



Cantor Fitzgerald Healthcare Conference

October 1, 2018

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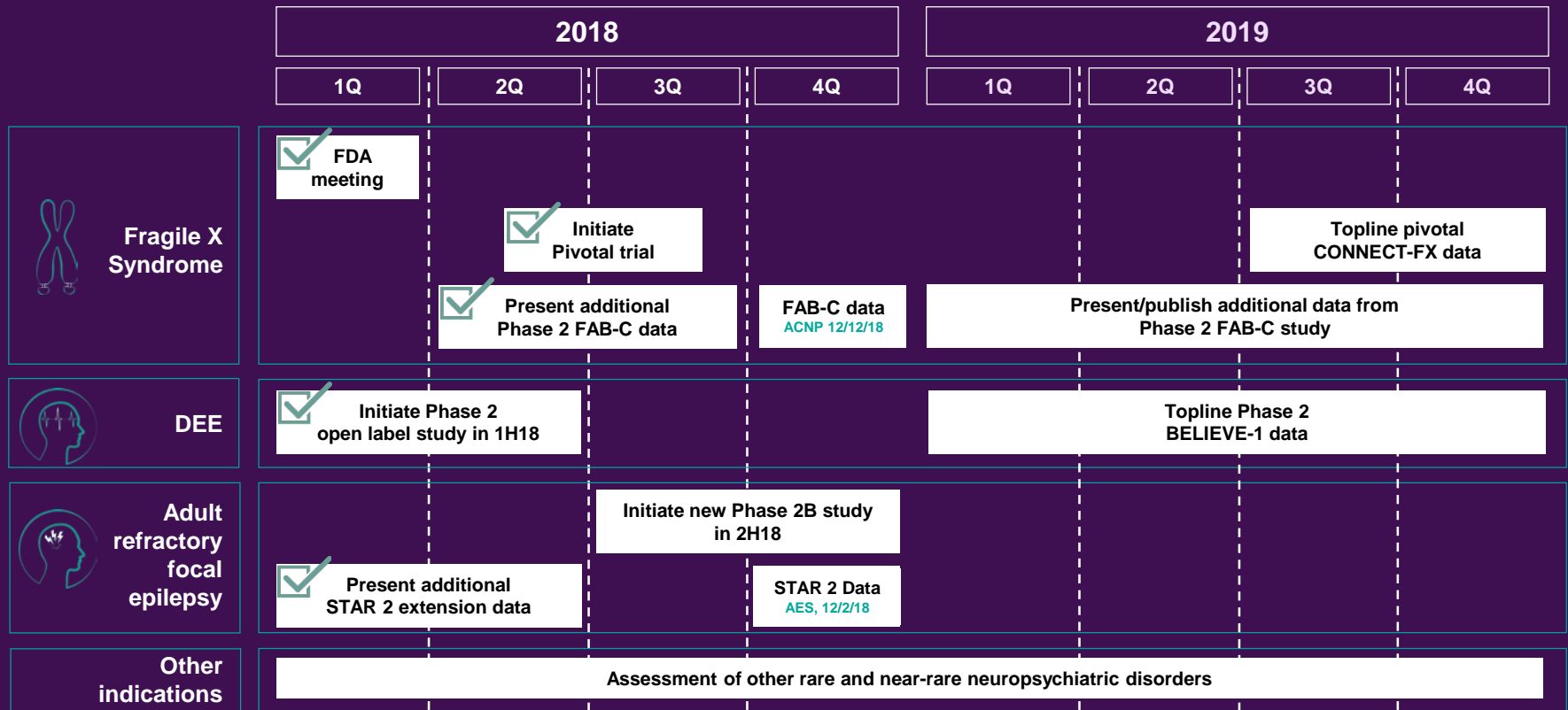
Zynerba Pharmaceuticals (NASDAQ: ZYNE)

A Rare/Near-Rare Neuropsychiatric Company

- Development efforts focused in rare and near rare neuropsych disorders
- Focused on high unmet medical needs; translating into multi-billion dollar market opportunity
- Opportunities for efficient development and commercialization strategy
- Experienced team; proven development and commercialization track record in transdermal delivery, orphan diseases, neurology, psychiatry
- Well capitalized with cash runway into the first half of 2020
- Multiple expected near term milestones



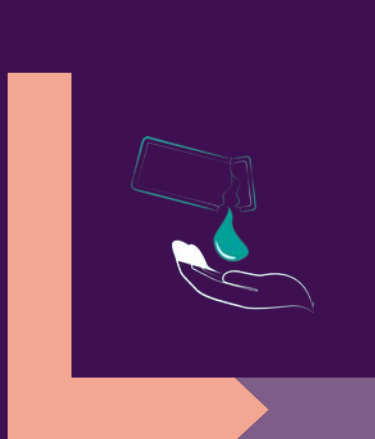
Expected 2018 and 2019 Milestones



ZYN002 Cannabidiol (CBD) Gel

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

Differentiated



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

Unique MOA



Transdermal

Formulation delivers
CBD through the
epidermis and into the
circulatory system

Neuropsych Indications

Potential utility in rare /
near-rare neuropsychiatric
conditions
Orphan Drug designation in
Fragile X Syndrome





Fragile X Syndrome

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.





Fragile X Clinical Program

Recent ZYN002 Development Progress

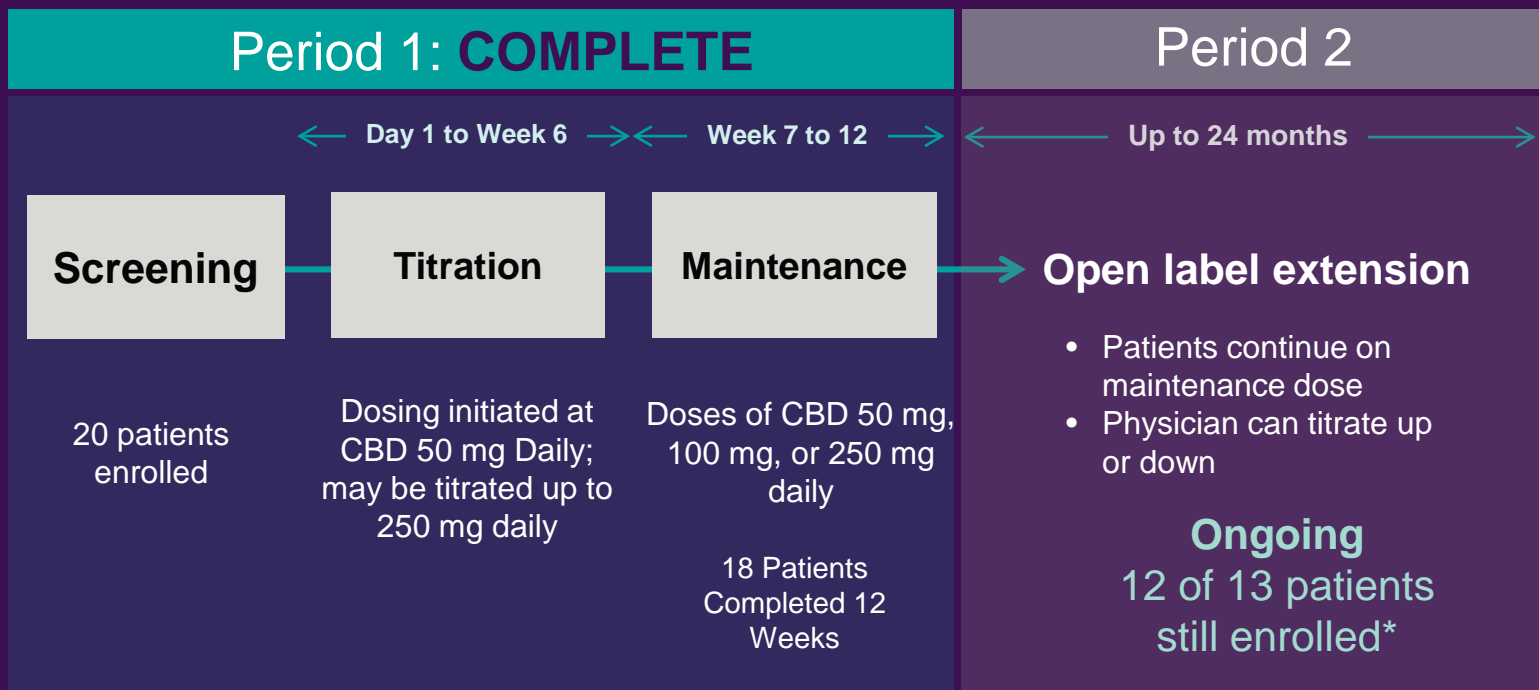
- Presented new FAB-C open label Phase 2 data at the 16th NFXF Conference (July 2018)
 - Achieved primary / numerous secondary efficacy endpoints with statistical significance vs. baseline at 12 weeks
 - 12-week improvements sustained through 38 weeks of treatment
- Initiated CONNECT FX: a pivotal trial underway in pediatric and adolescent FXS patients
 - Initiated July 2018
 - Top line results expected in 2H2019





FAB-C Open Label Phase 2 Trial

Treatment of **F**ragile X Syndrome **A**nxiety and **B**ehavioral **C**hallenges with CBD



*As of September 2018

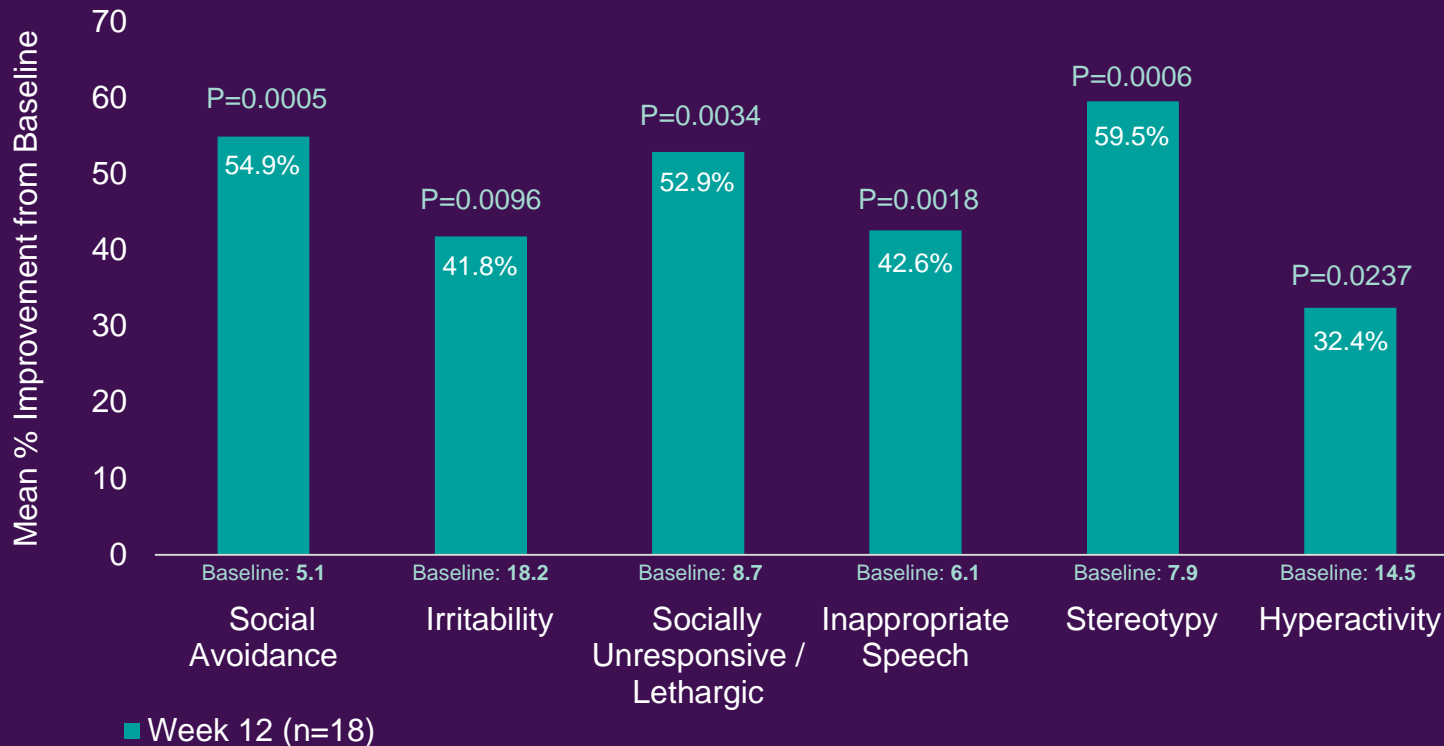




FAB-C Open Label Phase 2

Week 12: ABC-C_{FXS} Mean Score

Percent Improvement in Behavioral Symptoms of FXS





FAB-C ABC-C_{FXS} Subscales

Week 12: Percent Improvement vs. 3rd Party Data*



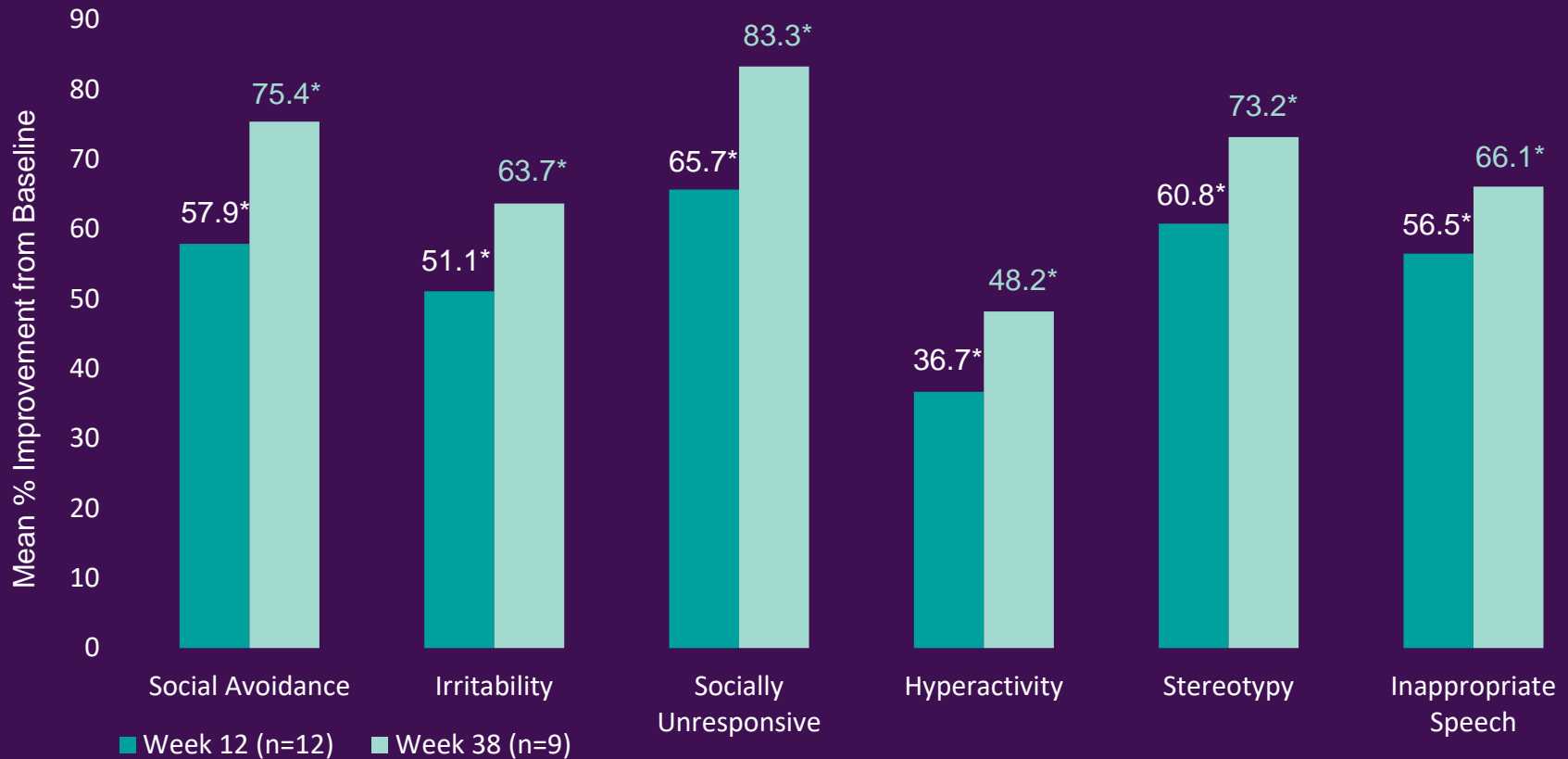
* Ligsay, A., Van Dijck, A., Nguyen, D. V., Lozano, R., Chen, Y., Bickel, E. S., et al. (2017). A randomized double-blind, placebo-controlled trial of ganaxolone in children and adolescents with fragile x syndrome. *Journal of Neurodevelopmental Disorders*, 9:26.



FAB-C Open Label Phase 2

Week 38: ABC-C_{FXS} Mean Score

Percent Improvement in Behavioral Symptoms of FXS



*P ≤ 0.012





FAB-C Open Label Phase 2

Safety Summary Through 38 Weeks

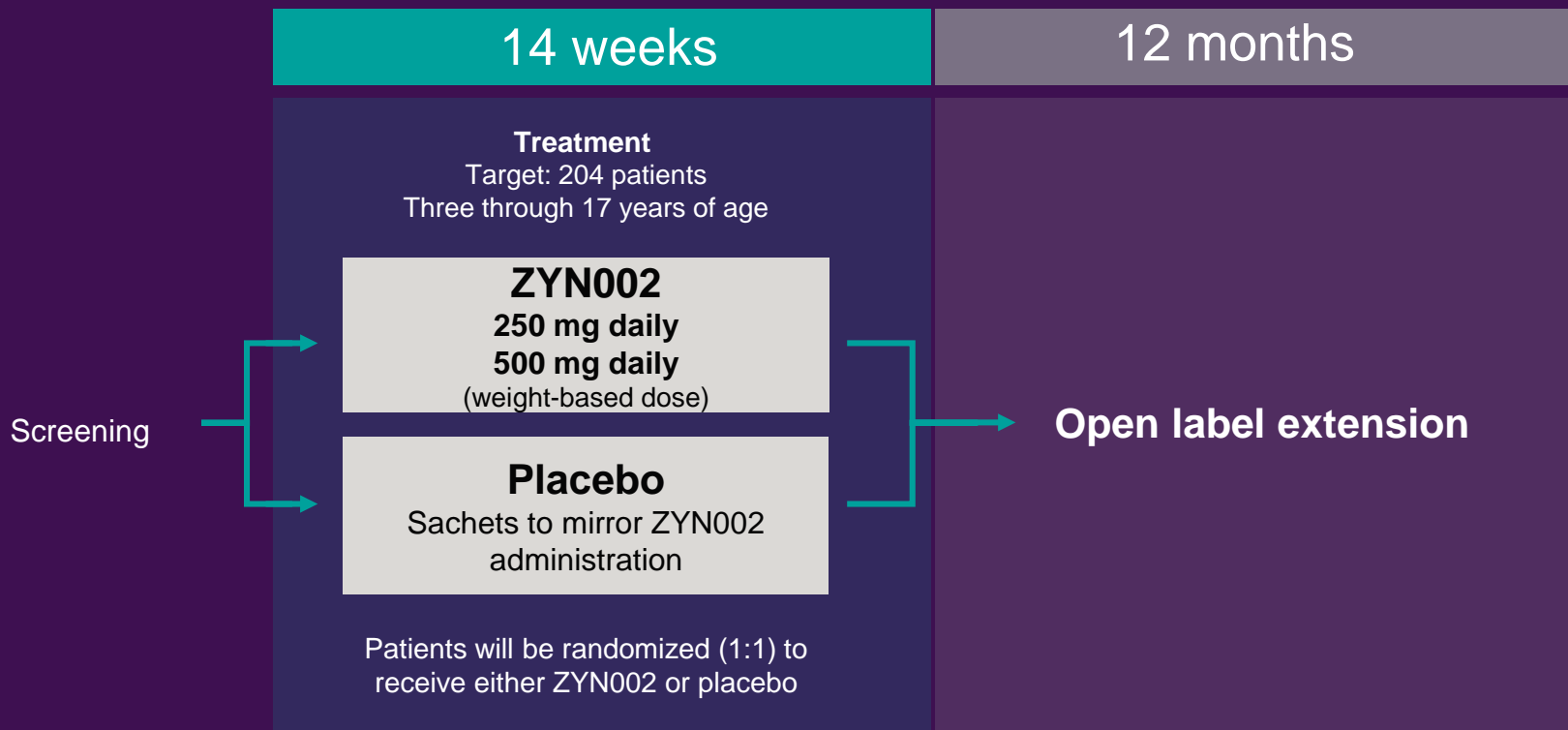
- Well tolerated, consistent with previously reported data; no SAEs
- No clinically meaningful trends in vital signs, ECG, or clinical safety labs including LFTs; no THC detected in plasma
- Two siblings discontinued in Period 1 of study
 - One for worsening of pre-existing eczema (not considered Tx-related)
 - One due to administrative reasons
- 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 unrelated to treatment with CBD
 - Most common: Gastroenteritis (14%), URTI (12%)
 - All considered not related and 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 CBD in DEE

BELIEVE 1 Trial Initiated in April 2018

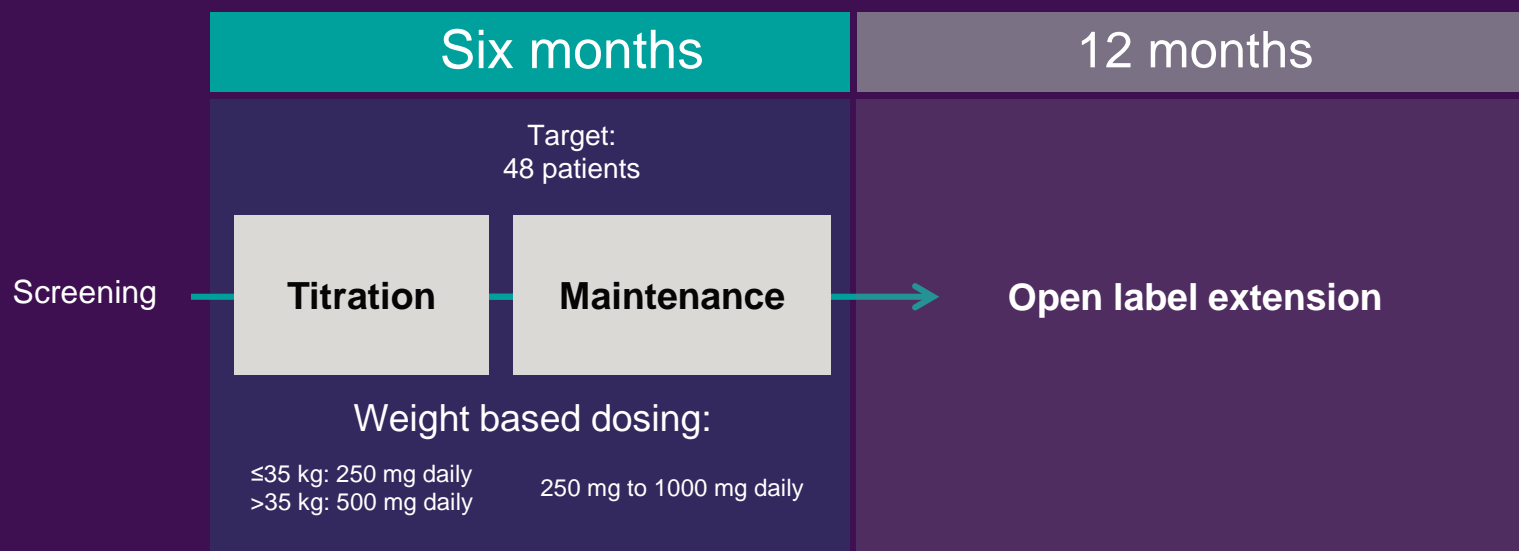
- Compelling rationale for utility of CBD in DEE
 - Third party clinical data show impact of CBD on seizures and behavioral issues in children
- Patient enrollment in BELIEVE 1 Phase 2 study ongoing
 - Six month multi-dose study in DEE patients (3 through 17 years)
 - Being conducted in Australia and New Zealand
 - Approximately half may have Dravet or LGS
 - Primary efficacy assessment: change in seizure frequency
 - Results expected in 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





Adult Refractory Focal Epilepsy



Adult Refractory Focal Epilepsy

Phase 2B Study Initiation Anticipated in 2H2018

- STAR 2 data suggest continued improvement in seizure control in ZYN002 patients through 12 months of open label exposure
- Expect to initiate Phase 2B double blind placebo controlled study in 2H2018

Adult Refractory Focal Epilepsy

- Focal seizures: most common epilepsy in adults
- Substantial U.S. market
 - ~500K refractory patients
- New treatment options with improved quality of life (safety and efficacy) needed

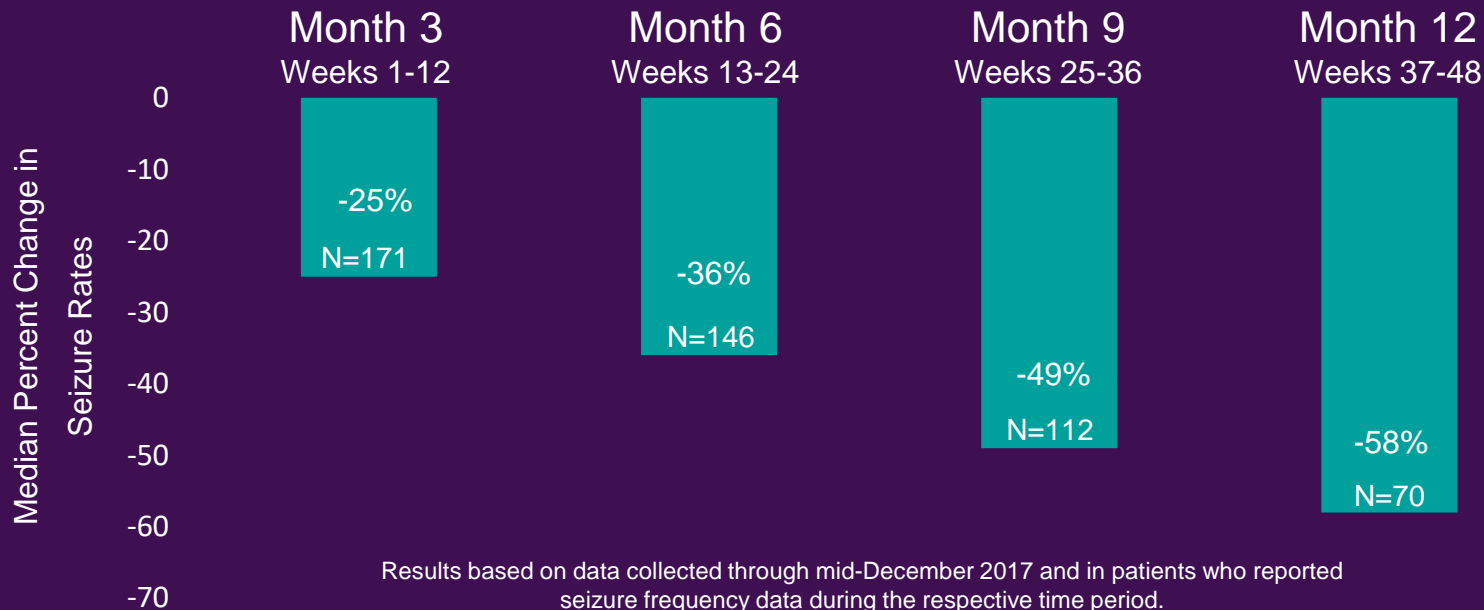


Long Term STAR 2 Efficacy Data



Median Percent Change in Seizure Rates at Months 3, 6, 9, and 12

All ZYN002-treated patients in STAR



Presented at AAN 2018: P4.468

“Transdermal Cannabidiol (CBD) Gel for the Treatment of Focal Epilepsy in Adults”





Proposed Phase 2b Study

Initiation Anticipated in 2H2018

Expected Trial Design*

- Well powered double-blind placebo controlled study
 - Randomization stratified by baseline seizure rate and gender
 - To enroll patients with moderate to severe epilepsy
 - Trial duration: 16 to 24 weeks
- To be conducted in U.S., Australia and New Zealand
- Primary endpoint: reduction from baseline in focal seizures
- 1:1:1 ratio (low dose: high dose: placebo)

*Note: Subject to change due to further regulatory, clinical and other considerations.

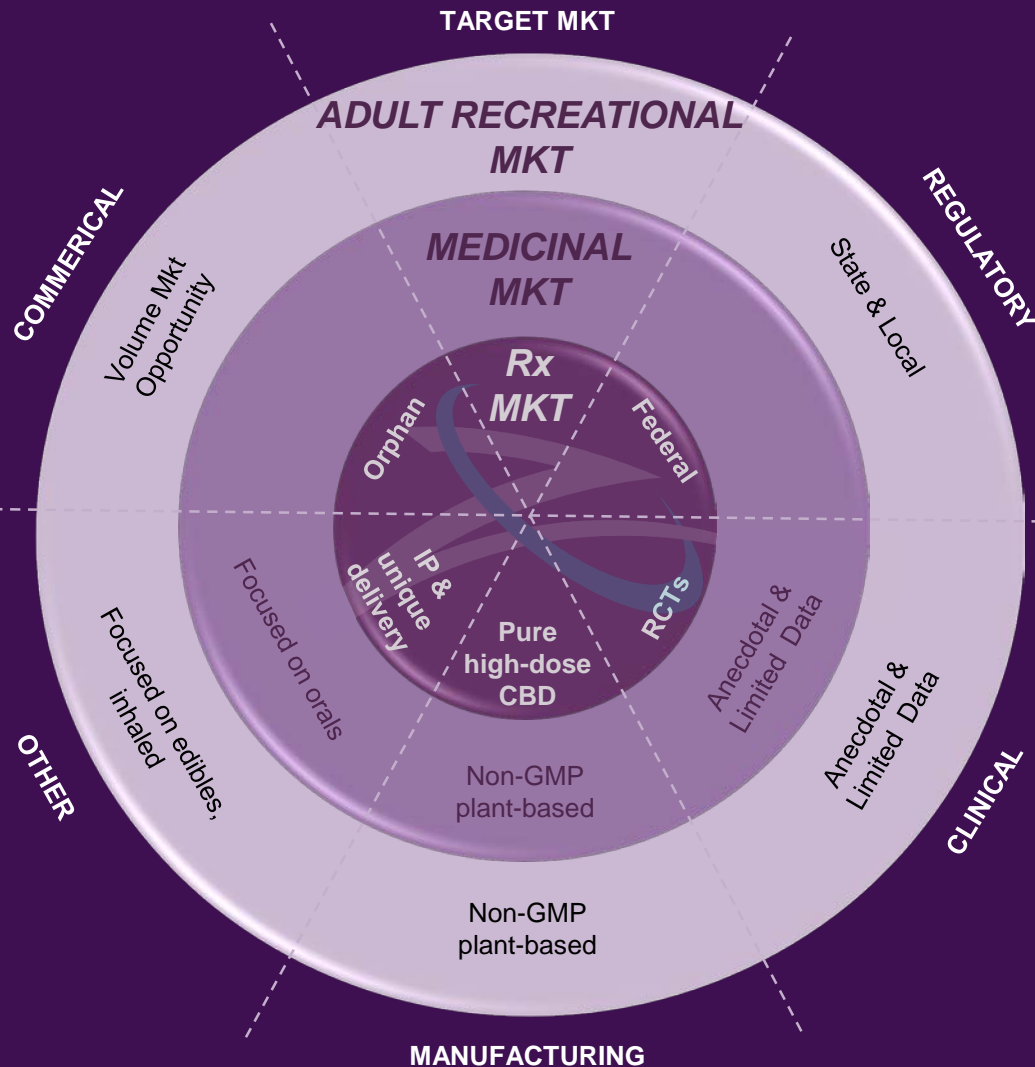


Financial Strength

- Cash and cash equivalent position of \$43.1 million as of June 30, 2018
- Net proceeds of July 2018 follow-on offering were \$30.0 million
- Combined current cash and cash equivalents position is expected to be sufficient to fund operations and capital requirements into 1H2020



Zynerba within the Macro-Cannabis Space



Potential Advantages of ZYN002*

Target Market

- Rare/near-rare conditions
- Specialty markets, pediatrics

Other

- IP: transdermal CBD
- Avoids GI tract & 1st pass metabolism

Regulatory

- Fed compliant (FDA/DEA/others)
- First FXS indicated product

Commercial

- Multi-billion dollar opportunity
- Opportunity for efficient commercial strategy
- Rx insurance coverage
- Lower cost to patient
- Consistent orphan drug pricing across indications
- Potential licensing/partnering opportunity

Clinical

- Randomized, well-controlled clinical trials
- Established efficacy, safety and dosing

Manufacturing

- GMP
- Consistent product
- Scale-able
- Attractive pharma margins

*Pending FDA approval

Commercial Strategy

ZYN002

United States

- On own, assuming FDA approval

Ex-US

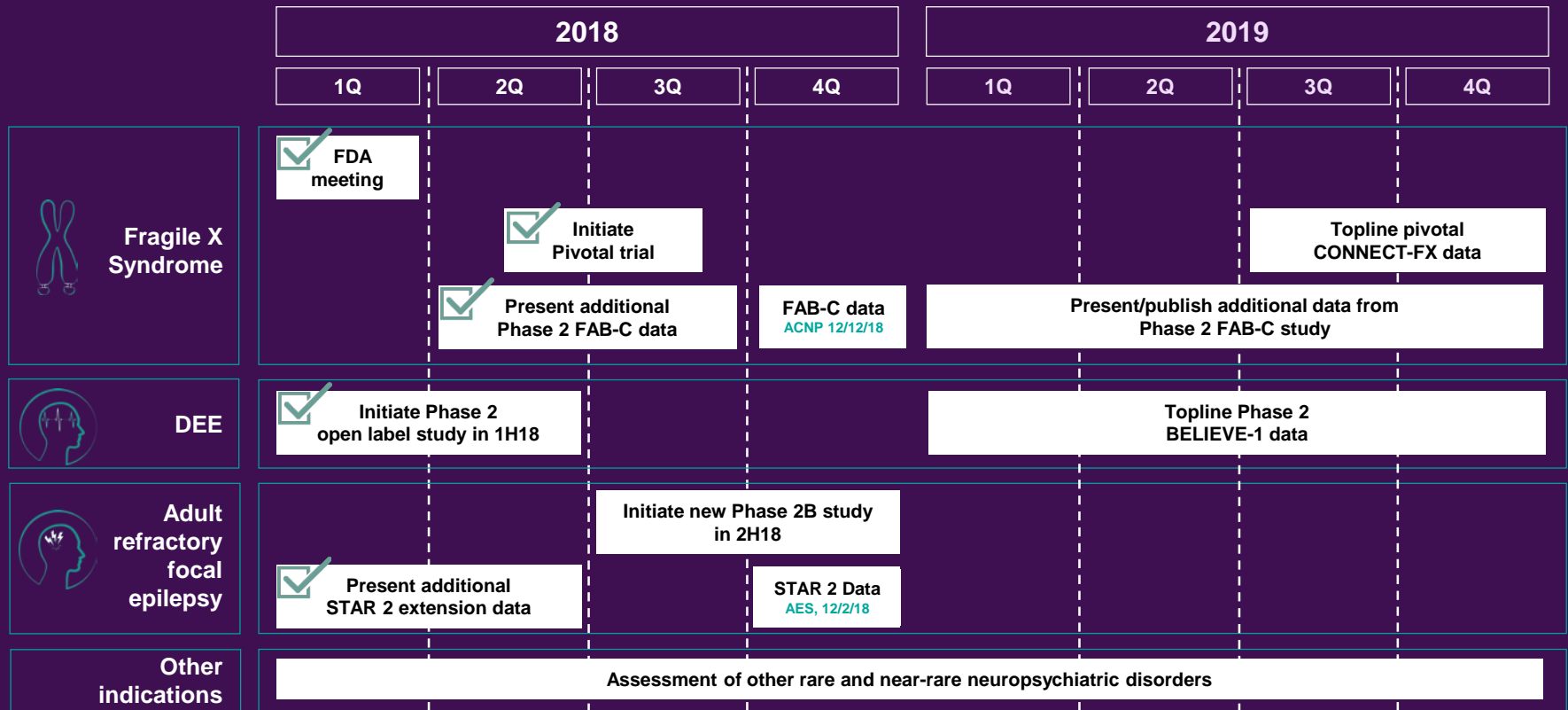
- Options:
 - On own
 - Partnering*

* Partnering opportunities

- Partner ZYN002 (ex-US)
- New indications
- Co-development / out-licensing ZYN001



Expected 2018 and 2019 Milestones





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