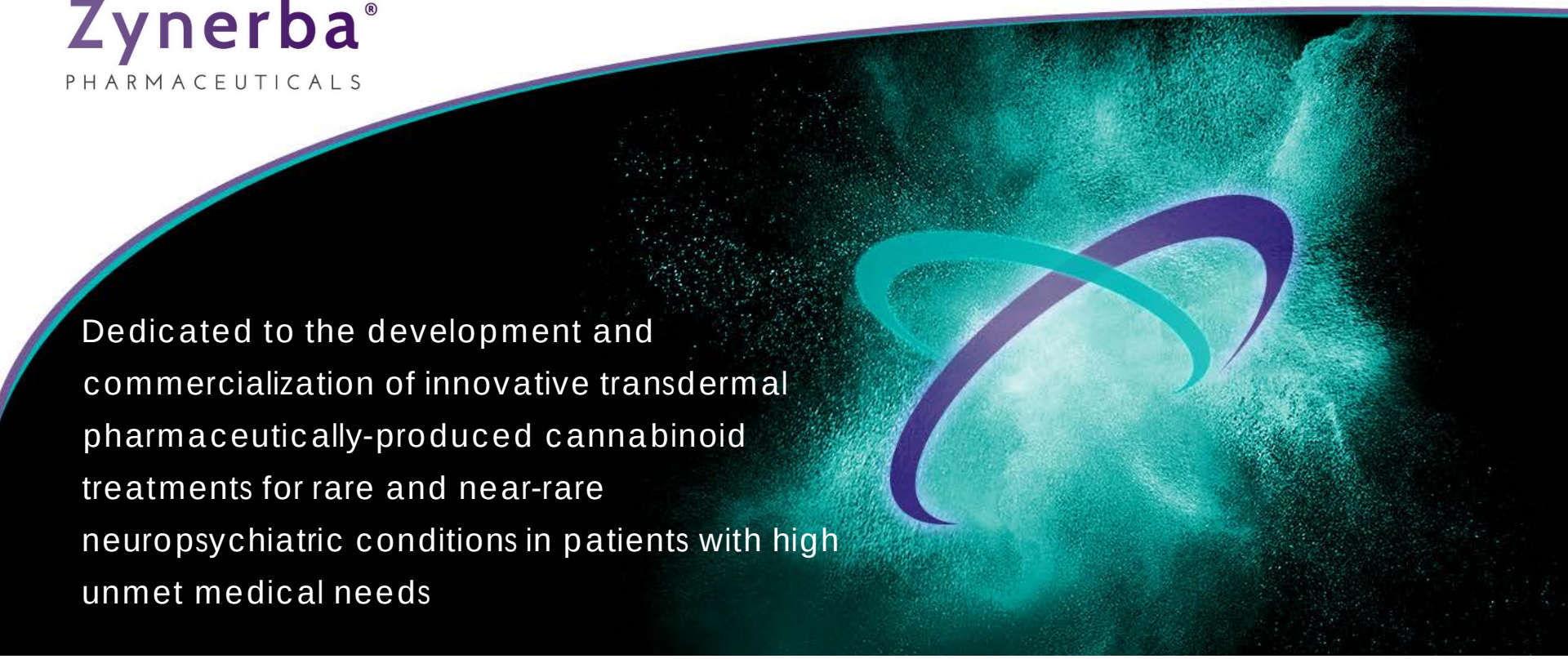
Zynerba®
PHARMACEUTICALS



Dedicated to the development and commercialization of innovative transdermal pharmaceutically-produced cannabinoid treatments for rare and near-rare neuropsychiatric conditions in patients with high unmet medical needs

April 2018

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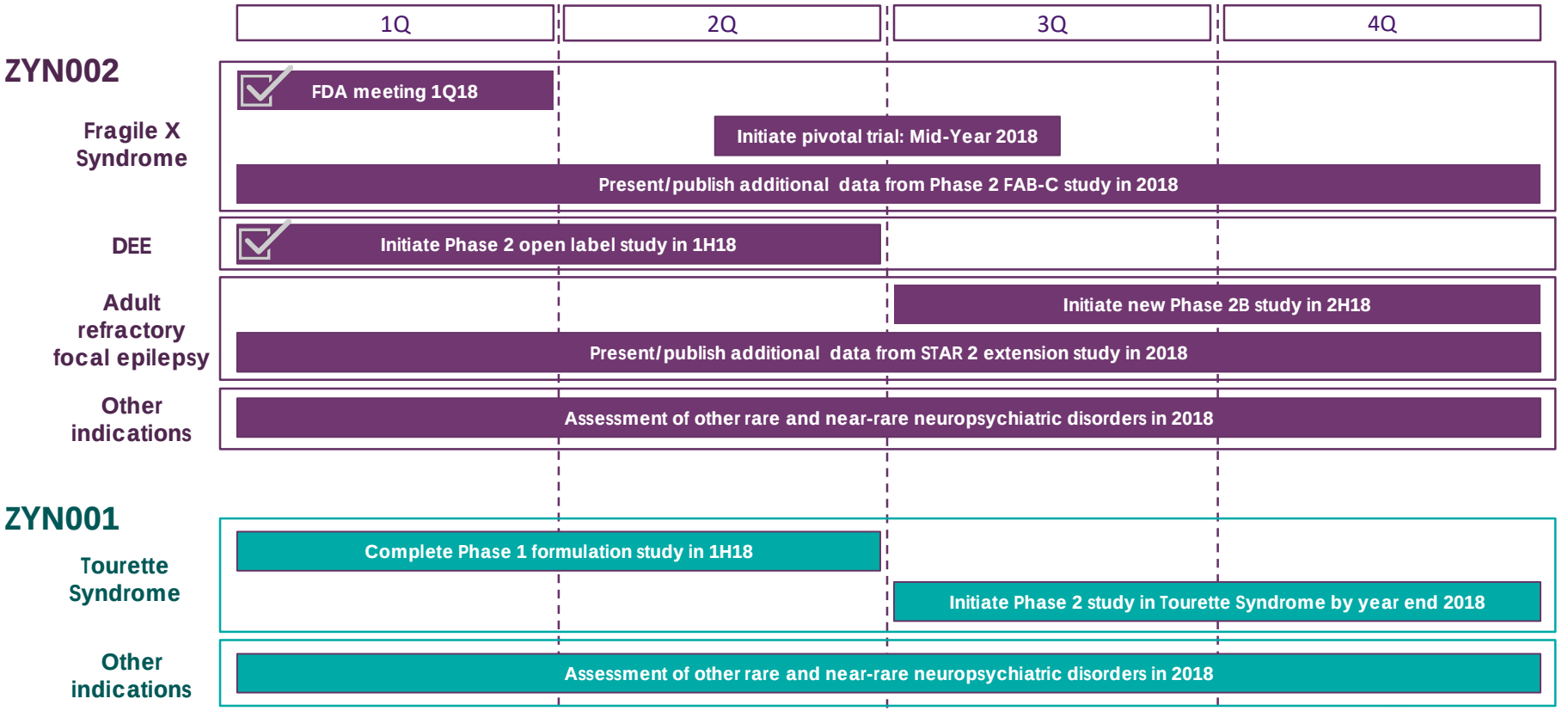
Zynerba Pharmaceuticals
A Rare/Near-Rare Neuropsychiatric Company

- Two patent protected compounds: ZYN002 (CBD gel) and ZYN001 (THC pro-drug patch)
- Focused on high unmet medical needs
  - Fragile X syndrome (FXS): ~71K U.S. patients; no approved products
  - Developmental and epileptic encephalopathies (DEE): ~45K U.S. patients
  - Adult refractory focal epilepsy: ~500K U.S. patients remain uncontrolled on existing AEDs
  - Tourette Syndrome (TS): ~200K U.S. patients have the most severe form of TS
- Opportunities for efficient development and commercialization strategy
  - Orphan drug designation provides opportunity for rapid development/approval
  - Other regulatory designations available; if granted, can accelerate approval of drugs meeting criteria
  - Targeted physician audience = modest commercial investment
  - Potential for consistent Orphan drug pricing across indications (>$25K per patient per year for ZYN002)
- Experienced team with proven development and commercialization track record in transdermal delivery, orphan diseases, neurology, and psychiatry
- Well capitalized with cash runway well into 2019
- Multiple expected near term milestones

Zynerba® PHARMACEUTICALS

Expected 2018 Milestones

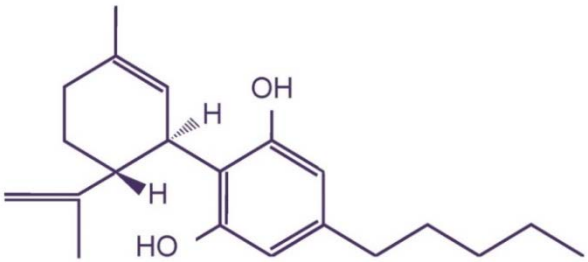


Zynerba® PHARMACEUTICALS

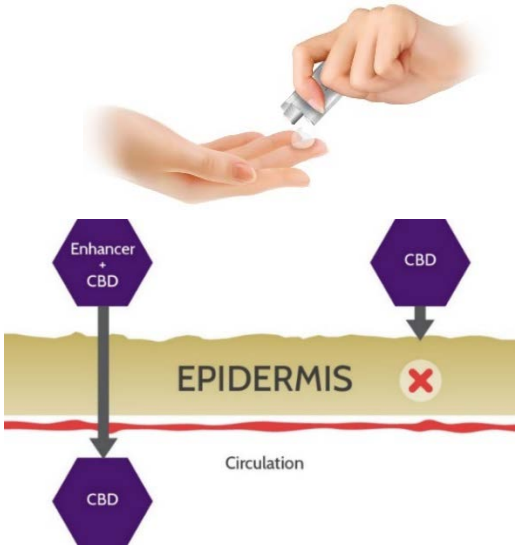
ZYN002
Cannabidiol (CBD) Gel

- **First and only patent-protected permeation-enhanced pharmaceutically-produced cannabidiol (CBD) gel formulated for transdermal delivery**
  - **CBD binds to multiple receptors and may mediate a number of pathways, including the endocannabinoid pathway**
  - **Patented formulation increases the delivery of CBD through the layers of the epidermis and into the circulatory system**

CBD



Transdermal gel delivery



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Fragile X Syndrome (FXS)
Preparing for 2018 Pivotal Study

FXS

- Rare genetic developmental disability in ~71,000 U.S. patients
- Leading known cause of inherited intellectual disability and ASD
- Symptoms including significant behavioral, social, and cognitive deficits
- Symptoms linked to deficiencies in the endocannabinoid system caused by FMR1 mutation

- U.S. Orphan Drug Designation for use of CBD as a treatment of Fragile X (Feb. 2016)
- Positive open label Phase 2 data (Sept. 2017):
  - Achieved primary and numerous secondary endpoints with statistical significance vs. baseline
  - Extremely well tolerated
- Conducted positive meeting with FDA (Jan. 2018)
- Expect to initiate single pivotal trial in pediatric and adolescent FXS patients mid-year 2018 to support NDA
- Results expected in 2019

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Developmental & Epileptic Encephalopathies (DEE)
New Phase 2 Program

DEE

- Category including a number of rare and ultra-rare severe brain disorders that manifest with seizures in children and cause severe cognitive and behavioral impacts
- ~45,000 U.S. children and adolescents with DEE
- Includes Doose, Dravet, Lennox-Gastaut, and West Syndromes, etc.
- Highly resistant to treatment

- Third party clinical data show impact of CBD on seizures and behavioral issues in children
- BELIEVE 1 Phase 2 study underway
  - Six month multi-dose study in ~50 DEE patients (3 to <18 years)
  - Primary efficacy assessment: change in seizure frequency
- Results expected in 2019

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Adult Refractory Focal Epilepsy
Phase 2B Anticipated in 2018

Adult Refractory Focal Seizures

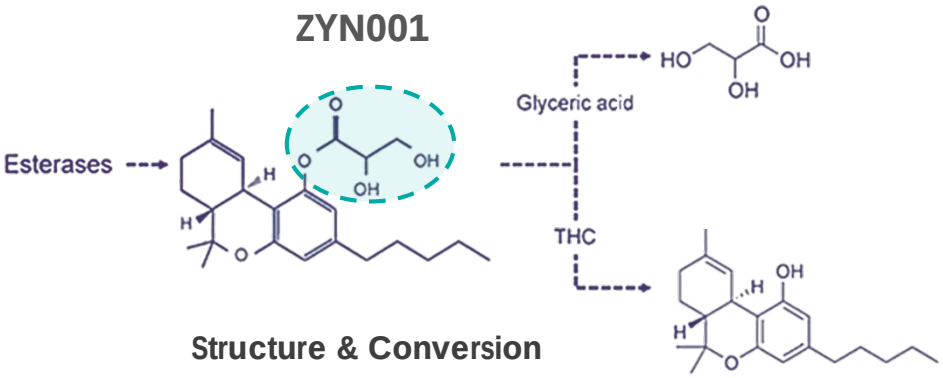
- Focal seizures are the most common epilepsy in adults
- Substantial U.S. market
  - ~500,000 refractory patients
- New treatment options with improved quality of life (safety and efficacy) needed

- STAR 2 data suggest clinically meaningful response with longer term use of ZYN002
  - Consistent improvements in median seizure rate at three, six and nine months of treatment with ZYN002
  - Updated STAR 2 data accepted as Late Breaking poster at 2018 AAN (April 25, 2018)
- Learnings from Phase 2 STAR 1 study and open label STAR 2 extension provide input into Phase 2b trial design
  - Planned modifications include increased baseline seizure frequency, patient count, and trial duration
- Expect to initiate ~300 patient double blind placebo controlled study in 2H2018

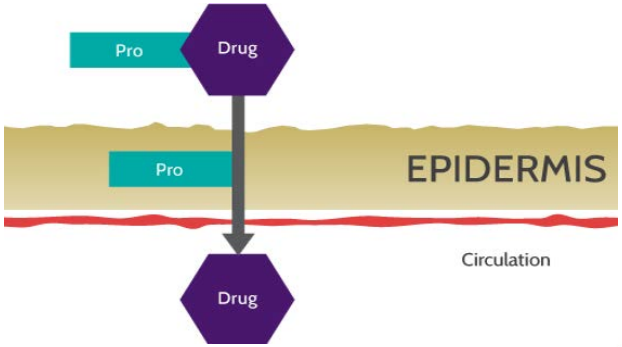
Zynerba® PHARMACEUTICALS

ZYN001
THC Pro-Drug Patch

- **Patent-protected pharmaceutically-produced D-glyceric acid ester-Δ9-tetrahydrocannabinol (THC) in a transdermal patch**
- **ZYN001 is a pro-drug**
  - **A drug administered in an inactive or less active form, designed to enable more effective delivery, and then converted into a different form through a normal metabolic process**
  - **Unlike THC, ZYN001 is able to be efficiently absorbed through the skin via transdermal delivery**
  - **After crossing the stratum corneum, ZYN001 is hydrolyzed to THC and glyceric acid under physiological conditions**
  - **THC binds multiple cannabinoid receptors and may mediate a number of pathways, including the endocannabinoid pathway**



Structure & Conversion



Delivery

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Potential for THC in Tourette Syndrome (TS)

Tourette Syndrome

- Neurodevelopmental disorder characterized by motor / vocal tics
  - Evident in early childhood
  - ~200K U.S. pts have most severe form
  - Up to 1:100 exhibit milder and less complex symptoms
- Central cannabinoid receptor system believed to play role in Tourette Syndrome pathology

- Third party double blind, placebo controlled studies show activity of THC in TS
- Phase 1 formulation work expected to be completed in 1H2018
- Phase 2 study in Tourette Syndrome expected to initiate in late 2H2018

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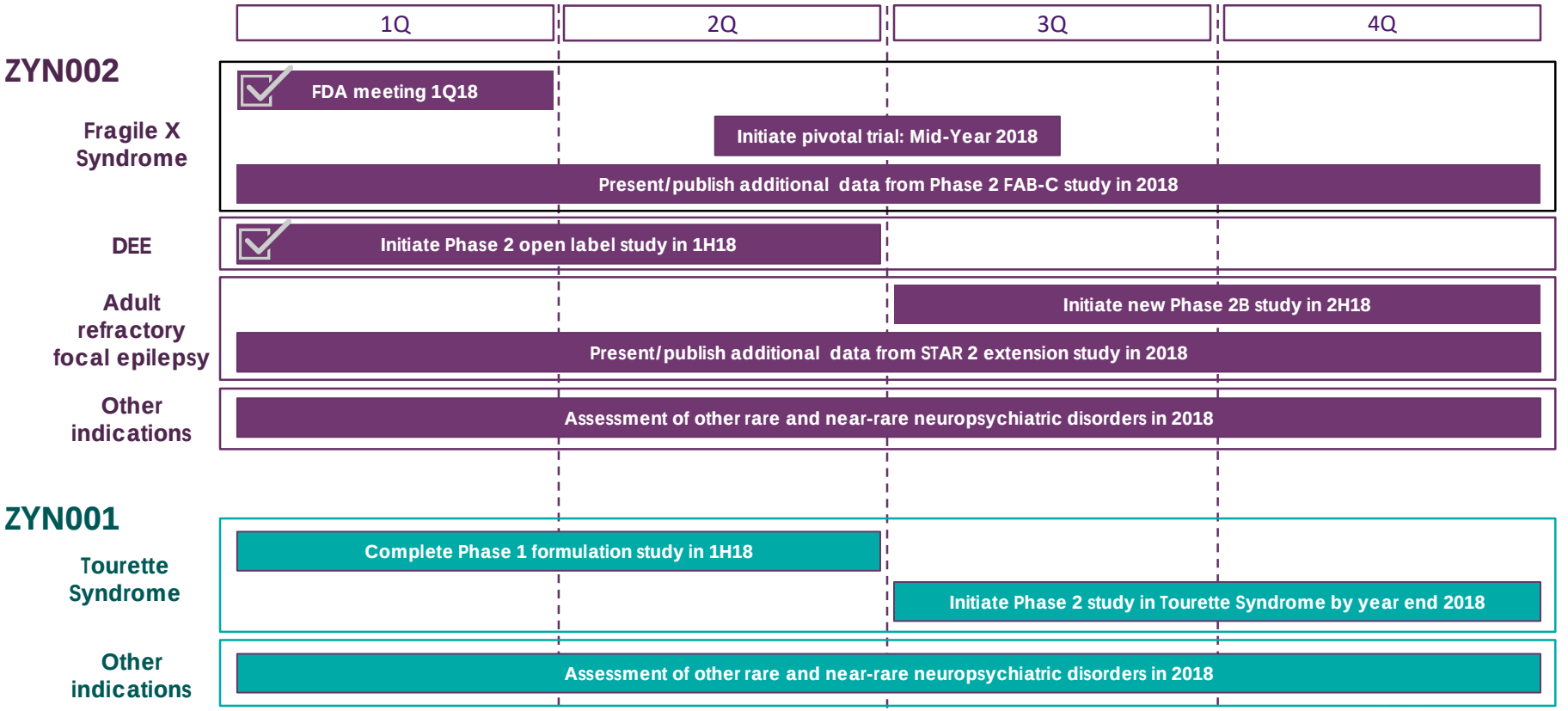
Expected 2018 Milestones



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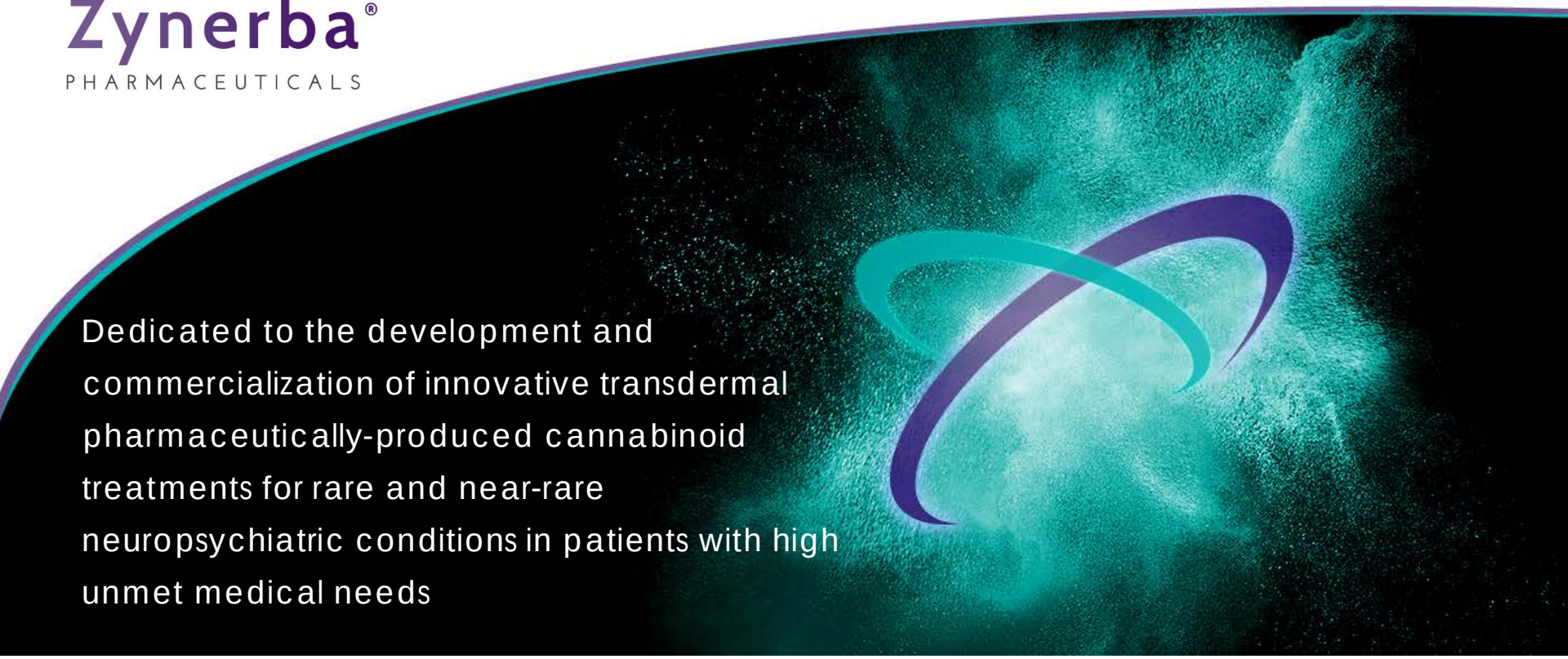

Dedicated to the development and commercialization of innovative transdermal pharmaceutically-produced cannabinoid treatments for rare and near-rare neuropsychiatric conditions in patients with high unmet medical needs

April 2018

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ZYN002
CBD Gel Clinical Program

Fragile X Syndrome

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Fragile X Syndrome (FXS)
The Endocannabinoid (EC) System is a Critical Pathway

- **Rare genetic developmental disability; leading known cause of both inherited intellectual disability and autism spectrum disorder**
- **Symptoms linked to deficiencies in the endocannabinoid system**
  - **ECs form system of neurotransmitters regulating emotional responses, behavioral reactivity to context, social interaction**
  - **FMR1 mutation in FXS causes dysregulation of the EC system resulting in significant social, behavioral, and cognitive deficits**
  - **Modulation of EC system with CBD may have therapeutic potential in ameliorating some of those symptoms**
  - **Strong scientific rationale in FXS validated by Phase 2 FAB-C clinical data**

U.S. Orphan Drug Designation for use of CBD as a treatment of Fragile X syndrome has been granted by the FDA (Feb. 2016)

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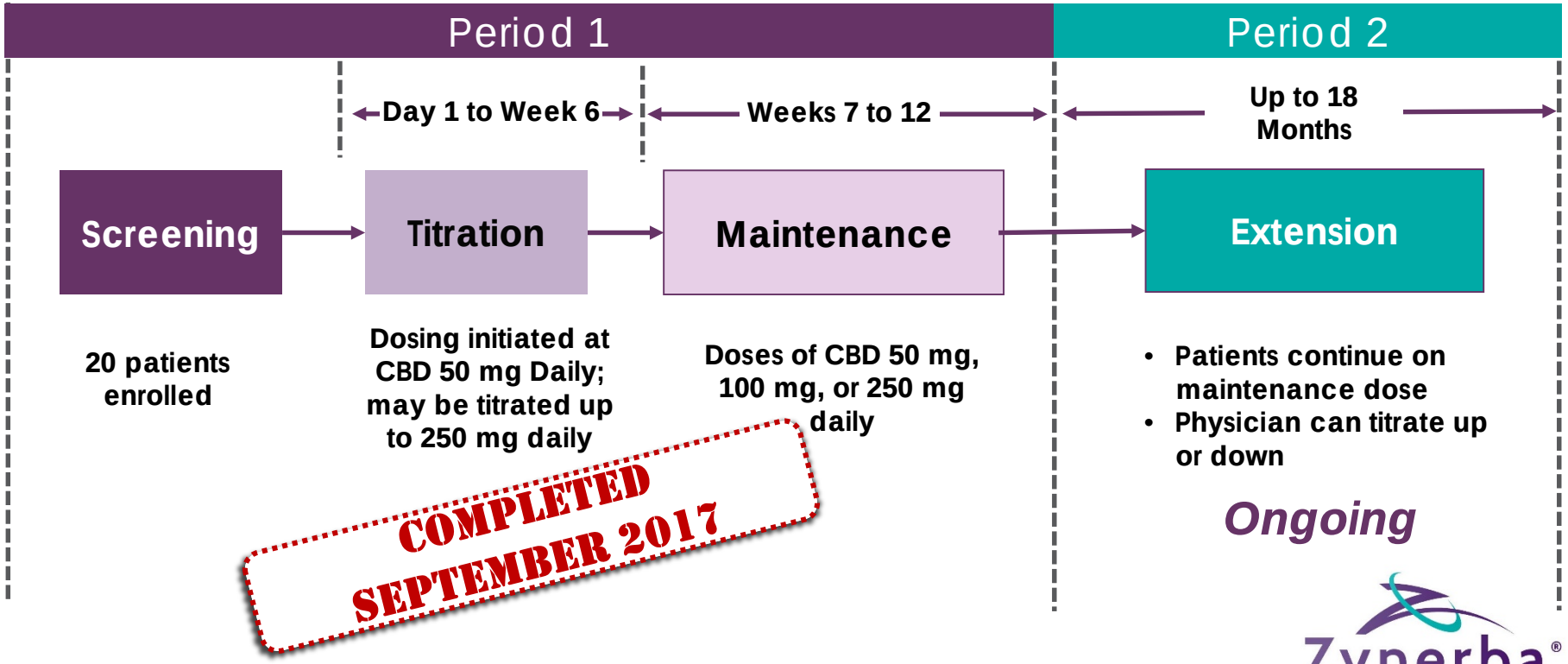
Fragile X Syndrome Open Label Phase 2
Trial Design

Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD (FAB-C)



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Positive FAB-C Open Label Phase 2 Efficacy Data
Primary Endpoint: ADAMS Total Score

ADAMS total score	Improvement vs. baseline (N=20)
Changes in Anxiety, Depression and Mood	46% *(p<0.0001)*

ADAMS subscales	Improvement vs. baseline (N=20)
General Anxiety	54% (p<*0.0001*)
Social Avoidance	53% *(p<0.0002)*
Compulsive Behavior	50% *(p=0.0262)*
Manic/Hyperactive Behavior	35% *(p=0.0003)*
Depressed Mood	29% *(p=0.1417)*

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Positive FAB-C Open Label Phase 2 Efficacy Data
Key Secondary Endpoint: ABC-FXS

ABC-FXS subscale	Improvement vs. baseline (N=20)
Stereotypy: "Repetitive Movements"	**59%** *(p=0.0006)*
Social Avoidance: "Seeks Isolation"	**55%** *(p=0.0005)*
Socially Unresponsive/Lethargic: "Does Not Pay Attention"	**53%** *(p=0.0034)*
Inappropriate Speech: "Repeats Words or Phrases"	**43%** *(p=0.0018)*
Irritability: "Has Temper Tantrums"	**42%** *(p=0.0096)*
Hyperactivity: "Disrupts Group Activities"	**33%** *(p=0.0194)*

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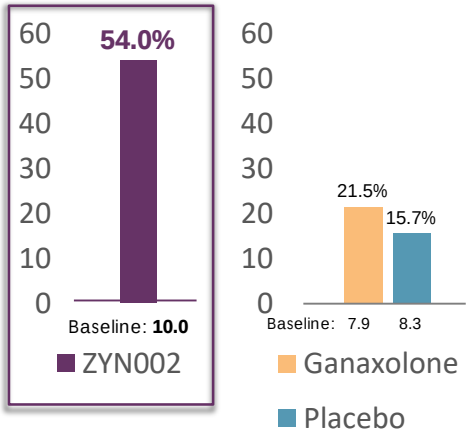
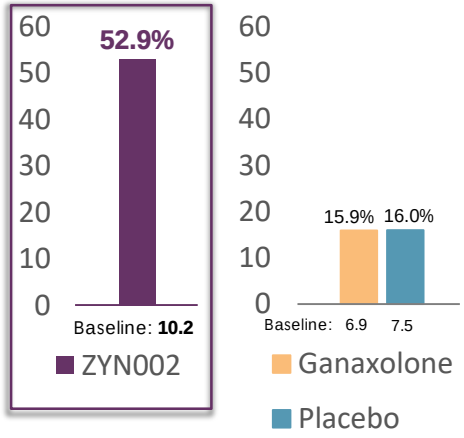
ADAMS Subscales

Week 12: Percent Improvement vs. 3rd party data*

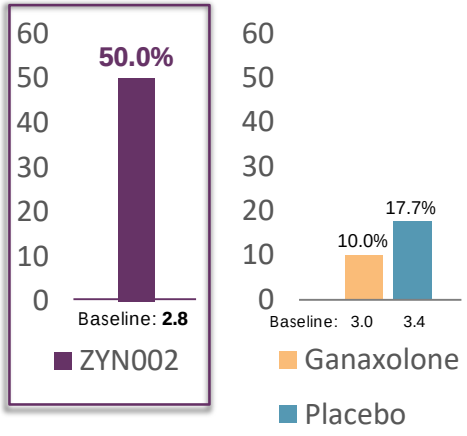
General Anxiety



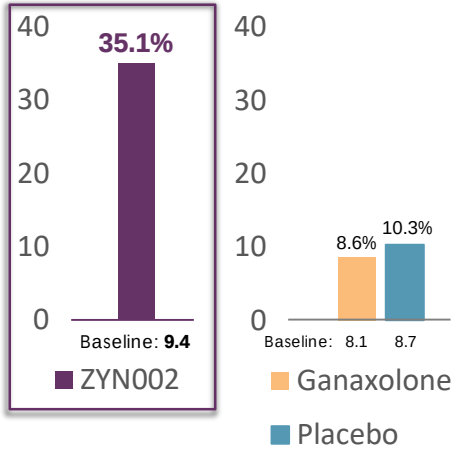
Social Avoidance



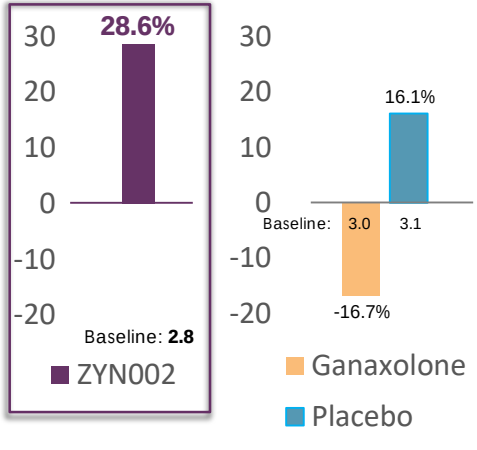
Compulsive Behavior



Manic/hyperactive Behavior



Depressed Mood



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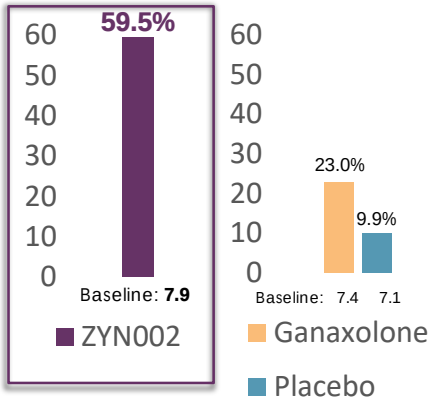
* Ligsay, A., Van Dijck, A., Nguyen, D. V., Lozano, R., Chen, Y., Bickel, E. S., et al. (2017). A randomized double-blind, placebo-controlled trial of ganaxolone in children and adolescents with fragile x syndrome. Journal of Neurodevelopmental Disorders, 9:26.

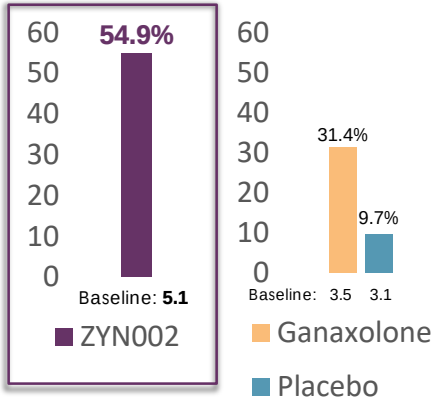
ABC-FXS Subscales

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

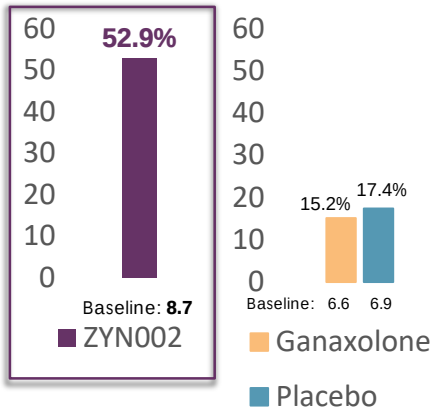
Stereotypy
Repetitive Movements



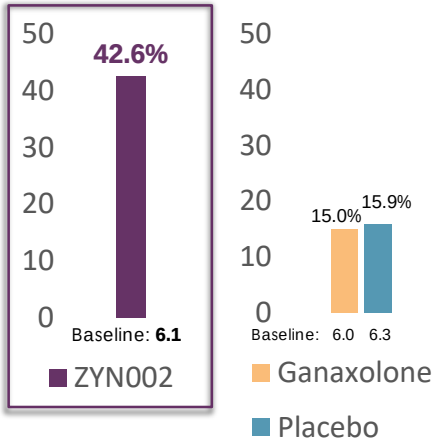
Social Avoidance
Seeks Isolation



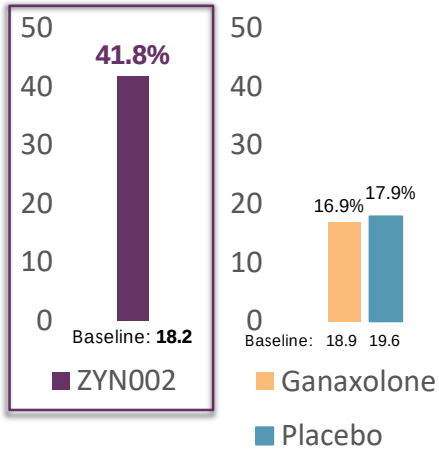
Socially Unresponsive / Lethargic
Does Not Pay attention



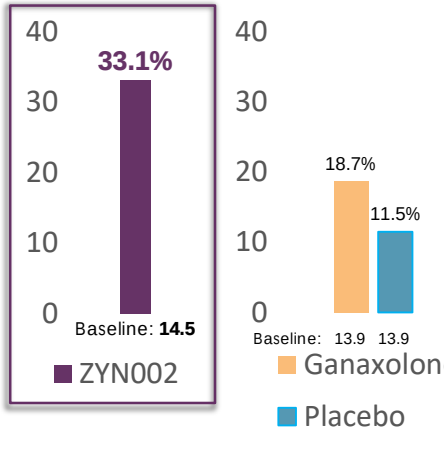
Inappropriate Speech
Repeats Words / Phrases



Irritability
Temper Tantrums



Hyperactivity
Disrupts Group Activities



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* 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.

Positive FAB-C Open Label Phase 2 Safety Data

- **Very well tolerated, consistent with previously reported clinical data; no SAEs**
- **Two sibling patients discontinued due to worsening of pre-existing eczema**
- **No drug-related GI events**
- **No THC was detected in the plasma**
- **13 patients continued into open label extension; 12 remain as of 4/2/18**
  - **Twelve patients have exceeded 9 months on ZYN002**
  - **Two patients have exceeded 12 months on ZYN002**

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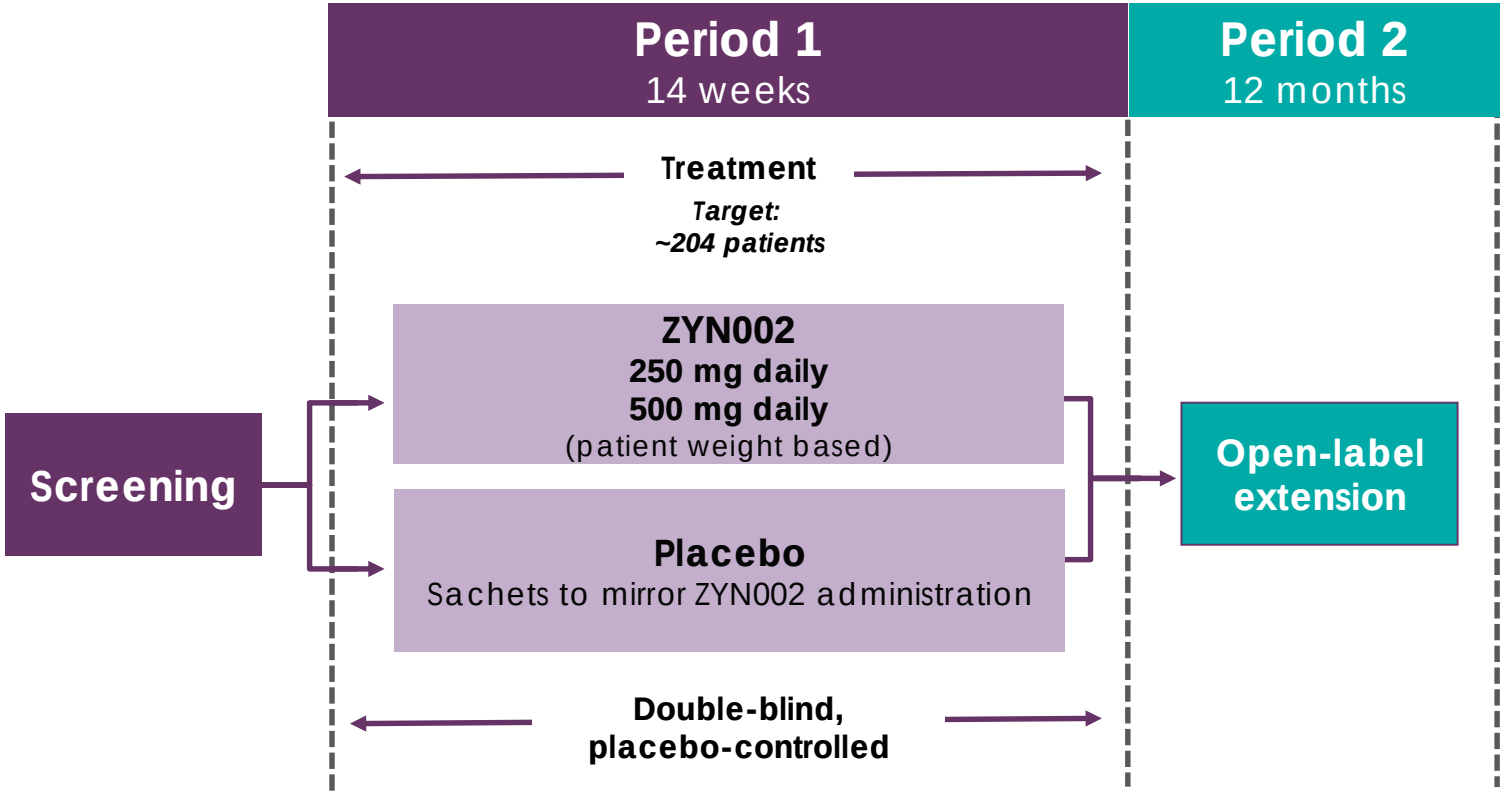
Fragile X Syndrome Pivotal Study
Proposed Trial Design*



Patients will be randomized (1:1) to receive either ZYN002 or placebo

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

ZYN002 in Fragile X Syndrome
Next Steps

- **Expect to begin pivotal trial in pediatric and adolescent patients with FXS mid-year 2018**
  - **204 patients from U.S., Australia and New Zealand**
  - **Key endpoints will assess observable behaviors: ABC-FXS**
  - **Top line data expected in 2019**
- **Assessing opportunities to present / publish full FAB-C data set as soon as possible in 2018**
  - **Targeting three FXS meetings June-August 2018**
- **Evaluating opportunities for FDA fast-track, breakthrough status, and/or priority review**

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ZYN002
CBD Gel Clinical Program

Developmental Epileptic Encephalopathies (DEE)

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Developmental and Epileptic Encephalopathies

DEE category includes:

- Doose Syndrome
- Dravet Syndrome
- Early Myoclonic Encephalopathy
- Epilepsy of Infancy With Migrating Focal Seizures
- Epilepsy with Generalized Tonic-Clonic Seizures alone (EGTCS)
- Juvenile Myoclonic Epilepsy (JME)
- Landau-Kleffner Syndrome
- Lennox-Gastaut Syndrome
- Ohtahara Syndrome (Early Infantile Epileptic Encephalopathy)
- West Syndrome / Infantile Spasms

- **Heterogeneous group of epilepsy syndromes associated with severe cognitive impairment and behavioral disturbances**
- **Syndromes involve:**
  - **Significant developmental impairment (*developmental* encephalopathies)**
  - **Regression of developmental progress (*epileptic* encephalopathies)**
- **Often progressive; highly resistant to treatment**
- **Improved seizure control may have a positive impact on development and quality of life**
- **Third party clinical data show impact of CBD on seizures and behavioral issues**

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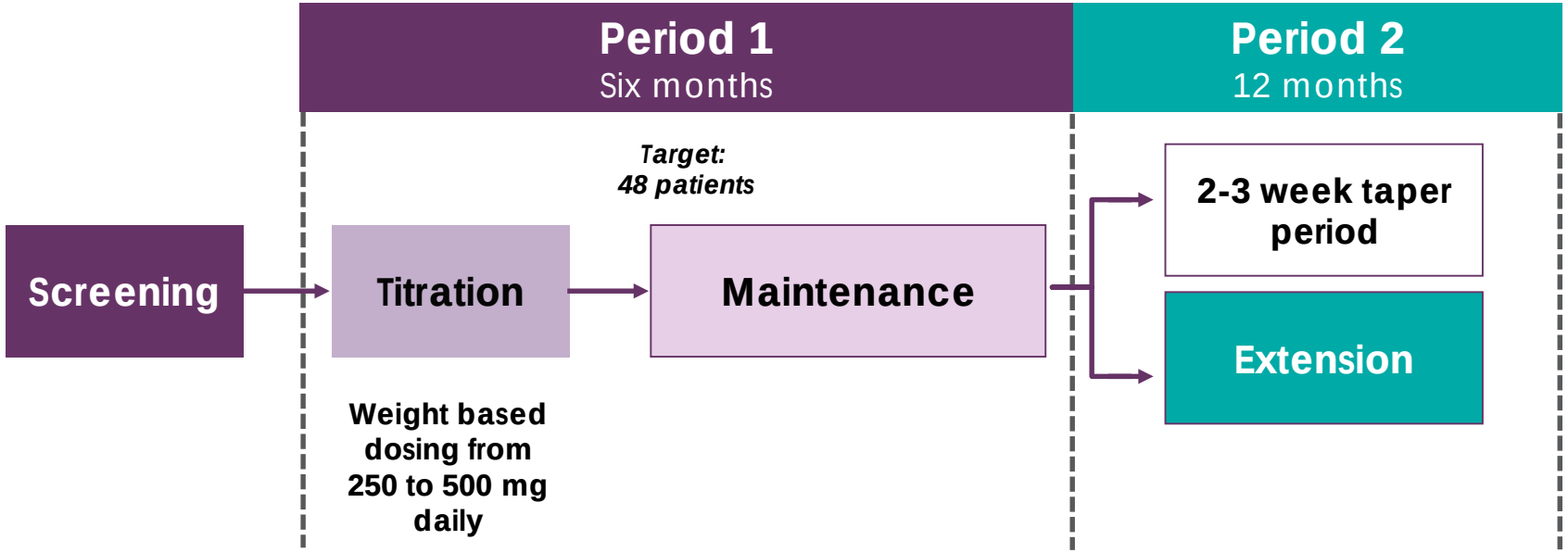
BELIEVE 1 DEE Open Label Phase 2 Study

Results Expected in 2019

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



- **Study initiated April 2018**
- **Primary efficacy assessment: change in seizure frequency**

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

ZYN002
CBD Gel Clinical Program

Adult Refractory Focal Epilepsy

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Adult Refractory Focal Epilepsy
Phase 2B Anticipated in 2018

Adult Refractory Focal Seizures

- Focal seizures are the most common epilepsy in adults
- Substantial US market
  - ~500,000 refractory patients
- New treatment options with improved quality of life (safety and efficacy) needed

- STAR 2 data suggest clinically meaningful response with longer term use of ZYN002
  - Consistent and improving median seizure rate at three, six and nine months of treatment with ZYN002
- Learnings from Phase 2 STAR 1 study and open label STAR 2 extension provide input into Phase 2B trial design
- Expect to initiate ~300 patient double blind placebo controlled Phase 2b study in 2H2018

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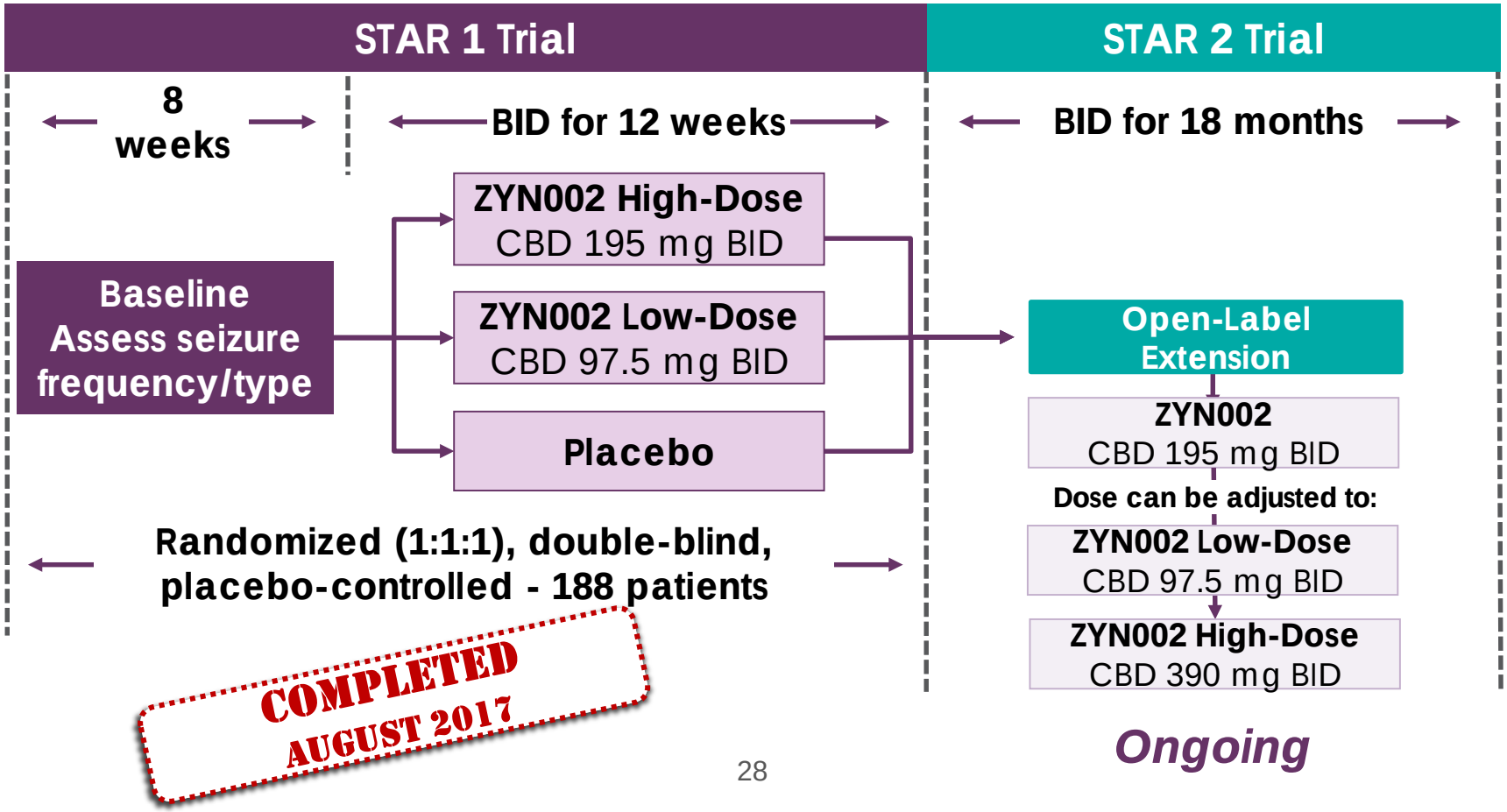
Epilepsy Phase 2 Clinical Study
Trial Design

Synthetic Transdermal CAnnabidiol for the TReatment of Epilepsy



Epilepsy Phase 2 Clinical Study
Demographics and Baseline Characteristics

STAR 1 patients	Placebo	195 mg ZYN002	390 mg ZYN002	Total
Pts Randomized	63	63	62	188
Sex	43% male 57% female	51% male 49% female	42% male 58% female	45% male 55% female
Pts Analyzed for efficacy	63	62	61	186
Pts completing study	62	57	55	174
Patients continuing into STAR 2				171
Baseline median seizure rate	10.5	14.0	10.1	10.6 (3-335)
AEDs				Median: 3.0 Mean: 2.5
Primary endpoint: Percent reduction in baseline seizures	8.7%	18.4%	14.0%	

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Epilepsy Phase 2 Clinical Study
STAR 1 and STAR 2 Results

STAR 1

- **Company believes study missed primary endpoint due to bimodal distribution of placebo patient responses :**
  - **>50% reductions in focal seizures in ~¼ of placebo patients**
  - **13 of these 15 patients were female**
- **Strong separation from placebo seen at >15 baseline seizures**
- **Excellent tolerability**

STAR 2

- **Low dropout rate to date**
- **93 patients have reached 9 mo. of drug exposure; 67 have reached 12 months***
- **Excellent tolerability**
- **Data suggest clinically meaningful response with longer term use**

Updated STAR 2 data accepted to Emerging Science (Late Breaker) poster session at the 2018 American Academy of Neurology (AAN) meeting (April 25, 2018)

Learnings provide input into revised Phase 2B clinical trial design

*As of April 2, 2018

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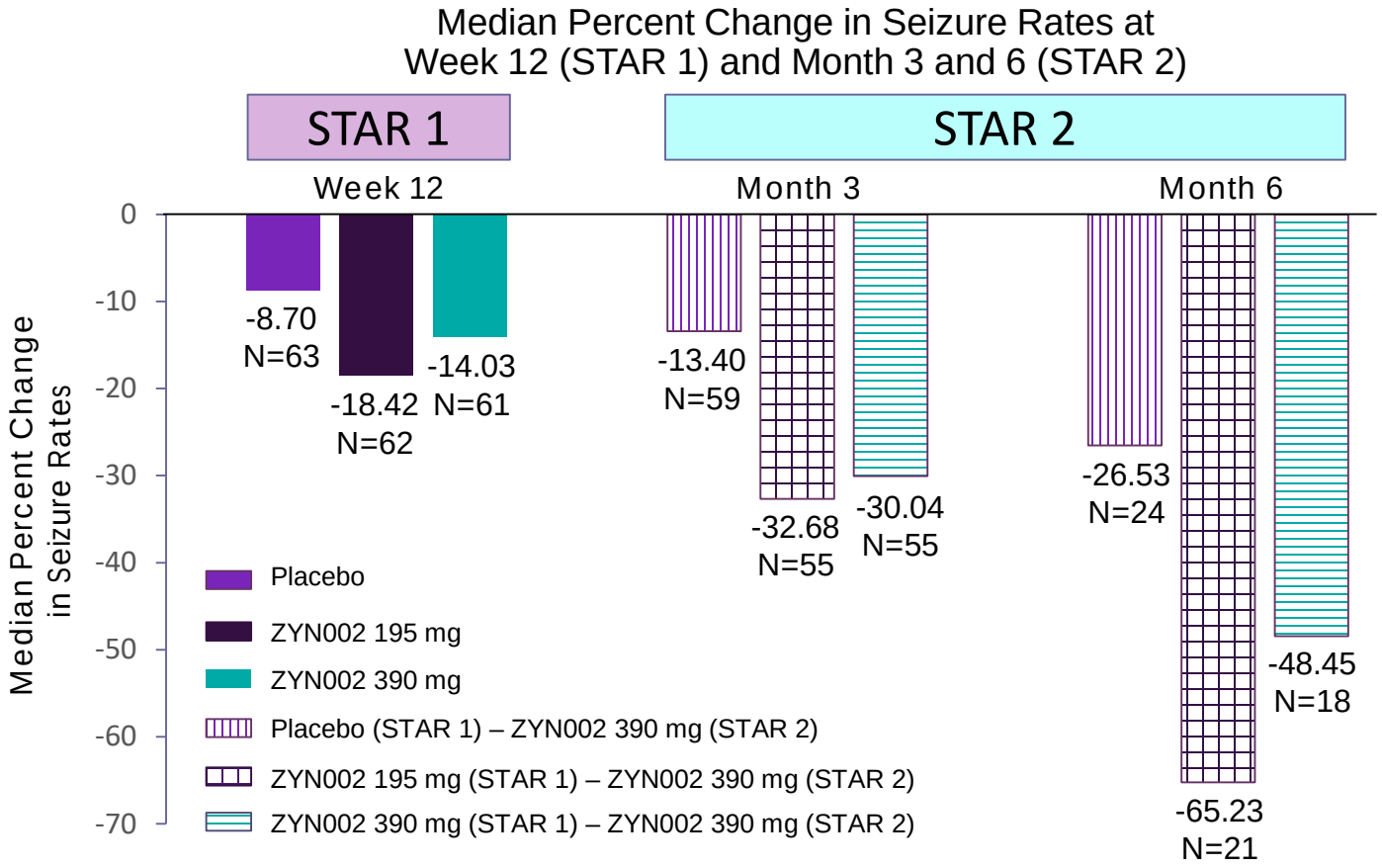
Data Presented at 2017 AES

STAR 1 and STAR 2 Efficacy Data



STAR 2 results based on data collected through mid-August 2017 and in patients who reported seizure frequency data during the respective time period.

Not all patients had reached 3 and 6 months in STAR 2

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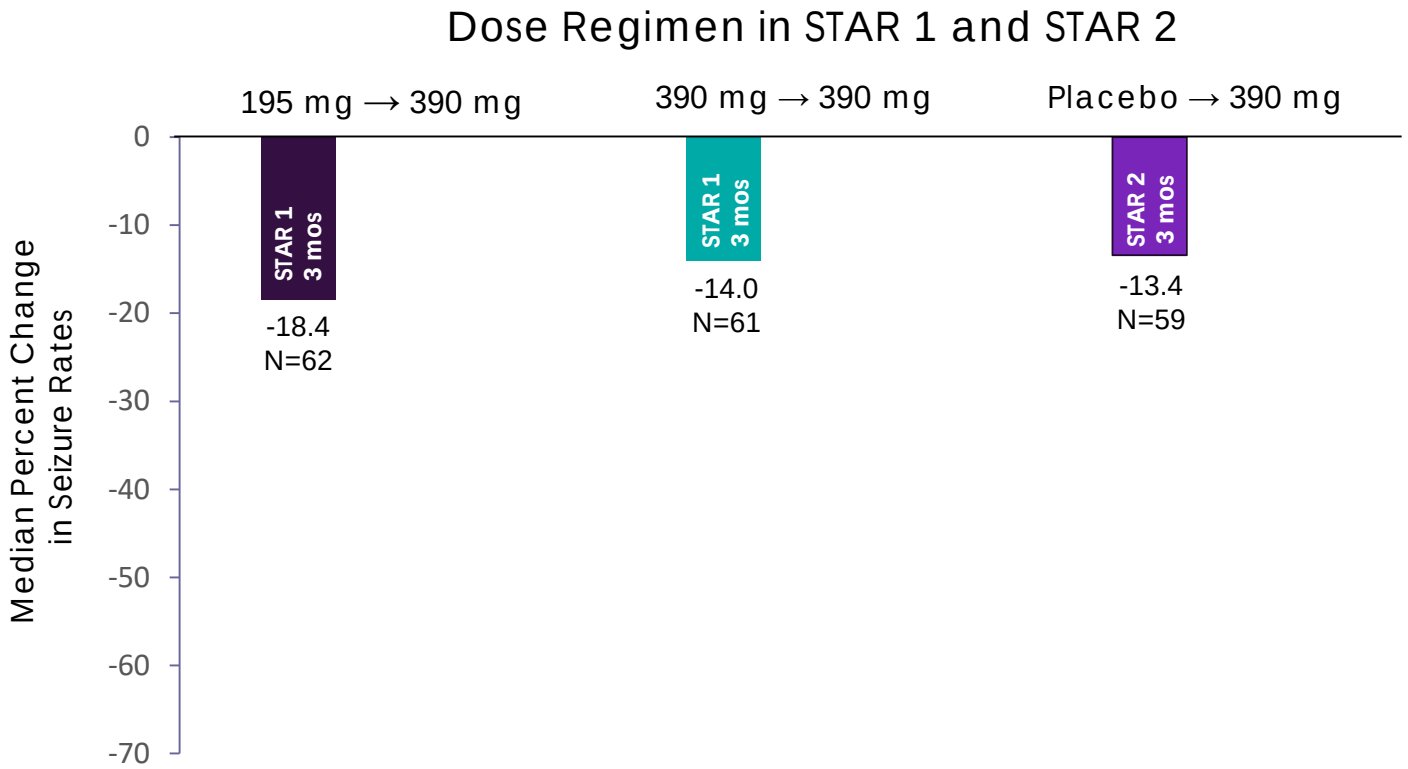
Consistent Results at Various Timeframes

Three Months on ZYN002



STAR 2 results based on data collected through mid-August 2017 and in patients who reported seizure frequency data during the respective time period.

Not all patients had reached 3 and 6 months in STAR 2 as of mid-August 2017

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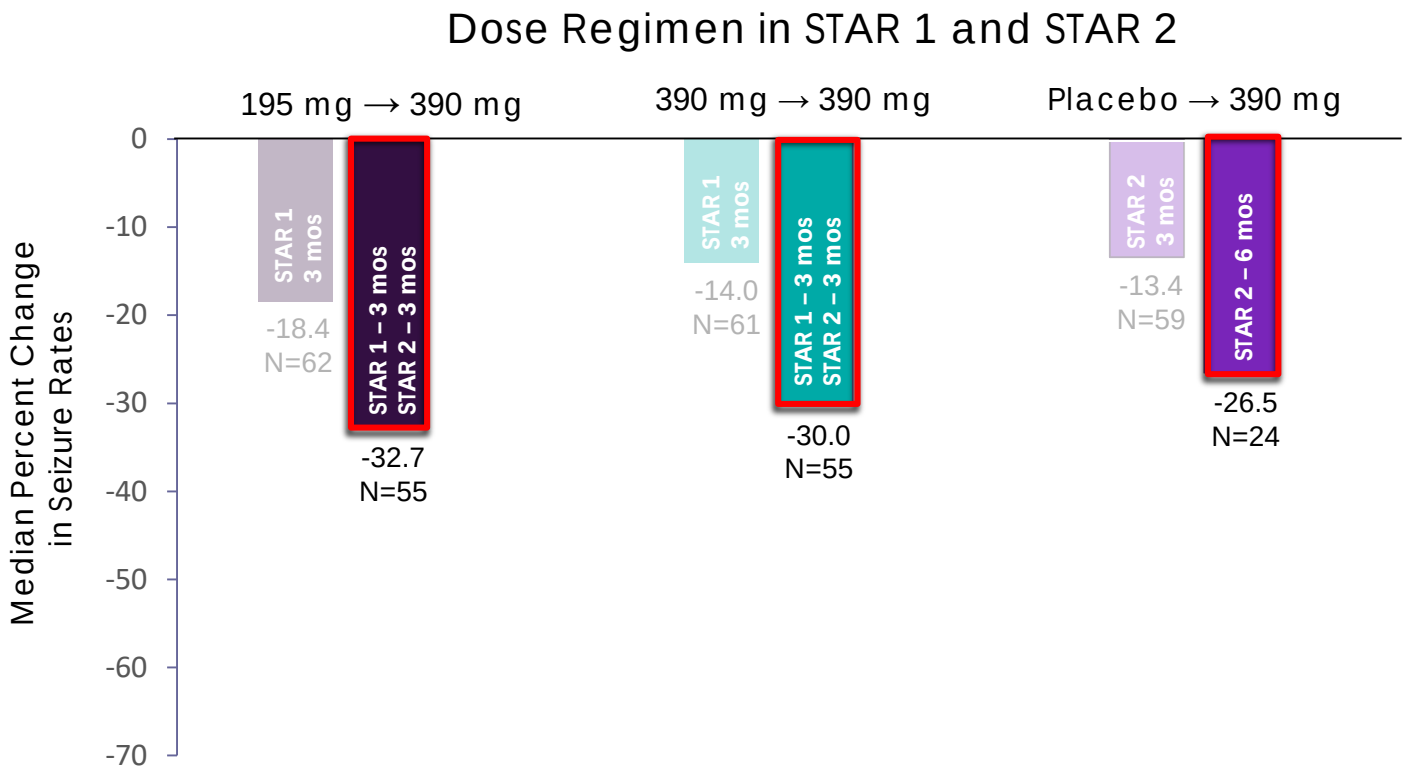
Consistent Results at Various Timeframes
Six Months on ZYN002



STAR 2 results based on data collected through mid-August 2017 and in patients who reported seizure frequency data during the respective time period.

Not all patients had reached 3 and 6 months in STAR 2 as of mid-August 2017

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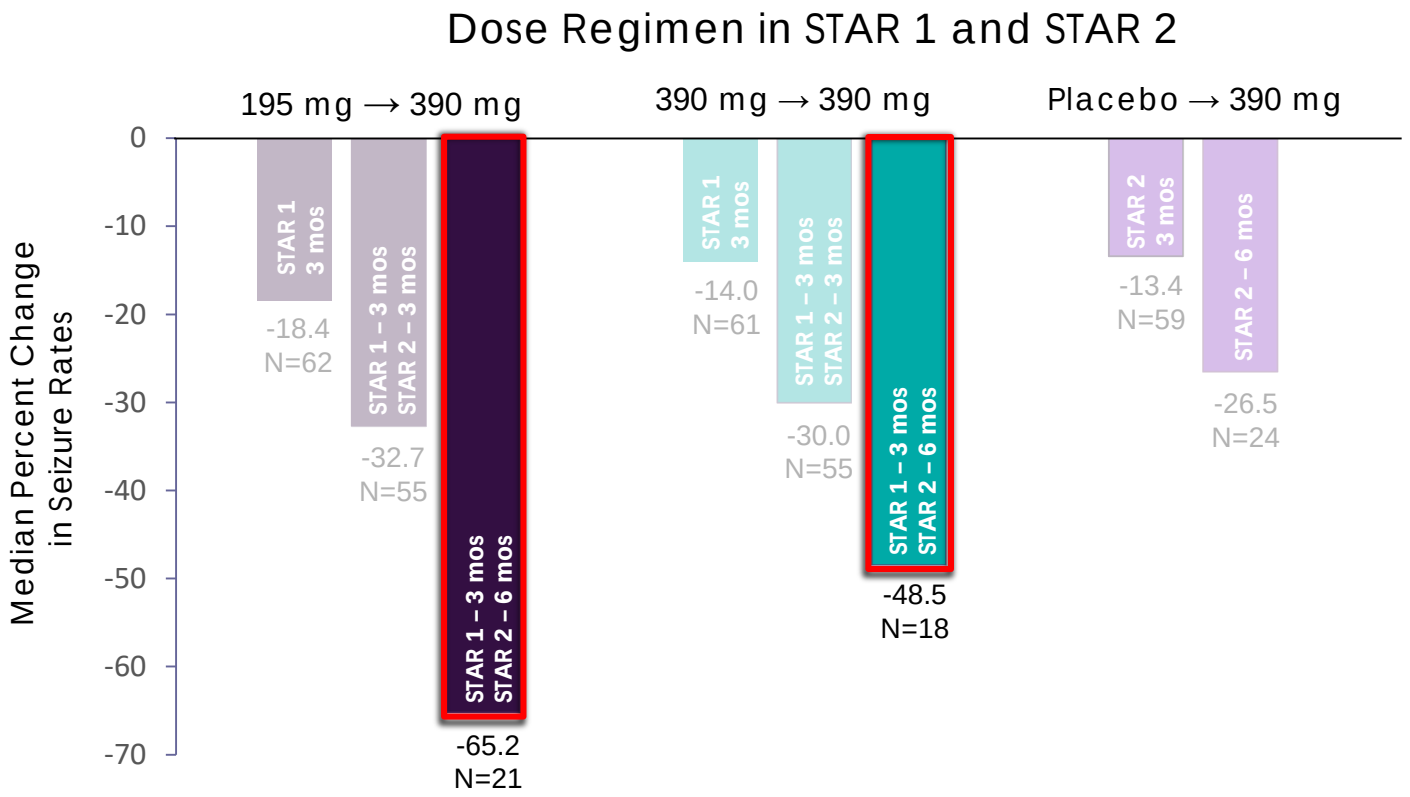
Consistent Results at Various Timeframes
Nine Months on ZYN002



STAR 2 results based on data collected through mid-August 2017 and in patients who reported seizure frequency data during the respective time period.

Not all patients had reached 3 and 6 months in STAR 2 as of mid-August 2017

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Proposed Phase 2b Study
Adult Refractory Focal Epilepsy

Trial design*

- ~300 patient double-blind placebo controlled study
- To be conducted in U.S., Australia and New Zealand
- Primary endpoint: reduction from baseline in focal seizures
- 1:1:1 ratio (195 mg: 780 mg: placebo)

Planned modifications

Learnings from STAR 1 and STAR 2 experience include:

- Stratified randomization by baseline seizure rate and gender
- Increase in patient count
- Increase trial duration
- Increase in baseline seizure frequency
  - Median seizure target: >15/month vs 10.6 in STAR 1

Expect to initiate study in 2H18

Open label extension to follow

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

Financial Strength
As of December 31, 2017

- **Cash and cash equivalent position of $62.5 million**
  - **Includes $3.0 million in net proceeds from shares sold in September and October 2017 under our ATM program**
- **Well capitalized, expect cash to fund operations well into 2019**

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Scientific Advisory Board

Elizabeth M. Berry-Kravis, MD, PhD	Professor, Department of Pediatrics, Rush Medical College
Craig A. Erikson, MD	Associate Professor, Department of Psychiatry and Behavioral Neuroscience, Cincinnati Children's Hospital
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Michael Rogawski, MD, PhD	Professor of Neurology, UC Davis Center for Neuroscience

Fragile X Syndrome Epilepsy

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Investor Relations

NASDAQ: ZYNE

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HC Wainwright: Oren Livnat

Piper Jaffray: Charles C. Duncan, PhD

Cantor Fitzgerald: Elemer Piros, PhD

Canaccord Genuity: Arlinda Lee, PhD

Seaport Global: Corey Davis

Oppenheimer: Derek Archila

Jefferies: Biren Amin, PhD

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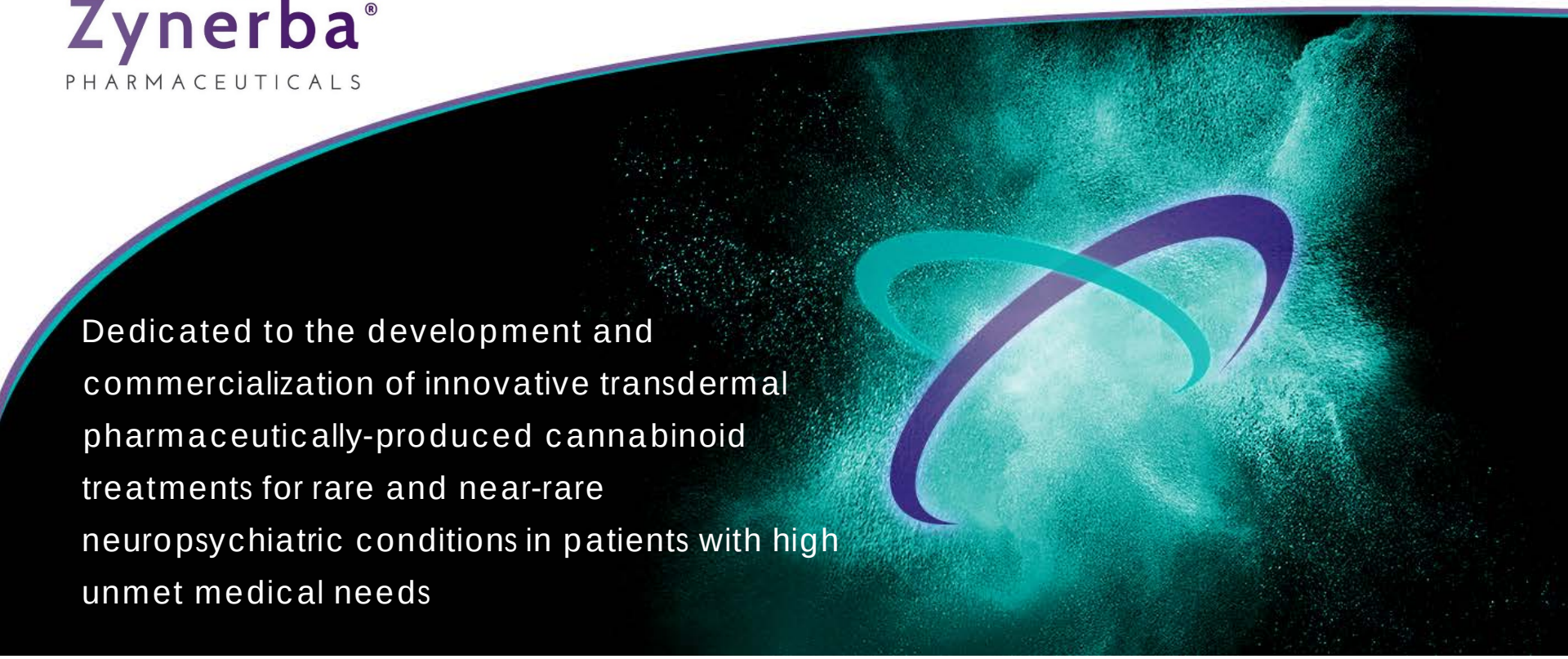

Dedicated to the development and commercialization of innovative transdermal pharmaceutically-produced cannabinoid treatments for rare and near-rare neuropsychiatric conditions in patients with high unmet medical needs

April 2018

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