31st Annual Roth Conference

March 19, 2019

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Zynerba Pharmaceuticals (NASDAQ: ZYNE)

A Rare/Near-Rare Neuropsychiatric Company

- Development efforts focused in rare and near rare neuropsych disorders
- Deep pipeline focused on high unmet medical needs; translating into multi-billion dollar market opportunity
  - Four clinical shots on goal: FXS, DEE, ASD, 22q
- Opportunities for efficient development and commercialization strategy
- Experienced team
  - Proven development and commercialization track record in transdermal delivery, orphan diseases, neurology, psychiatry
- Well capitalized
  - Cash runway expected into the first quarter of 2021, and beyond planned NDA filing and potential approval in FXS
- Multiple expected near term milestones

Deep Clinical Pipeline

Zygel™

Indication	Preclinical	Phase 1	Phase 2	Pivotal	2019 Milestones
Fragile X Syndrome (FXS)*					
		CONNECT-FX			Top line CONNECT-FX data: 2H2019
		FAB-C Open Label Extension			Additional long term FAB-C data: 2019
Developmental and Epileptic Encephalopathies (DEE)					
		BELIEVE 1			Top line BELIEVE 1 data: 3Q2019
Autism Spectrum Disorder (ASD) in pediatric patients					
		BRIGHT			Initiate Phase 2 open label study: 1H2019 ☑
22q Deletion Syndrome (22q)					
		Initiate 1H2019			Initiate Phase 2 open label study: 1H2019
Adult Refractory Focal Epilepsy					
		STAR 2 Open Label Extension			
Other neuropsychiatric conditions					
					Assess other neuropsychiatric conditions: 2019

*Orphan Drug Designation

Ongoing | Planned

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

Orphan Drug designation 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
  - ECs form 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
- Affects ~71K people in U.S.
- No approved drugs indicated for FXS

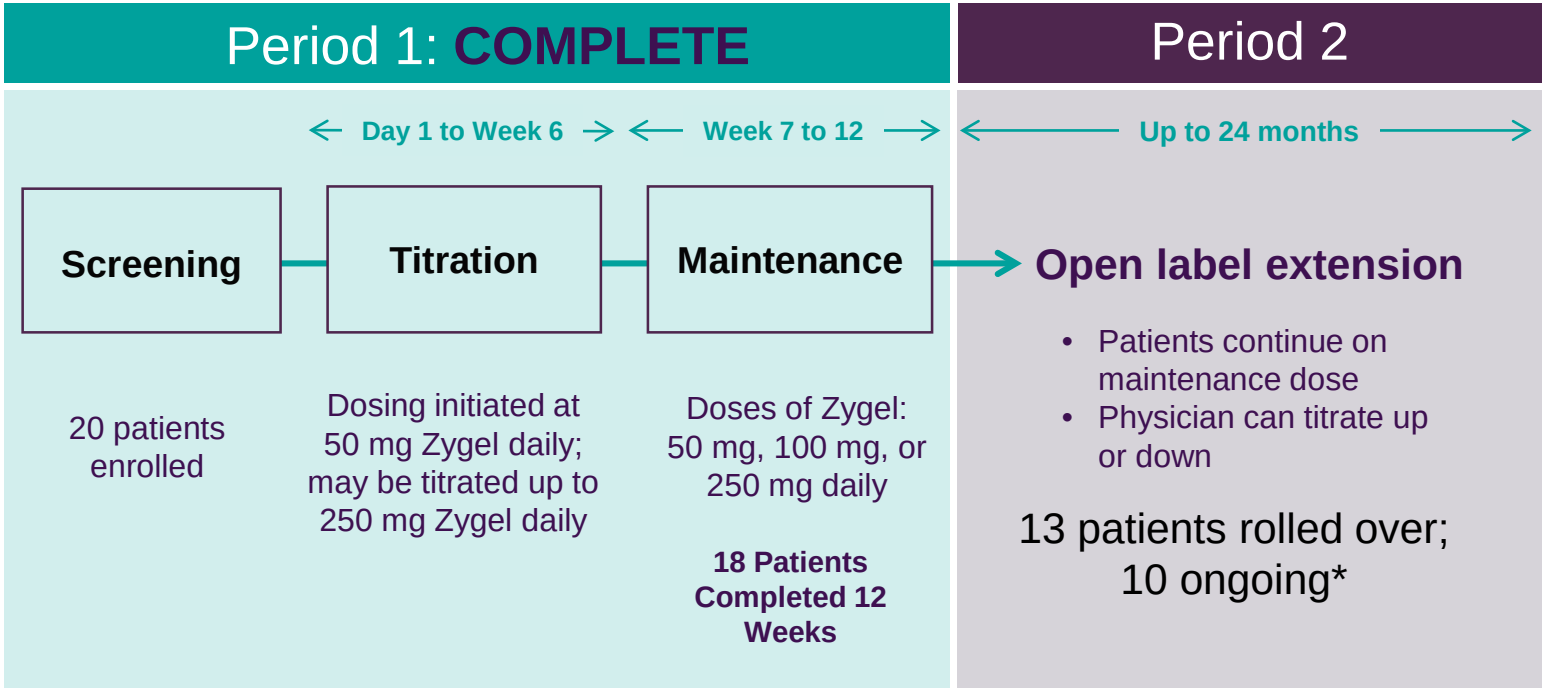
Fragile X Clinical Program

Recent Zygel Development Progress

- Presented 12-month FAB-C open label Phase 2 data at American College of Neuropsychopharmacology meeting (ACNP; Dec. 2018)
  - 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
- Enrollment ongoing in CONNECT-FX: a pivotal trial in pediatric and adolescent patients with FXS
  - Initiated July 2018
  - Top line results expected in 2H2019

FAB-C Open Label Phase 2 Trial Design

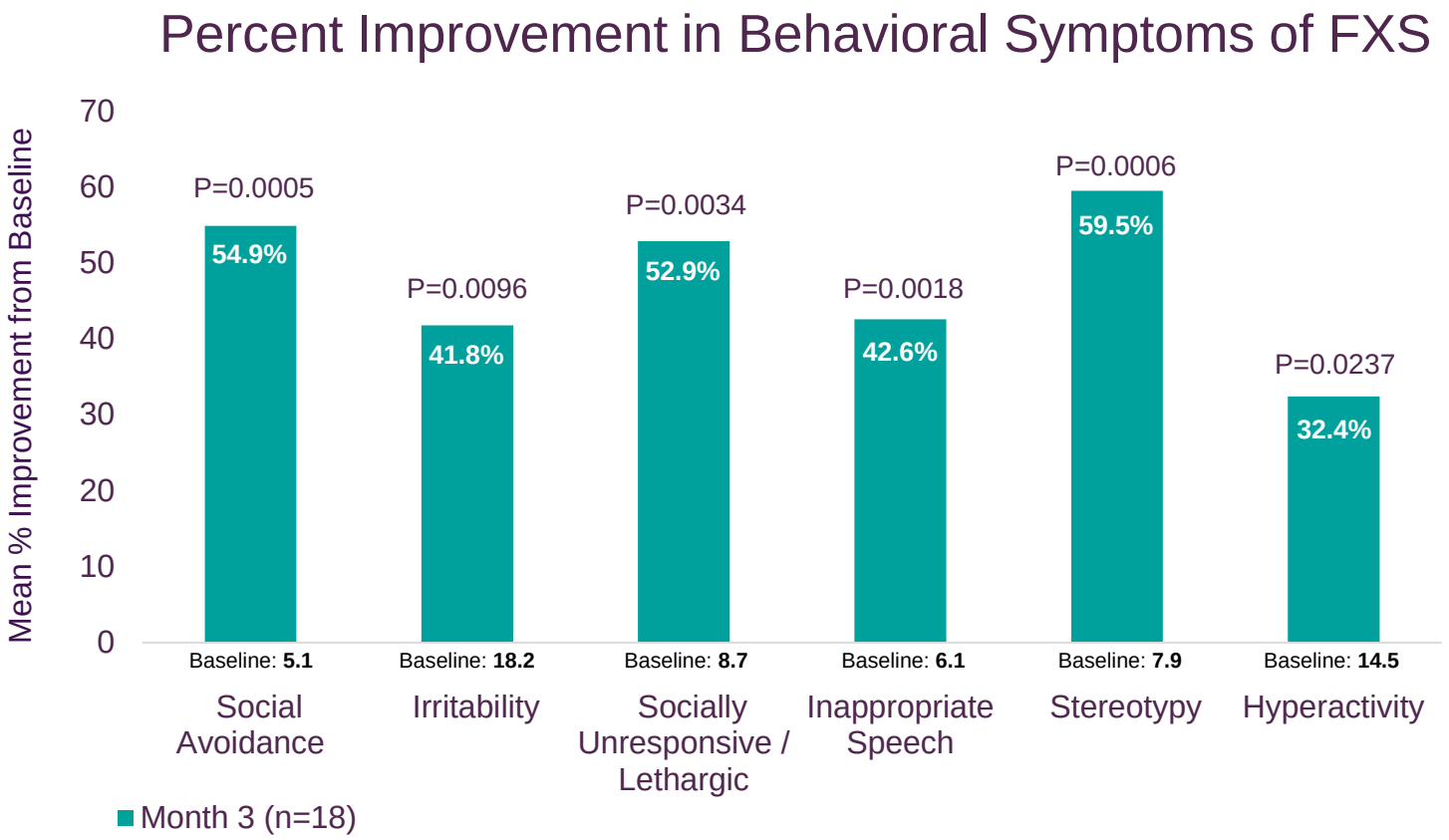
Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD



*As of March 10, 2019

FAB-C Open Label Phase 2

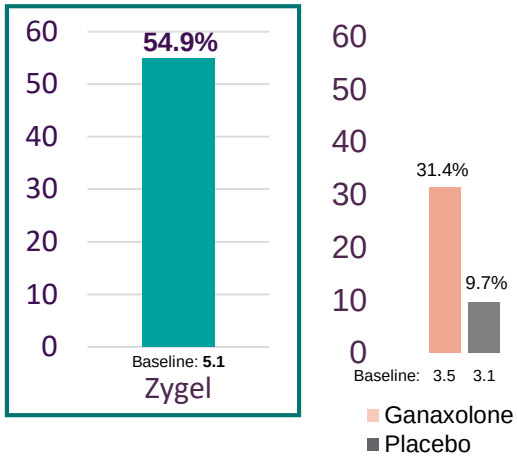
Month Three: ABC-C_{FXS} Mean Score



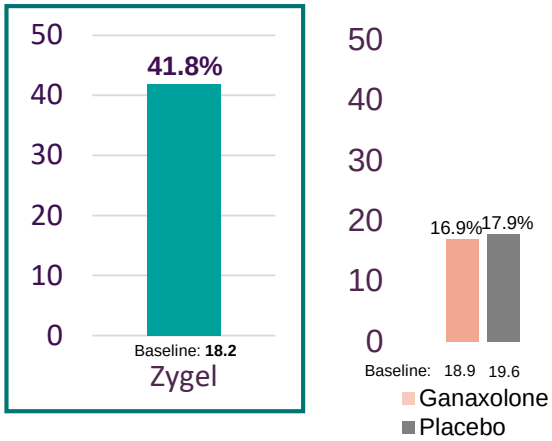
FAB-C ABC-C_{FXS} Subscales

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

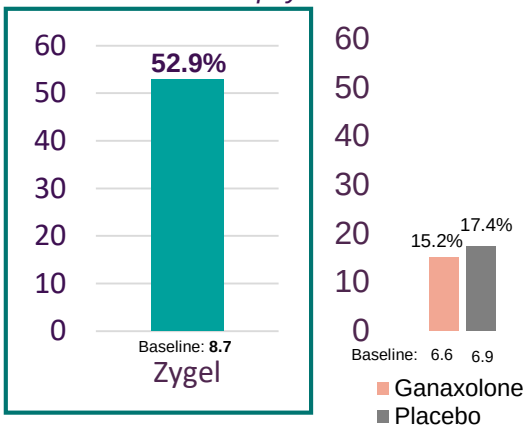
Social Avoidance
Seeks isolation



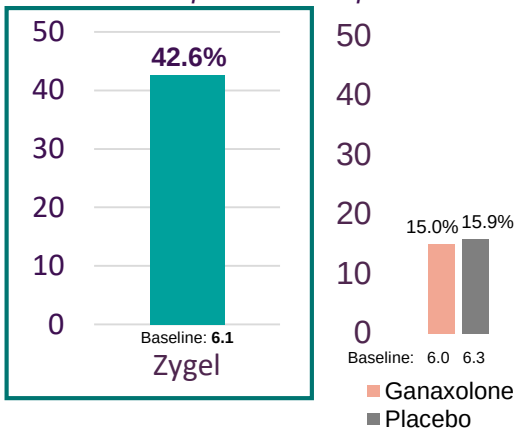
Irritability
Temper tantrums



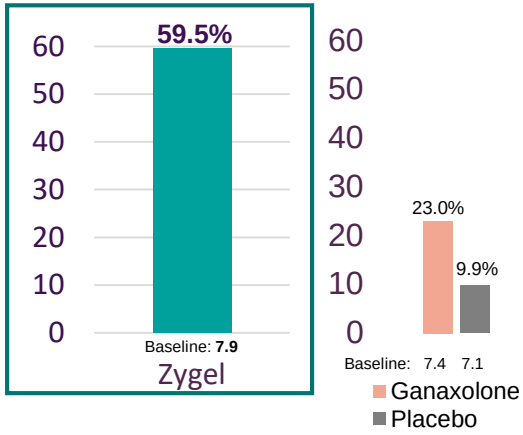
Socially Unresponsive / Lethargic
Does not pay attention



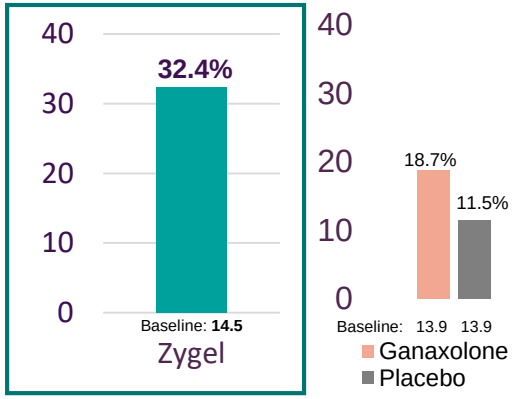
Inappropriate Speech
Repeats words / phrases



Stereotypy
Repetitive movements



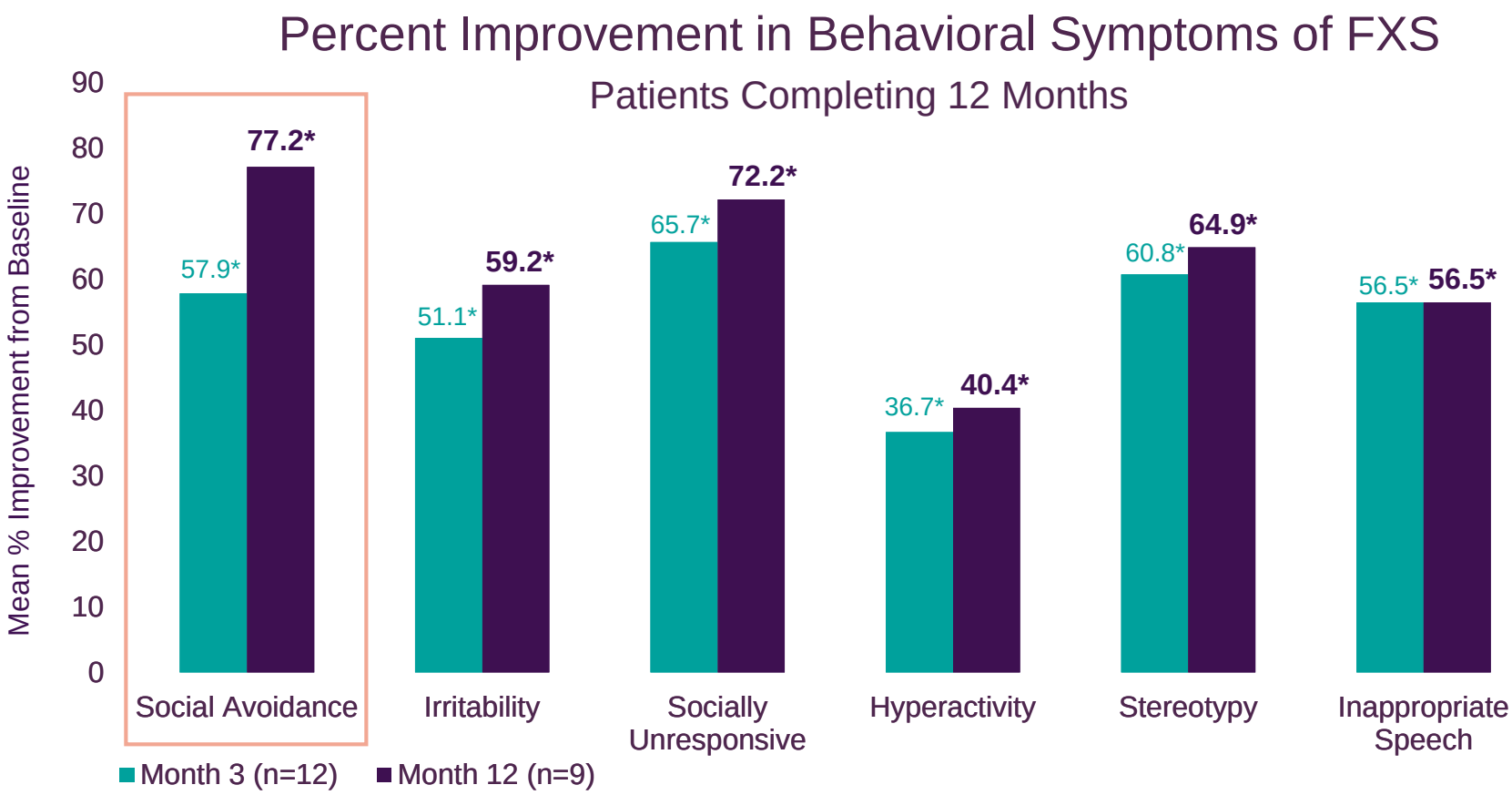
Hyperactivity
Disrupts group activities



* 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 College of Neuropsychopharmacology (ACNP) meeting, December 2018

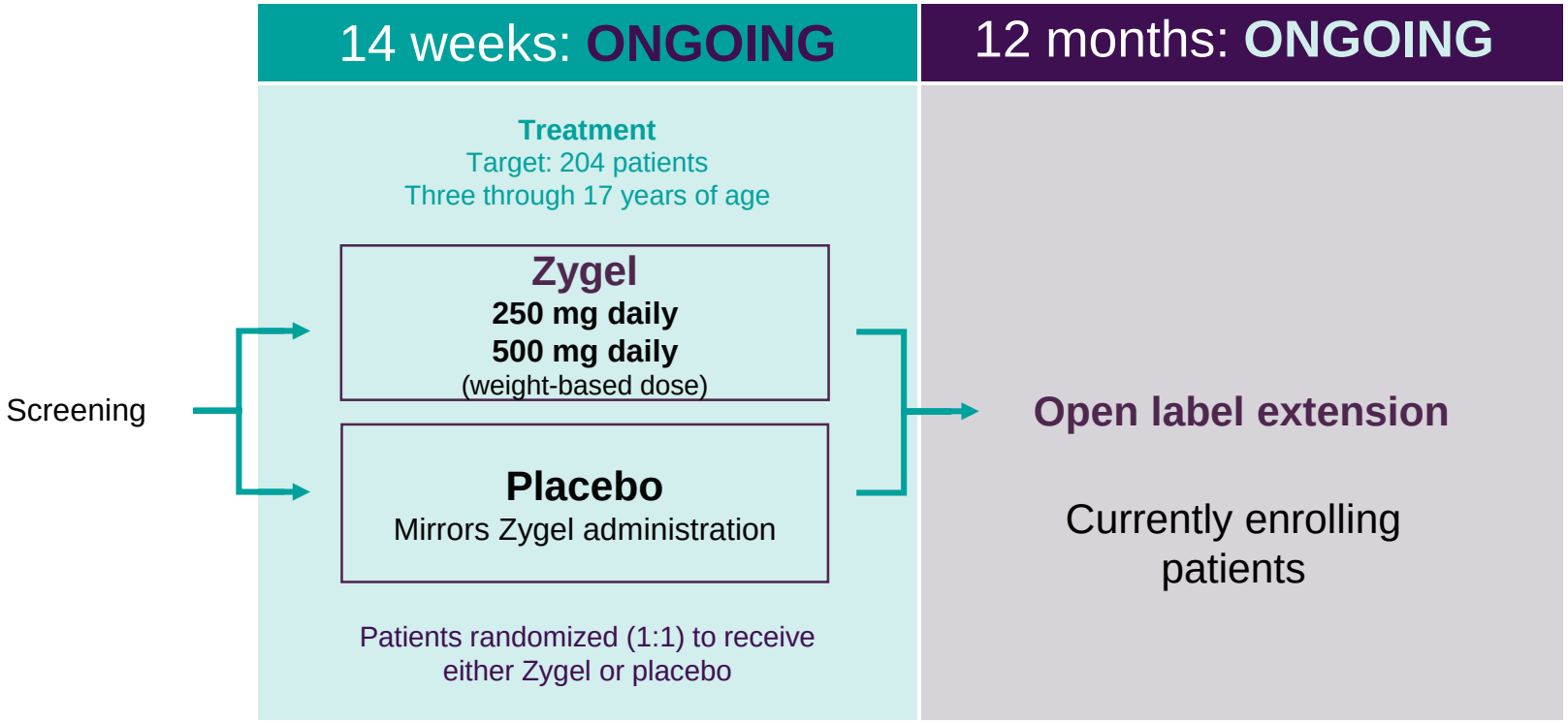
FAB-C Open Label Phase 2

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
  - Two 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

CONNECT-FX

Top Line Results Expected in 2H2019

- 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 fast-track, breakthrough status, and/or priority review

DEE
Developmental and Epileptic Encephalopathies

DEE Overview

- Heterogeneous group of rare / ultra rare epilepsy syndromes
- Severe cognitive impairment and behavioral disturbances
- Affects ~45K U.S. children & adolescents
- Syndromes involve:
  - Impaired development (developmental encephalopathies)
  - Regression of developmental progress (epileptic encephalopathies)
- Often progressive; highly resistant to treatment
- Improved seizure control may positively impact development and quality of life

DEE includes syndromes such as:

Doose Syndrome
Dravet Syndrome
Early Myoclonic Encephalopathy
Juvenile Myoclonic Epilepsy (JME)
Landau-Kleffner Syndrome
Lennox-Gastaut Syndrome (LGS)
Ohtahara Syndrome
West Syndrome / Infantile Spasms

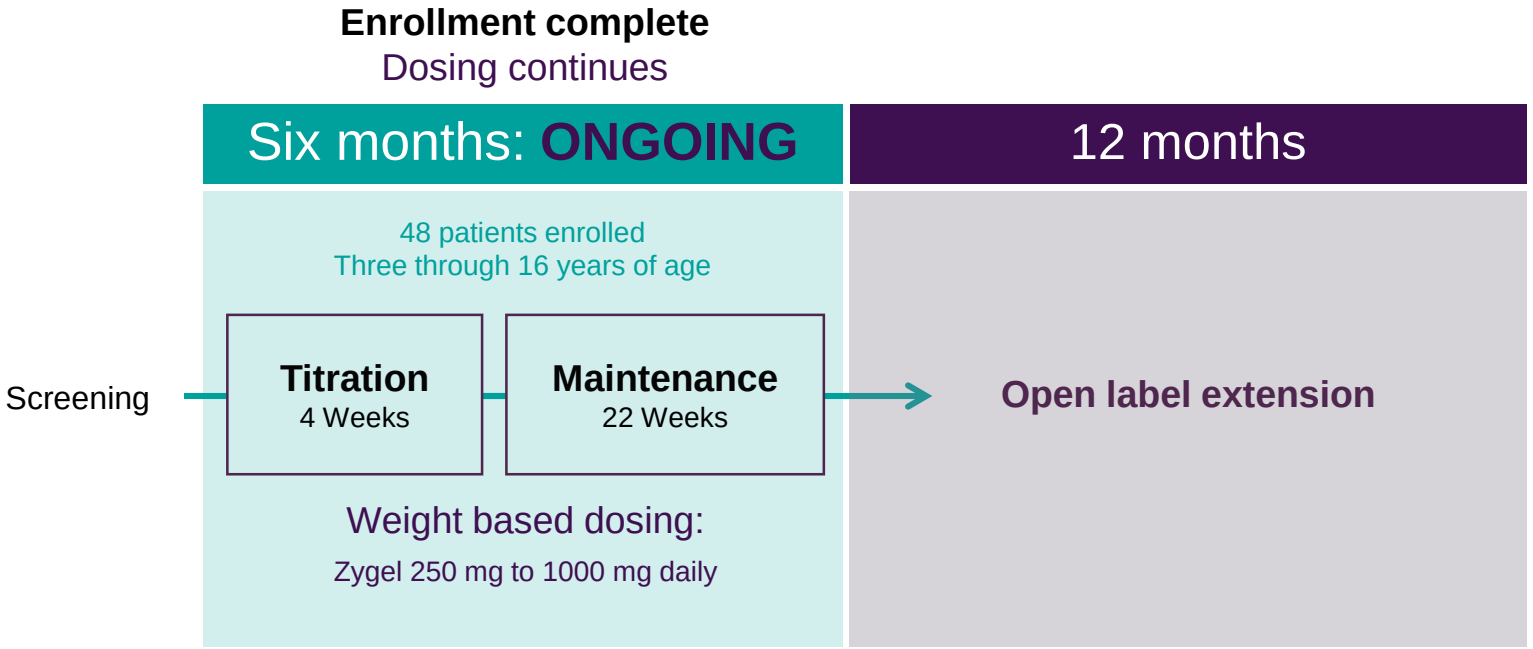
Developing Zygel in DEE

Enrollment Complete in BELIEVE 1 Trial

- Compelling rationale for utility of CBD in DEE
  - Third party clinical data show impact of CBD on seizures and behavioral issues in children
- Patient enrollment in BELIEVE 1 Phase 2 study complete
  - Six month multi-dose study in DEE patients (3 through 17 years)
  - Being conducted in Australia and New Zealand
  - Inclusion criteria require ≥5 generalized motor seizures during baseline
  - ~27% have Dravet or LGS
  - Primary efficacy assessment: change in seizure frequency
- Top line results expected in 3Q2019

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



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

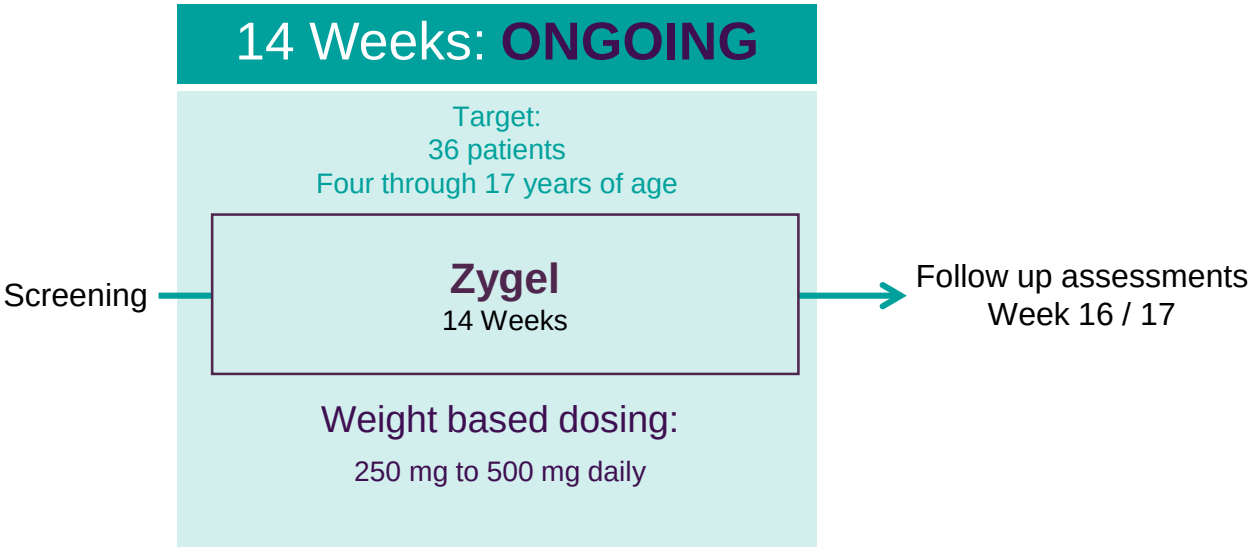
Developing Zygel in ASD

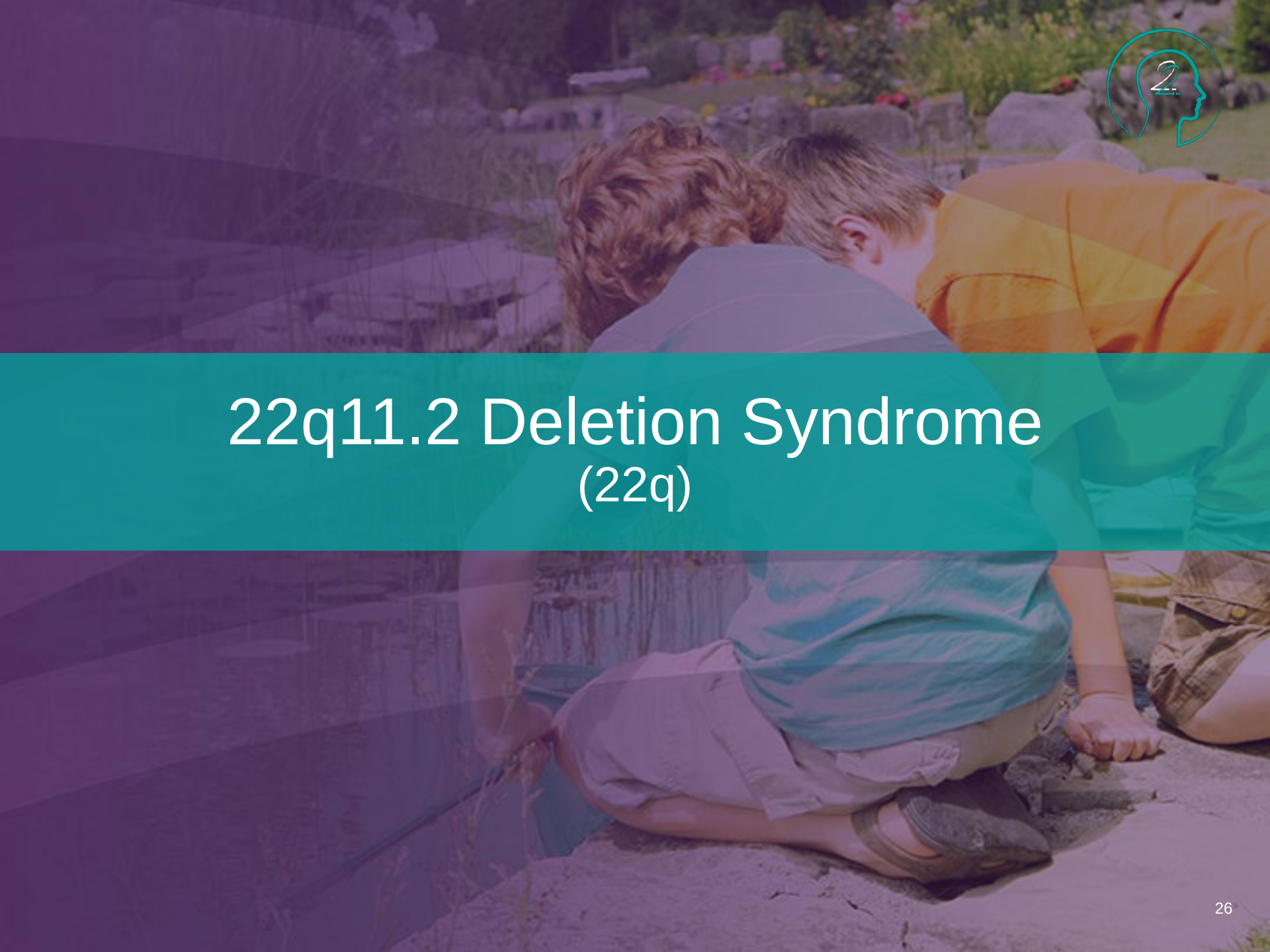
- Newer studies suggest ASD is linked to disruption in the endocannabinoid system
  - Altered anandamide (an endocannabinoid) signaling may contribute to ASD-related social and communication impairments
  - EC system modulates many cellular functions and molecular pathways altered in ASD: imbalanced 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
  - Exogenous CBD may modulate the endocannabinoid system and improve certain autism-related behaviors
- Phase 2 study underway in pediatric 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





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

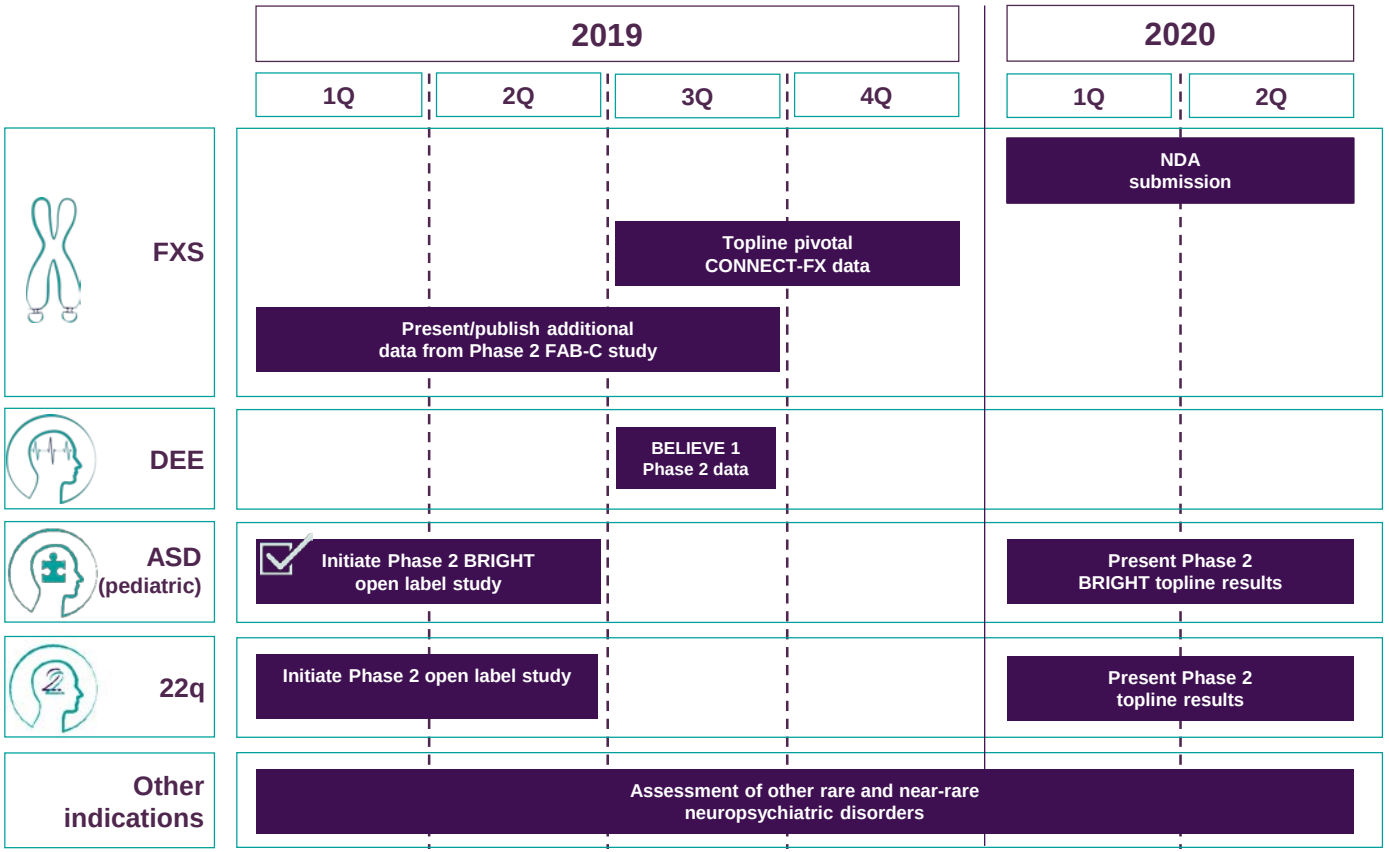
Developing Zygel in 22q

- CBD may treat neuropsychiatric symptoms in 22q due to activity as:
  - Agonist at serotonin 1A receptors
  - Antagonist at GPR55 receptors
  - Modulator of endocannabinoid system
- Anxiety may predict adaptive functioning, and is thought to heighten the risk of later development of psychotic disorders
  - Early control of anxiety may delay the development of psychosis
- Expect to initiate Phase 2 study in 22q in 1H2019
- Top line results expected in 1H2020

Financial Strength

- Clean balance sheet
  - No debt, 21.1M shares outstanding (as of 3/7/19)
- Strong cash and cash equivalent position
  - $59.8 million (as of 12/31/18)
  - Additional $18.1M in net cash proceeds from shares sold under ATM from 1/29/19 through 3/6/19
- Expected to be sufficient to fund operations and capital requirements beyond the planned NDA submission and potential approval in FXS and into the first quarter of 2021

Expected Milestones into 2020



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