Corporate Overview

August 2019

Forward-Looking Statements

THE STATEMENTS IN THIS PRESENTATION MAY INCLUDE FORWARD-LOOKING STATEMENTS WITHIN THE MEANING OF THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995. THESE STATEMENTS, AMONG OTHER THINGS RELATE TO THE FUTURE OPERATIONS, OPPORTUNITIES OR FINANCIAL PERFORMANCE OF ZYNERBA PHARMACEUTICALS, INC. WE MAY, IN SOME CASES, USE TERMS SUCH AS “PREDICTS,” “BELIEVES,” “POTENTIAL,” “PROPOSED,” “CONTINUE,” “ESTIMATES,” “ANTICIPATES,” “EXPECTS,” “PLANS,” “INTENDS,” “MAY,” “COULD,” “MIGHT,” “WILL,” “SHOULD” OR OTHER WORDS THAT CONVEY UNCERTAINTY OF FUTURE EVENTS OR OUTCOMES TO IDENTIFY THESE FORWARD-LOOKING STATEMENTS. SUCH STATEMENTS ARE SUBJECT TO NUMEROUS IMPORTANT FACTORS, RISKS AND UNCERTAINTIES THAT MAY CAUSE ACTUAL EVENTS OR RESULTS TO DIFFER MATERIALLY FROM THE COMPANY’S CURRENT EXPECTATIONS, INCLUDING THE FOLLOWING: THE COMPANY’S CASH AND CASH EQUIVALENTS MAY NOT BE SUFFICIENT TO SUPPORT ITS OPERATING PLAN FOR AS LONG AS ANTICIPATED; THE RESULTS, COST AND TIMING OF THE COMPANY’S CLINICAL DEVELOPMENT PROGRAMS, INCLUDING ANY DELAYS TO SUCH CLINICAL TRIALS RELATING TO ENROLLMENT OR SITE INITIATION; CLINICAL RESULTS FOR THE COMPANY’S PRODUCT CANDIDATES MAY NOT BE REPLICATED OR CONTINUE TO OCCUR IN ADDITIONAL TRIALS AND MAY NOT OTHERWISE SUPPORT FURTHER DEVELOPMENT IN A SPECIFIED INDICATION OR AT ALL; ACTIONS OR ADVICE OF THE U.S. FOOD AND DRUG ADMINISTRATION AND FOREIGN REGULATORY AGENCIES MAY AFFECT THE DESIGN, INITIATION, TIMING, CONTINUATION AND/OR PROGRESS OF CLINICAL TRIALS OR RESULT IN THE NEED FOR ADDITIONAL CLINICAL TRIALS; THE COMPANY’S ABILITY TO OBTAIN AND MAINTAIN REGULATORY APPROVAL FOR ITS PRODUCT CANDIDATES, AND THE LABELING UNDER ANY SUCH APPROVAL; AND THE COMPANY’S EXPECTATIONS REGARDING ITS ABILITY TO OBTAIN AND ADEQUATELY MAINTAIN SUFFICIENT INTELLECTUAL PROPERTY PROTECTION FOR ITS PRODUCT CANDIDATES. THESE AND OTHER RISKS ARE DESCRIBED IN OUR FILINGS WITH THE SECURITIES AND EXCHANGE COMMISSION, AVAILABLE AT WWW.SEC.GOV. ANY FORWARD-LOOKING STATEMENTS THAT THE COMPANY MAKES IN THIS PRESENTATION SPEAK ONLY AS OF THE DATE OF THIS PRESENTATION. THE COMPANY ASSUMES NO OBLIGATION TO UPDATE FORWARD-LOOKING STATEMENTS WHETHER AS A RESULT OF NEW INFORMATION, FUTURE EVENTS OR OTHERWISE, AFTER THE DATE OF THIS PRESENTATION.

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™
  - Four clinical shots on goal: FXS, DEE, ASD, 22q
- 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	2019/2020 Milestones
Fragile X Syndrome (FXS)*					
	CONNECT-FX				Top line pivotal CONNECT-FX data: 1H2020 File FXS NDA: 2H2020
	FAB-C Open Label Extension				Additional long term FAB-C data
Developmental and Epileptic Encephalopathies (DEE)					
	BELIEVE 1				Top line BELIEVE 1 data: September 2019
Autism Spectrum Disorder (ASD)					
	BRIGHT				Initiate Phase 2 open label study: 1H2019 ☑ Top line BRIGHT data: 1H2020
22q Deletion Syndrome (22q)					
	INSPIRE				Initiate Phase 2 open label study: 2Q2019 ☑ Top line INSPIRE data: 1H2020
Adult Refractory Focal Epilepsy					
	STAR 2 Open Label Extension				
Other neuropsychiatric conditions					
					Assess other neuropsychiatric conditions: 2019 & 2020

*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

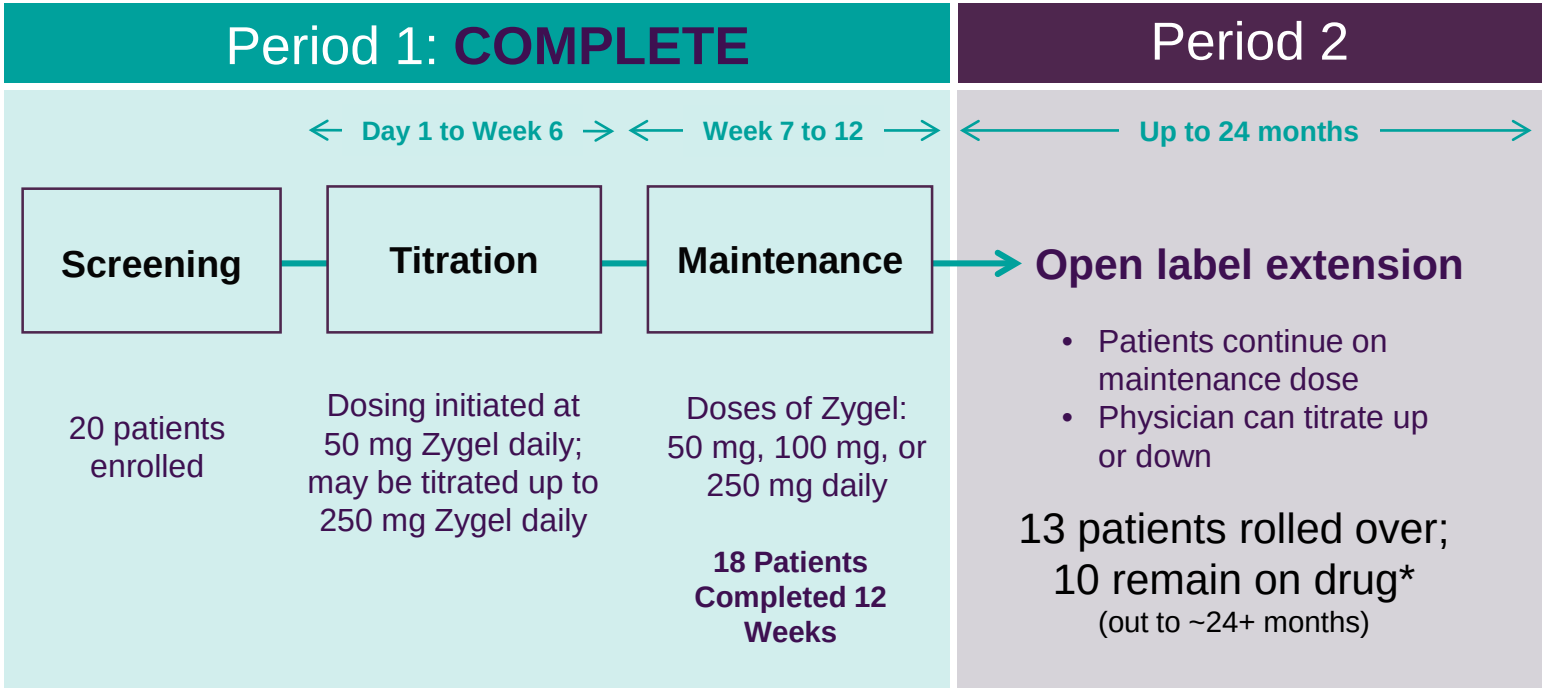
- Rare genetic developmental disability
- Leading known cause of both inherited intellectual disability and autism spectrum disorder
- Symptoms linked to deficiencies in the endocannabinoid (EC) system
  - System of neurotransmitters regulating emotional responses, behavioral reactivity to context, social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

Recent Development Progress in FXS

- Received FDA Fast Track designation for treatment of behavioral symptoms associated with FXS
- Recently issued US patent directed to methods of treating FXS with cannabidiol extends IP protection to 2038
- 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
- Enrollment ongoing in CONNECT-FX: a pivotal trial in pediatric and adolescent patients with FXS
  - Top line results expected in 1H2020

FAB-C Open Label Phase 2 Trial Design

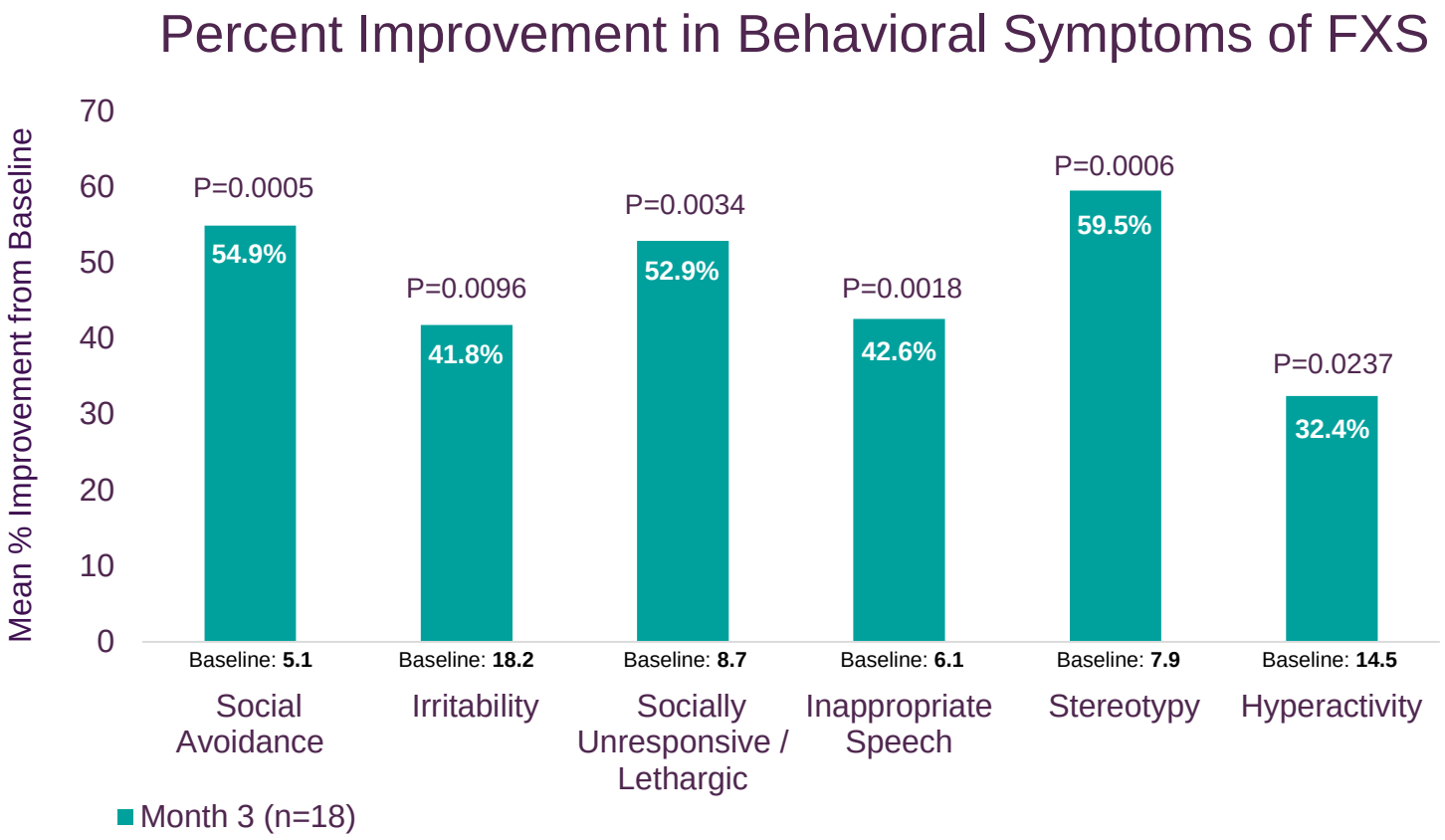
Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD



*As of July 31, 2019

FAB-C Open Label Phase 2

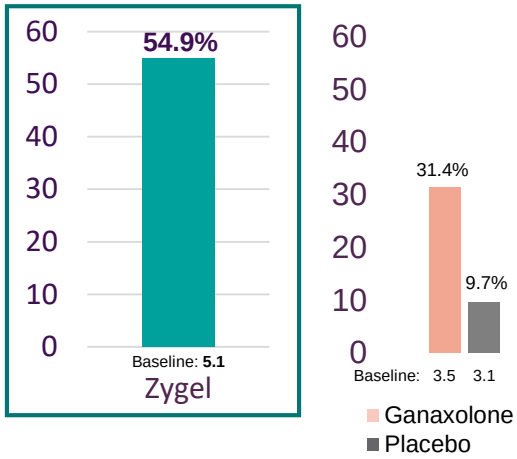
Month Three: ABC-C_{FXS} Mean Score



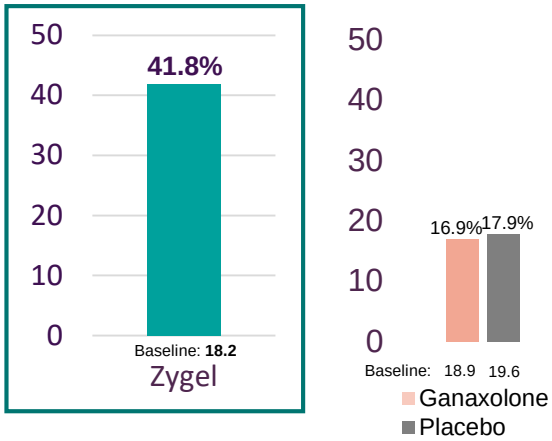
FAB-C ABC-C_{FXS} Subscales

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

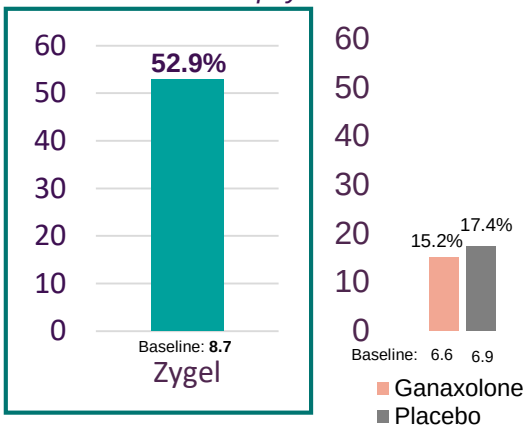
Social Avoidance
Seeks isolation



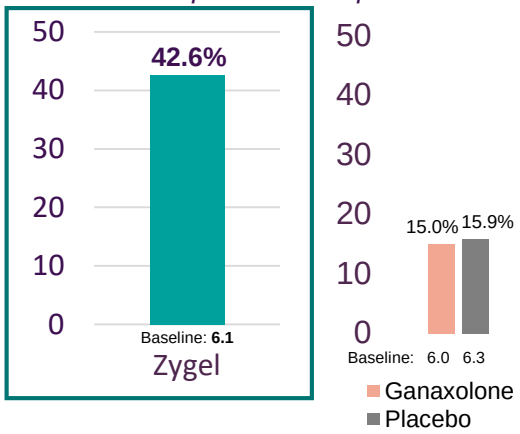
Irritability
Temper tantrums



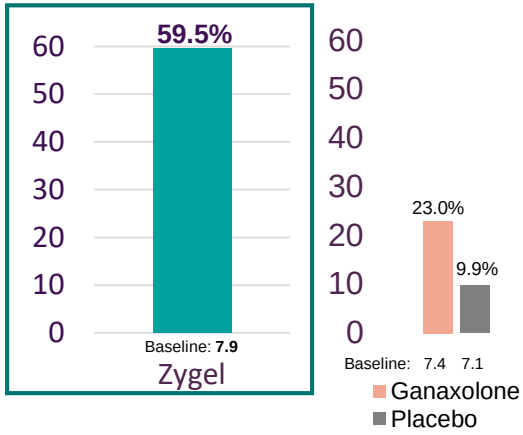
Socially Unresponsive / Lethargic
Does not pay attention



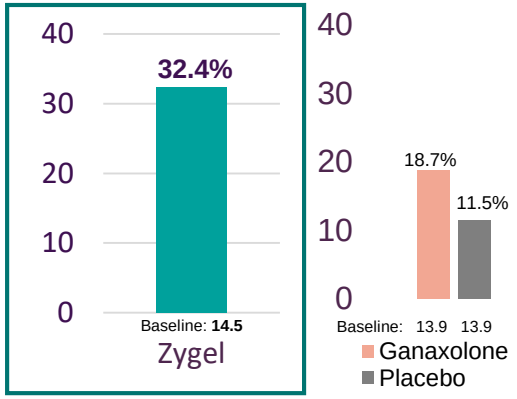
Inappropriate Speech
Repeats words / phrases



Stereotypy
Repetitive movements



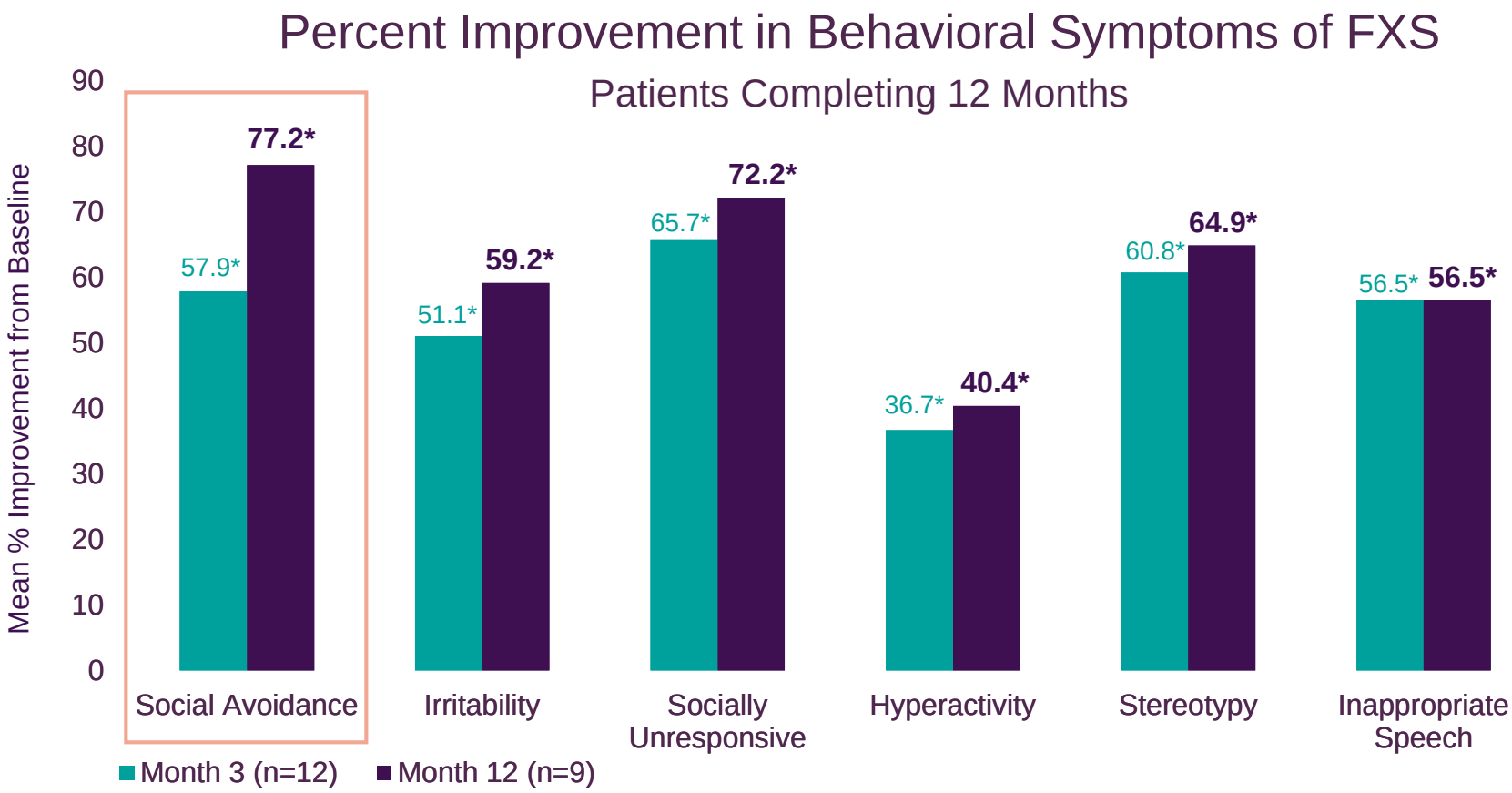
Hyperactivity
Disrupts group activities



* 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

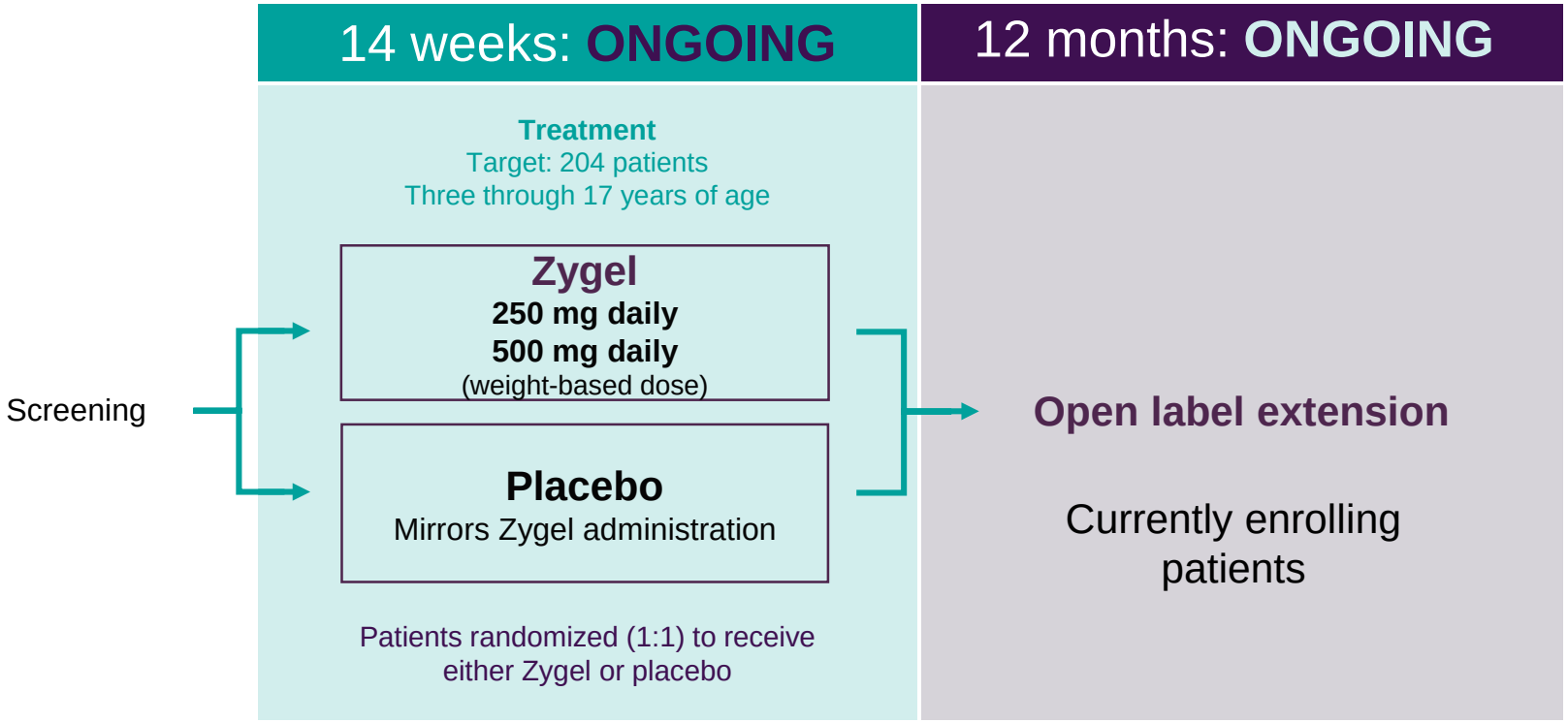
FAB-C Open Label Phase 2

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

CONNECT-FX

Top Line Results Expected in 1H2020

- 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

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

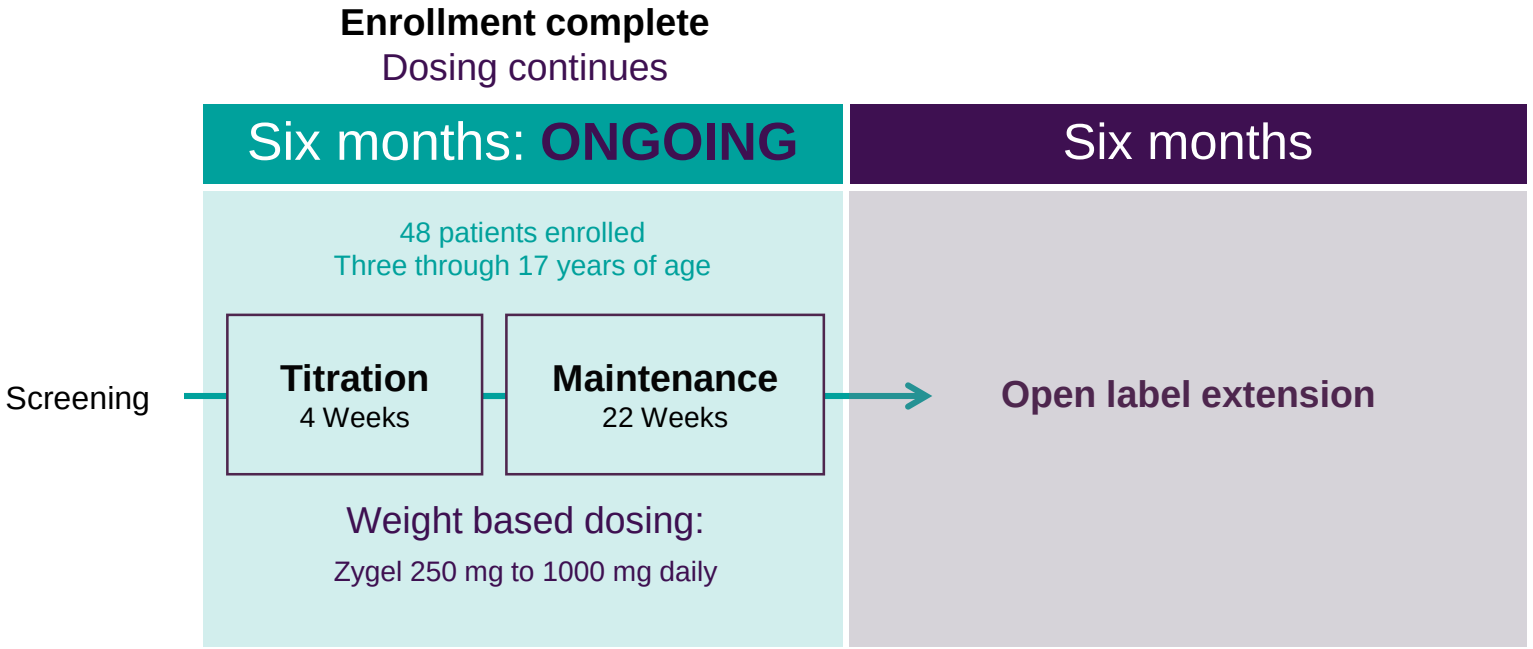
Developing Zygel in DEE

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 September 2019

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

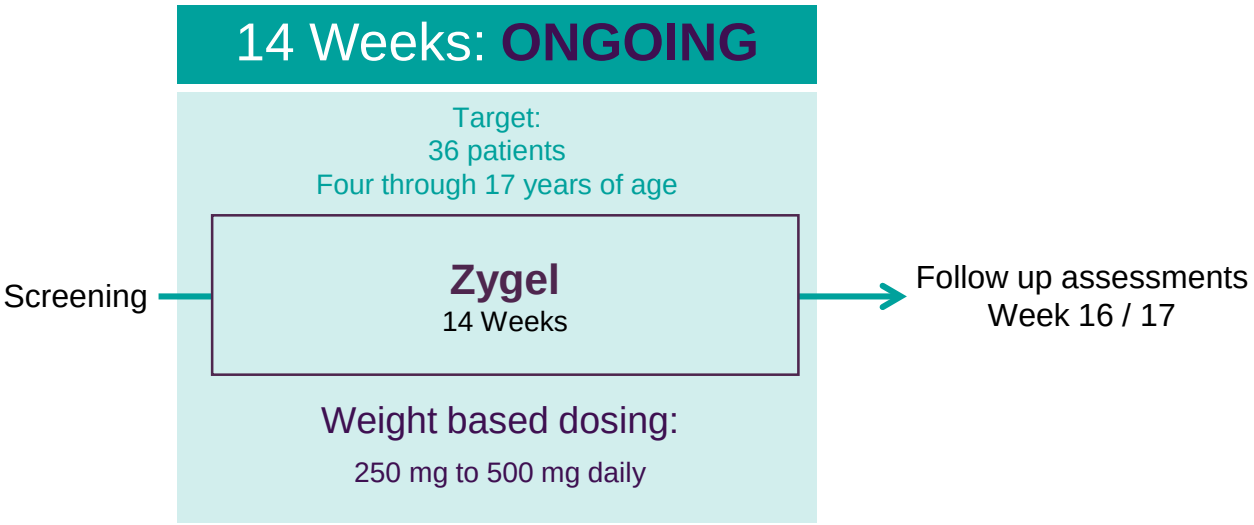
Developing Zygel in ASD

- Newer studies suggest ASD is linked to disruption in the 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

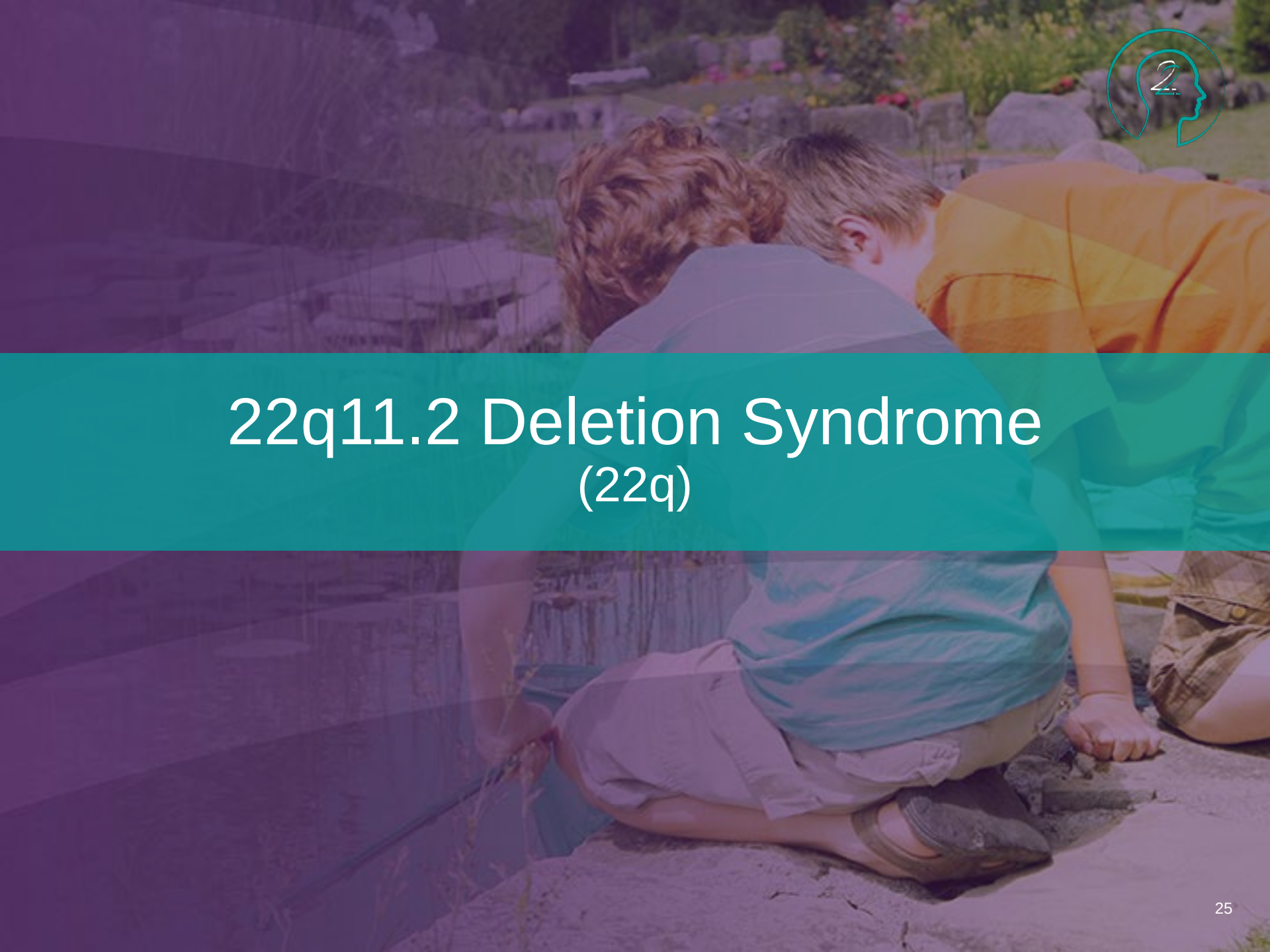
Open-LaBel ToleRabIlity and Efficacy Study of ZYN002 Administered as a Transdermal Gel to CHildren and AdolescenTs with Autism Spectrum Disorder

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

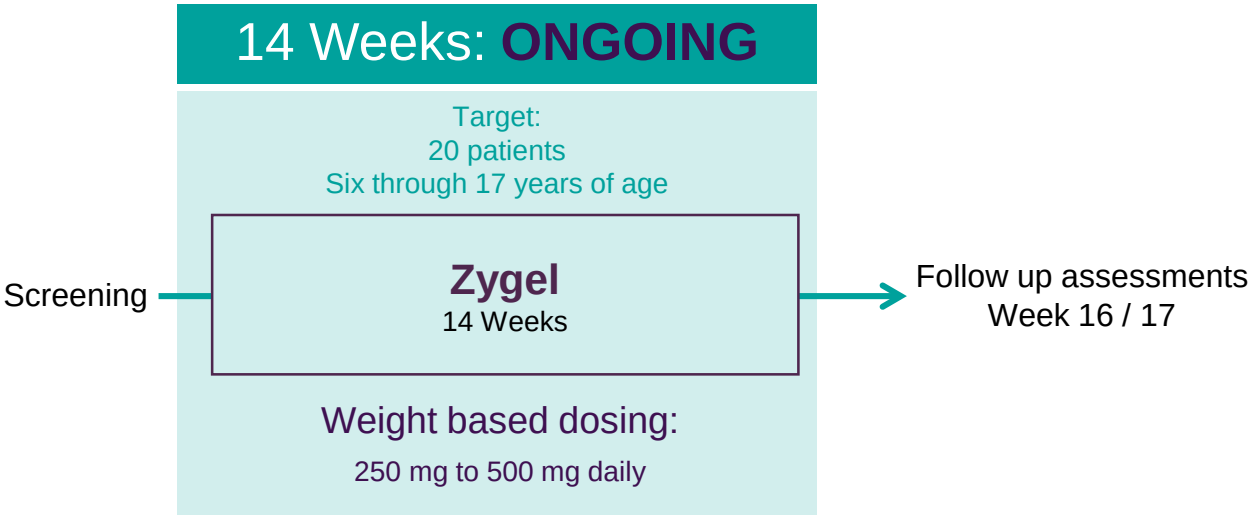
Developing Zygel in 22q

- 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



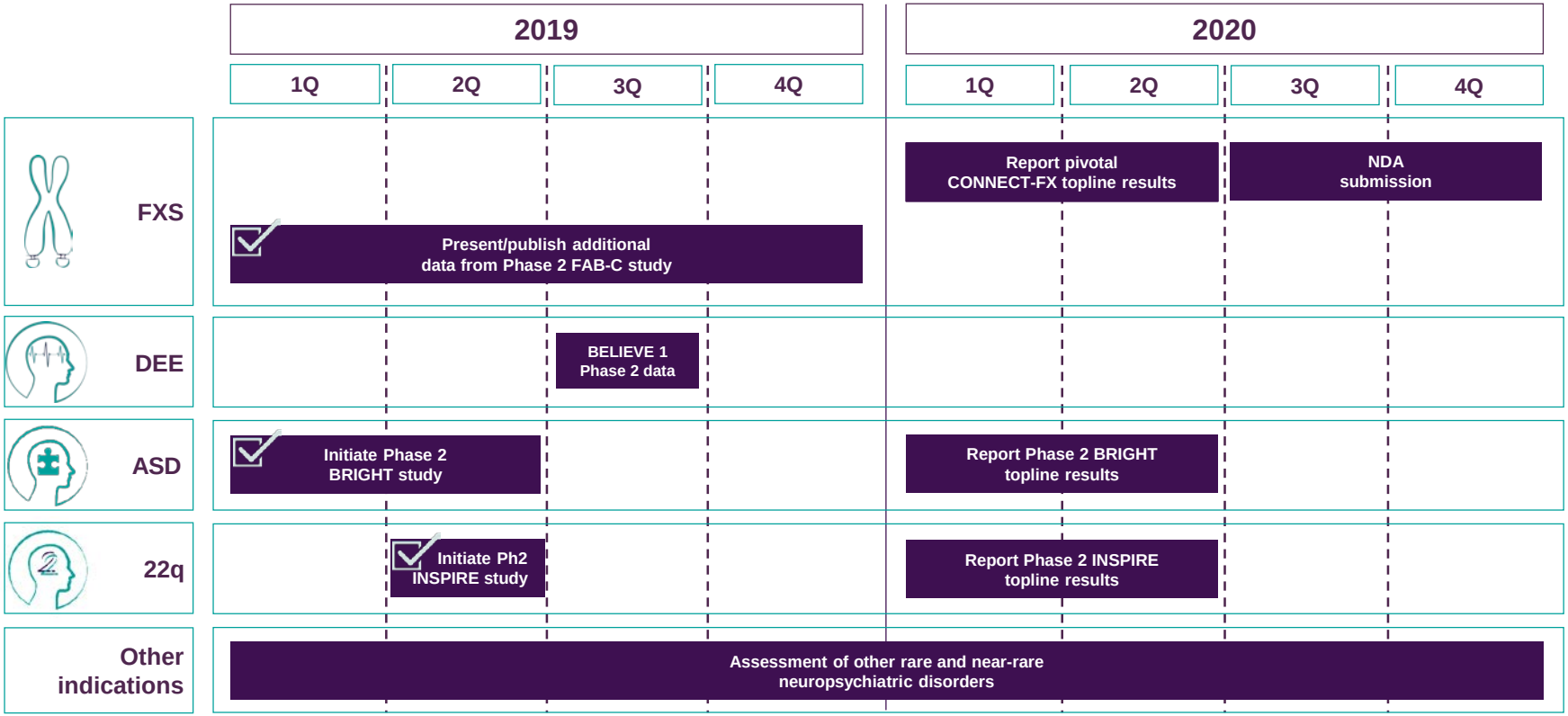
Efficacy assessments (week 14 vs baseline) include:

- 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 August 6, 2019)
- Cash and cash equivalent position of $88.7M as of June 30, 2019
  - Includes net proceeds of $27.0M from 2.1M shares sold and issued at a weighted average selling price of $13.50 per share during the second quarter of 2019 under ATM
- Advance Overseas Finding expected to generate an incremental $7.0 to $9.0 million over the next 18 to 24 months
- 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



Corporate Overview

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