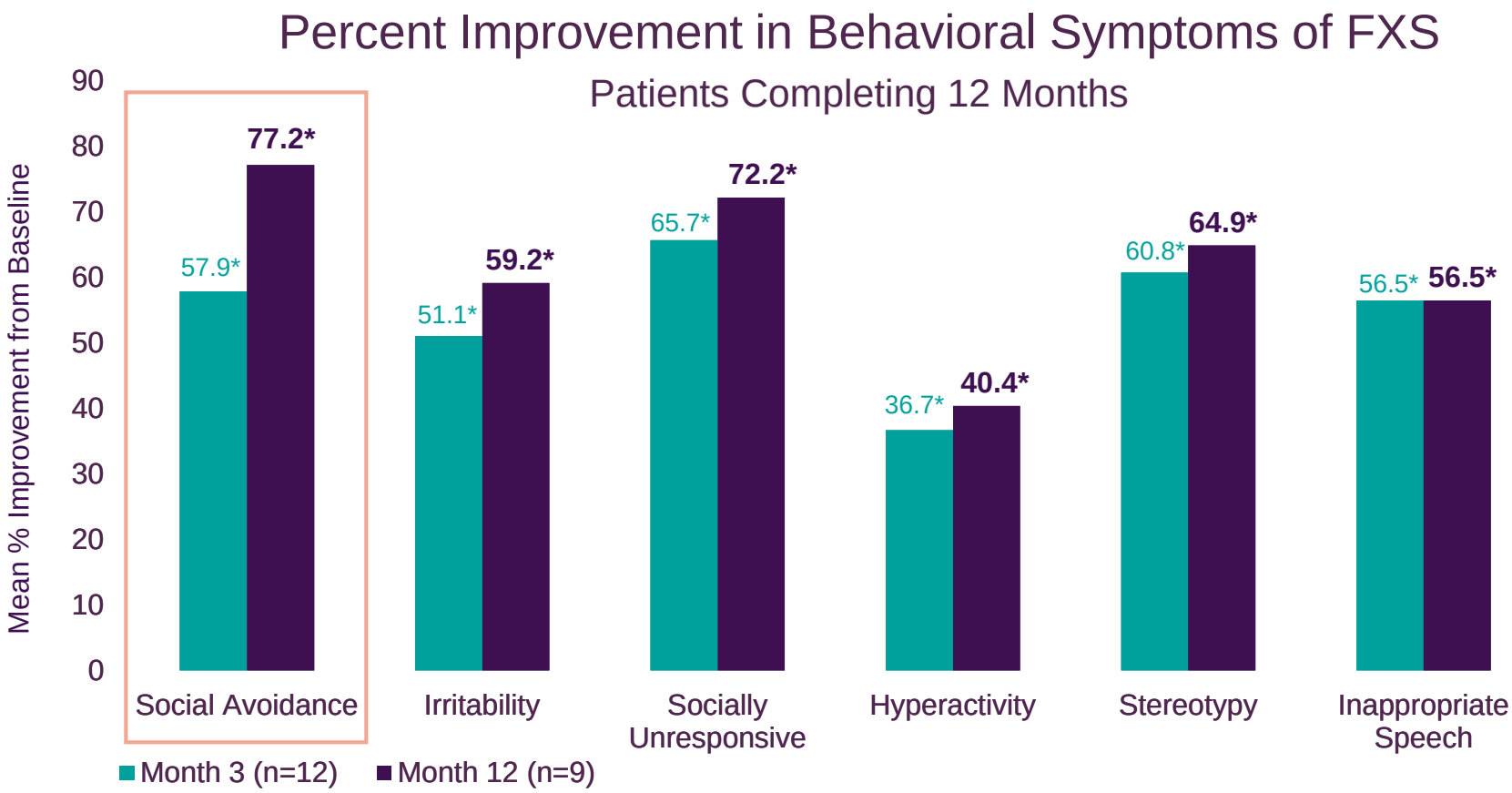
Hyperactivity
Disrupts group activities



* 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.

FAB-C Open Label Phase 2

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



*P ≤ 0.05

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

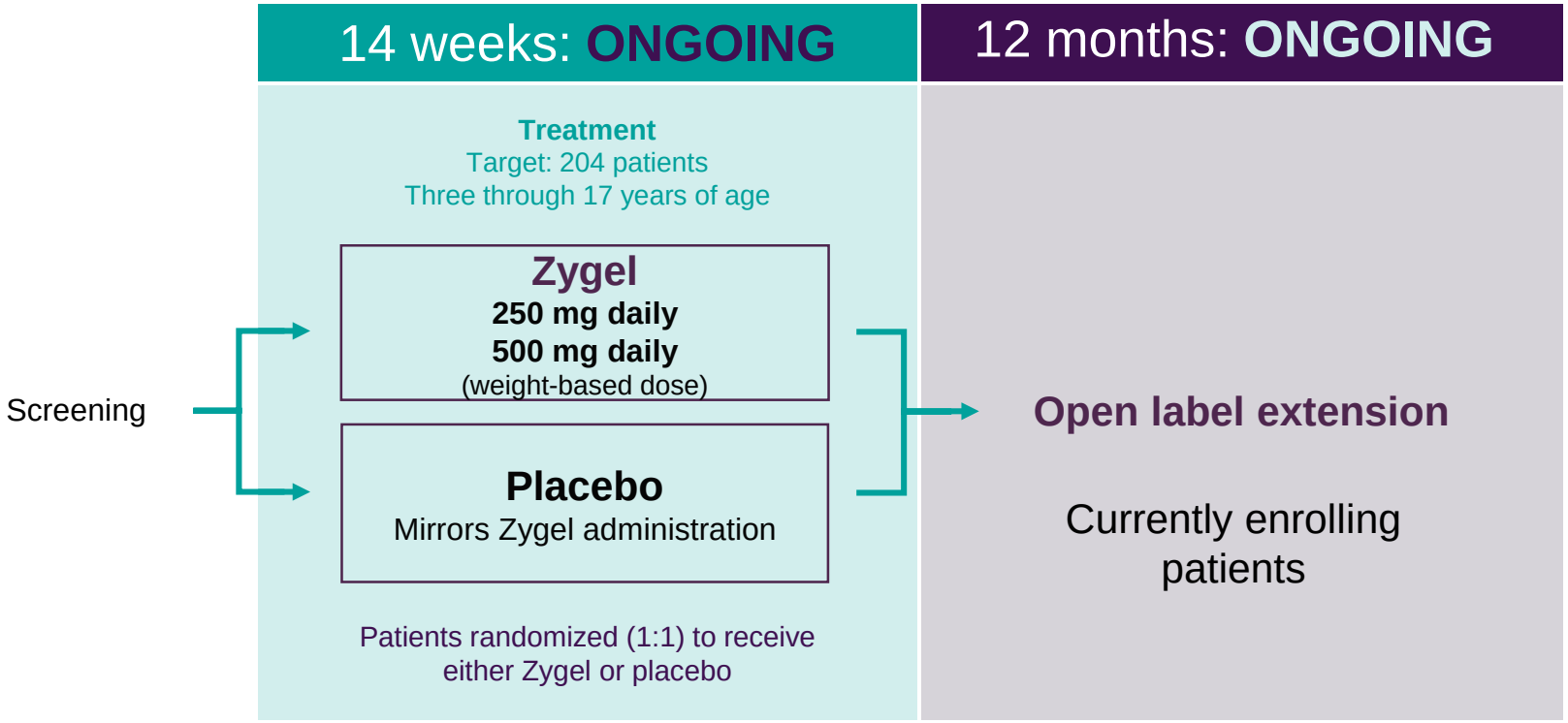
FAB-C Open Label Phase 2

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

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

CONNECT-FX

- With positive results, Zynerba intends to request a meeting with the FDA to:
  - Determine acceptability of data as basis for NDA filing
  - Seek advice on marketing authorization preparation
- Zynerba believes indication may include the treatment of behavioral symptoms associated with FXS
- Evaluating opportunities for FDA breakthrough status and/or priority review

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

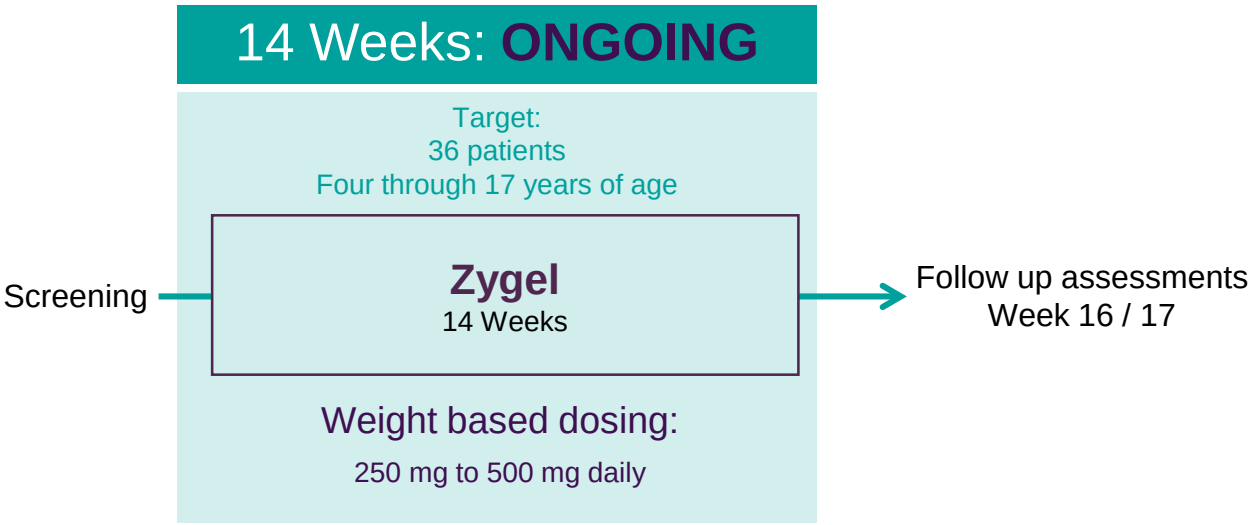
Developing Zygel in ASD

- 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
- Recent US patent directed to methods of treating ASD with synthetic cannabidiol provides IP protection to 2038
- Phase 2 study underway in pediatric and adolescent patients with ASD
- Top line results expected in 1H2020

BRIGHT Phase 2 Trial in ASD

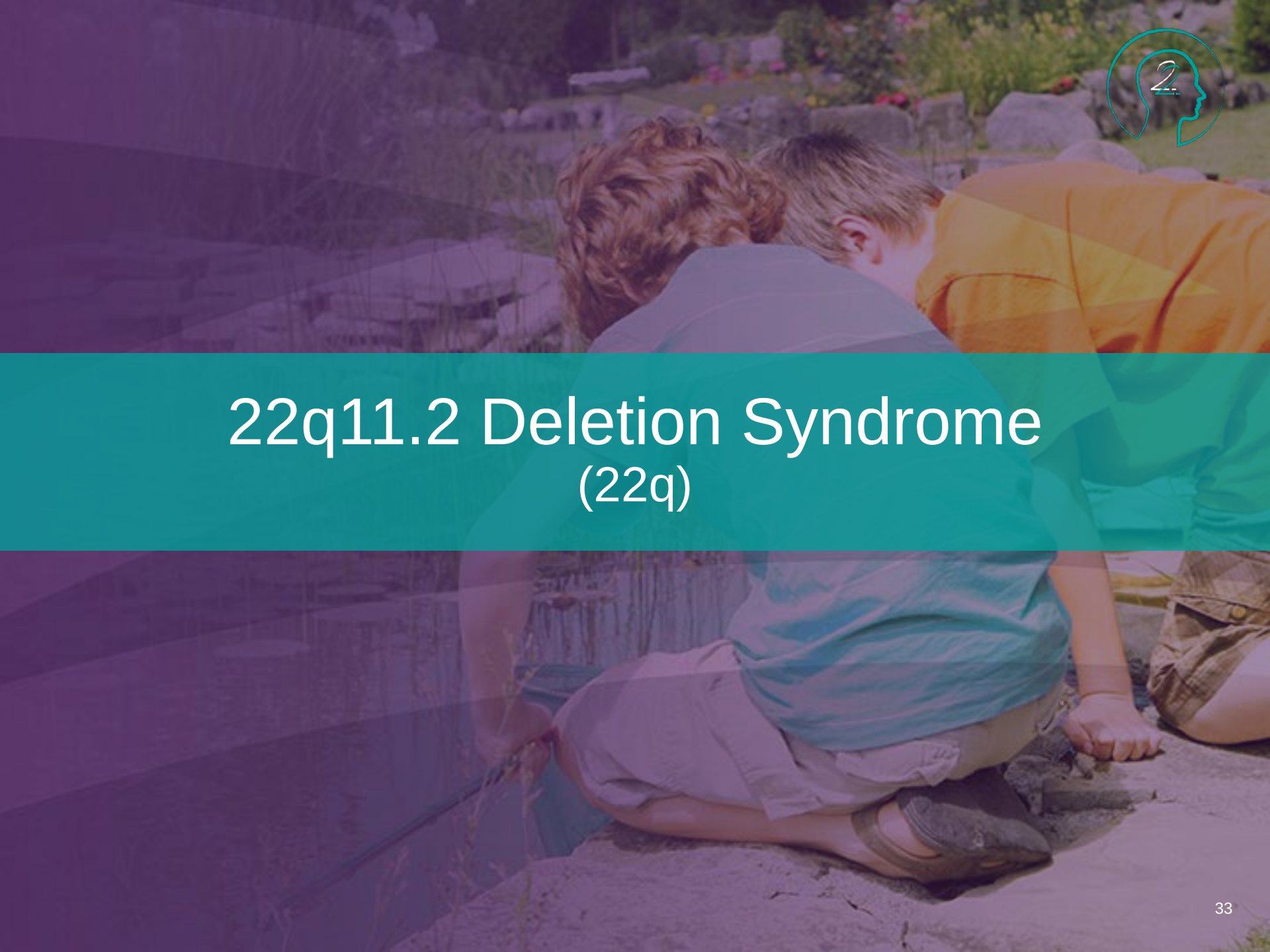
Open-LaBel ToleRabIlity and Efficacy Study of ZYN002 Administered as a Transdermal Gel to CHildren and AdolescenTs with Autism Spectrum Disorder

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 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

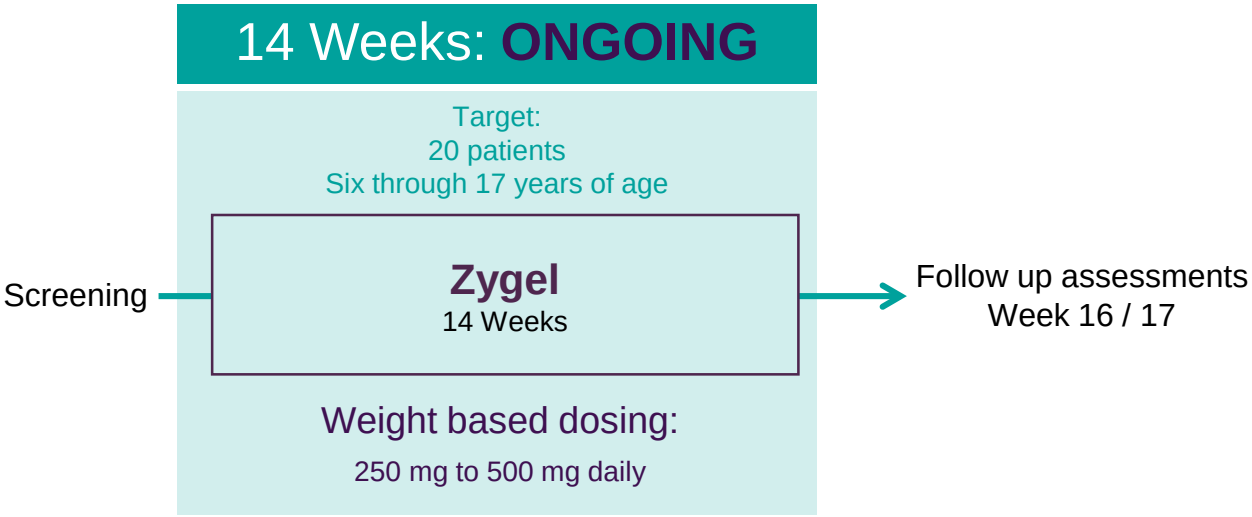
Developing Zygel in 22q

- CBD may treat neuropsychiatric symptoms in 22q due to activity as:
  - Agonist at serotonin 1A receptors
  - Antagonist at GPR55 receptors
  - Modulator of endocannabinoid system
- 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 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



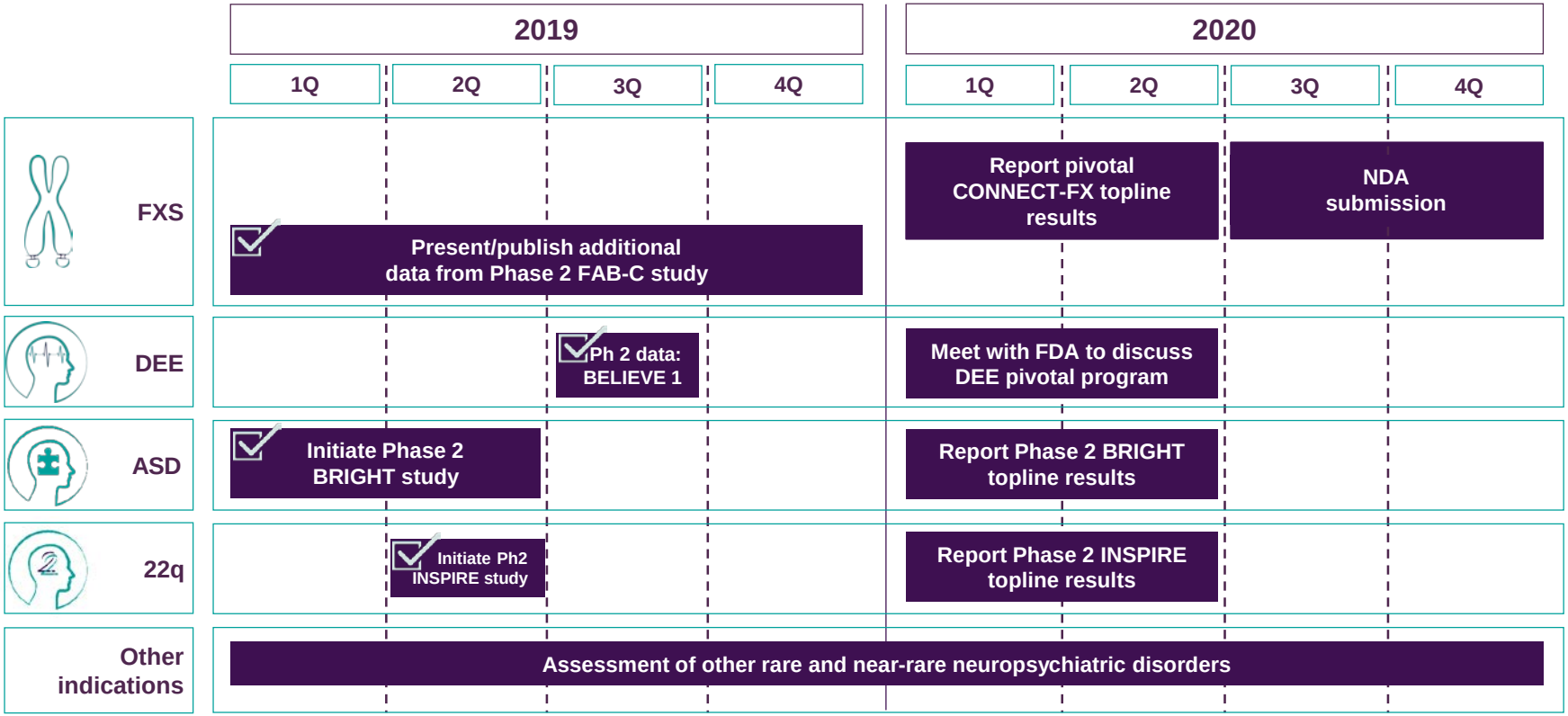
Efficacy assessments (week 14 vs baseline) include:

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

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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