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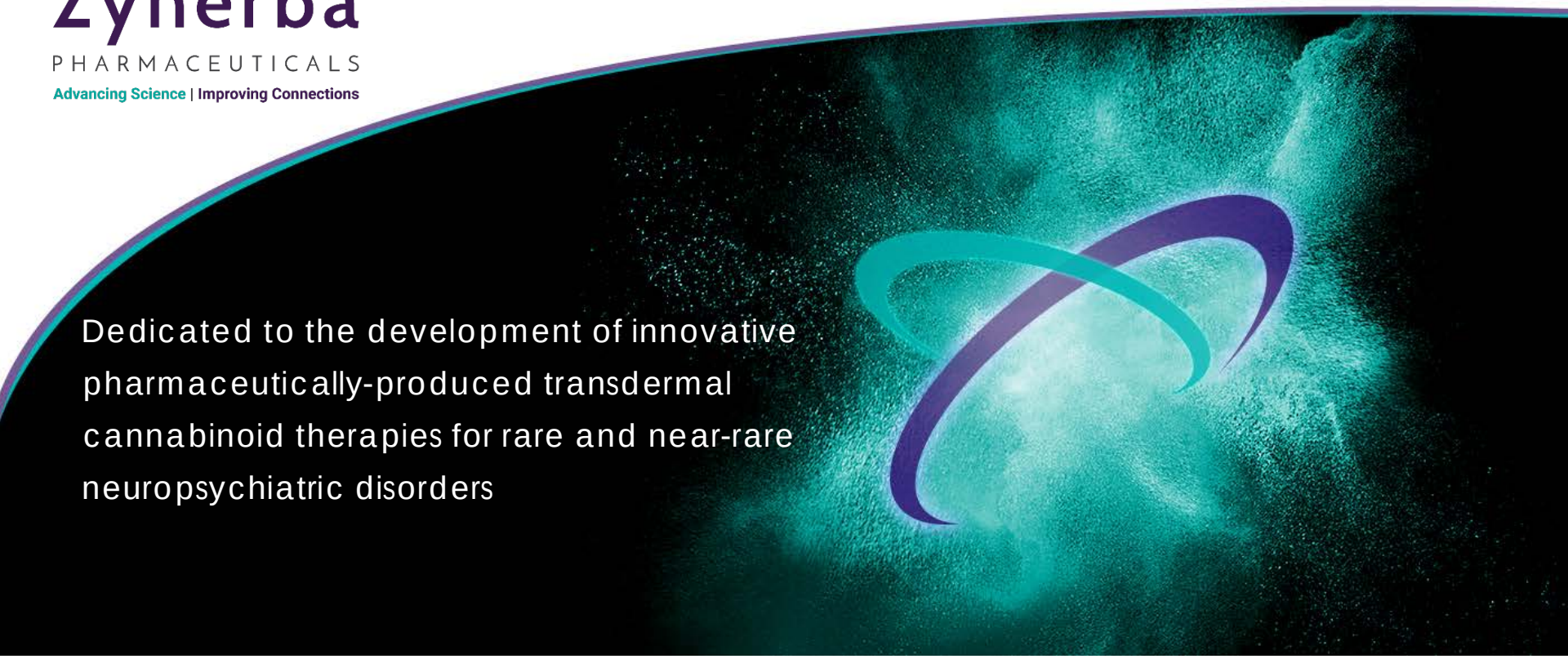

Dedicated to the development of innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders

July 2018

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Zynerba Pharmaceuticals
A Rare/Near-Rare Neuropsychiatric Company

- **Developing ZYN002 (CBD gel) in rare and near rare neuropsych disorders**
- **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**
- **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 into the second half of 2019**
- **Multiple expected near term milestones**

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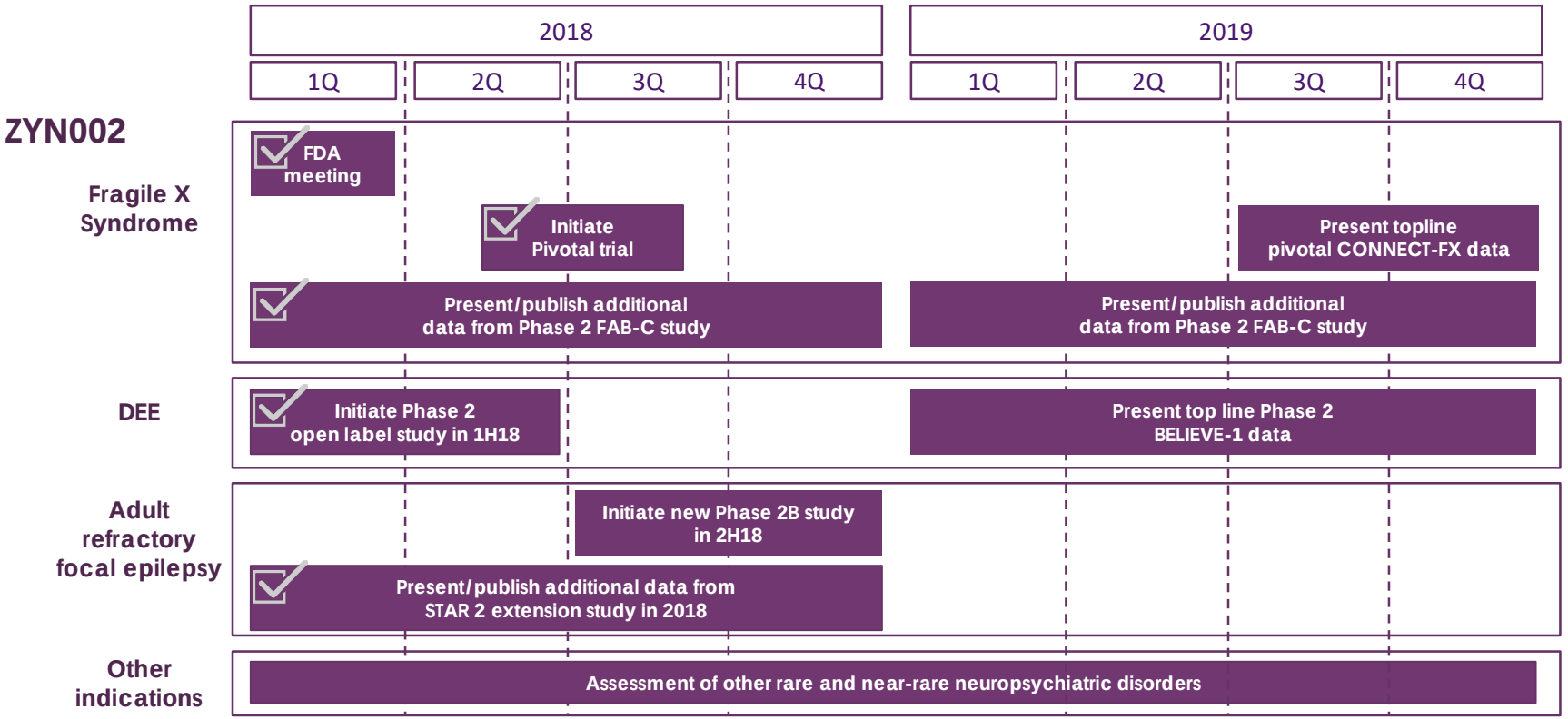
Expected 2018 and 2019 Milestones



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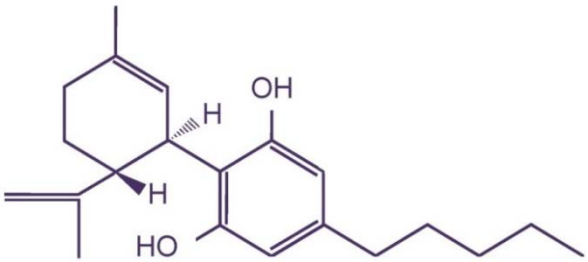
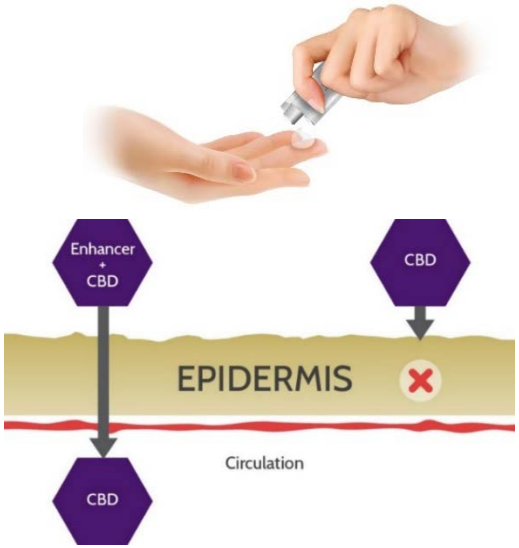
ZYN002
Cannabidiol (CBD) Gel

- **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)
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)

Fragile X Syndrome (FXS) Overview

FXS

- ~71,000 in U.S. patients with Fragile X
- Symptoms including significant behavioral, social, and cognitive deficits

- CONNECT FX: a pivotal trial now underway in pediatric and adolescent FXS patients
- Initiated July 2018; results expected in 2H2019
- With positive results, will request FDA meeting to determine acceptability of data for NDA submission*
- Presented significant and sustained FAB-C open label Phase 2 efficacy data at the 16th NFXF International FXS Conference (July 2018)
  - Achieved primary and numerous secondary efficacy endpoints with statistical significance vs. baseline
  - Significant improvements at 12 weeks were sustained through 38 weeks of treatment with ZYN002

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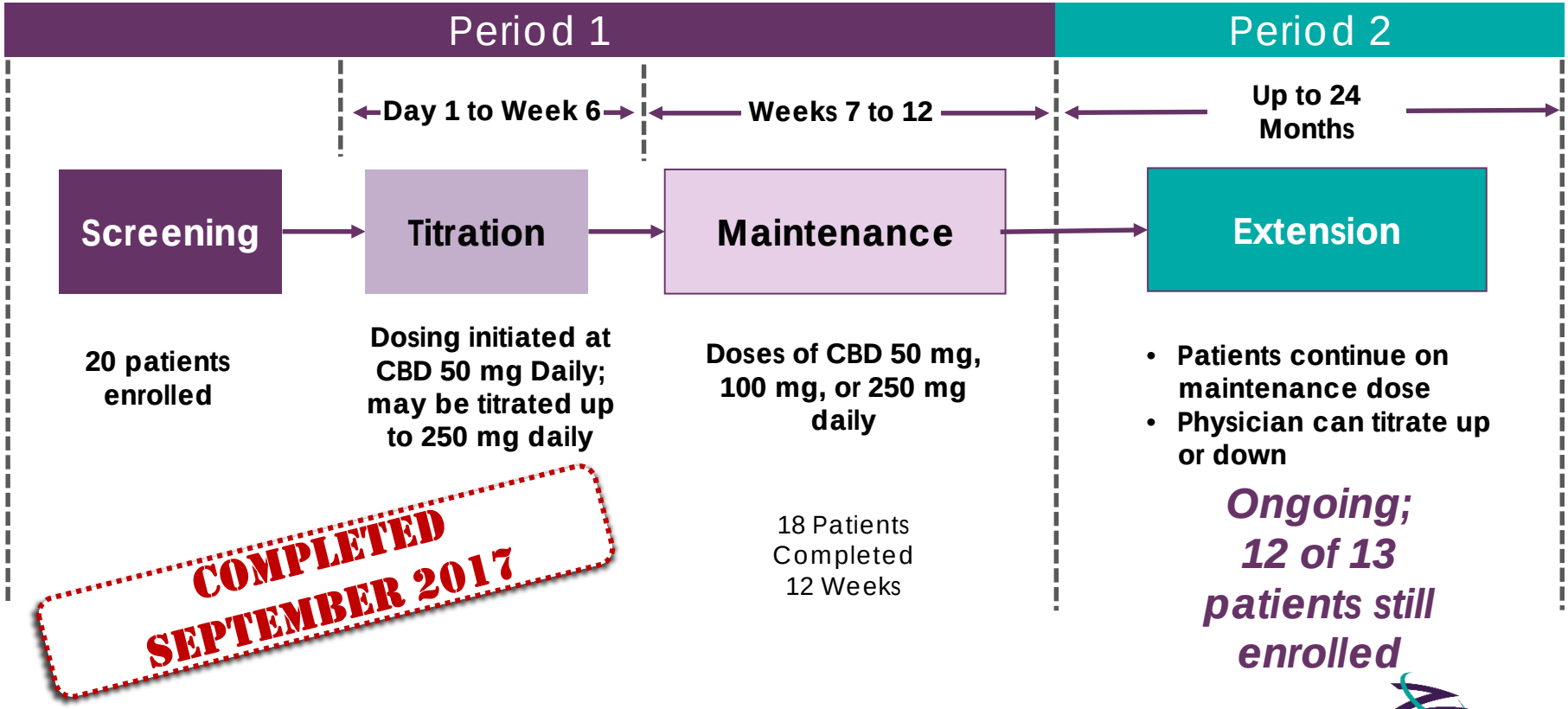
*Note: Subject to change due to further regulatory, clinical and other considerations.

FAB-C Open Label Phase 2 (6 to 17 y.o.)



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FAB-C 12-Week Efficacy Data: ADAMS

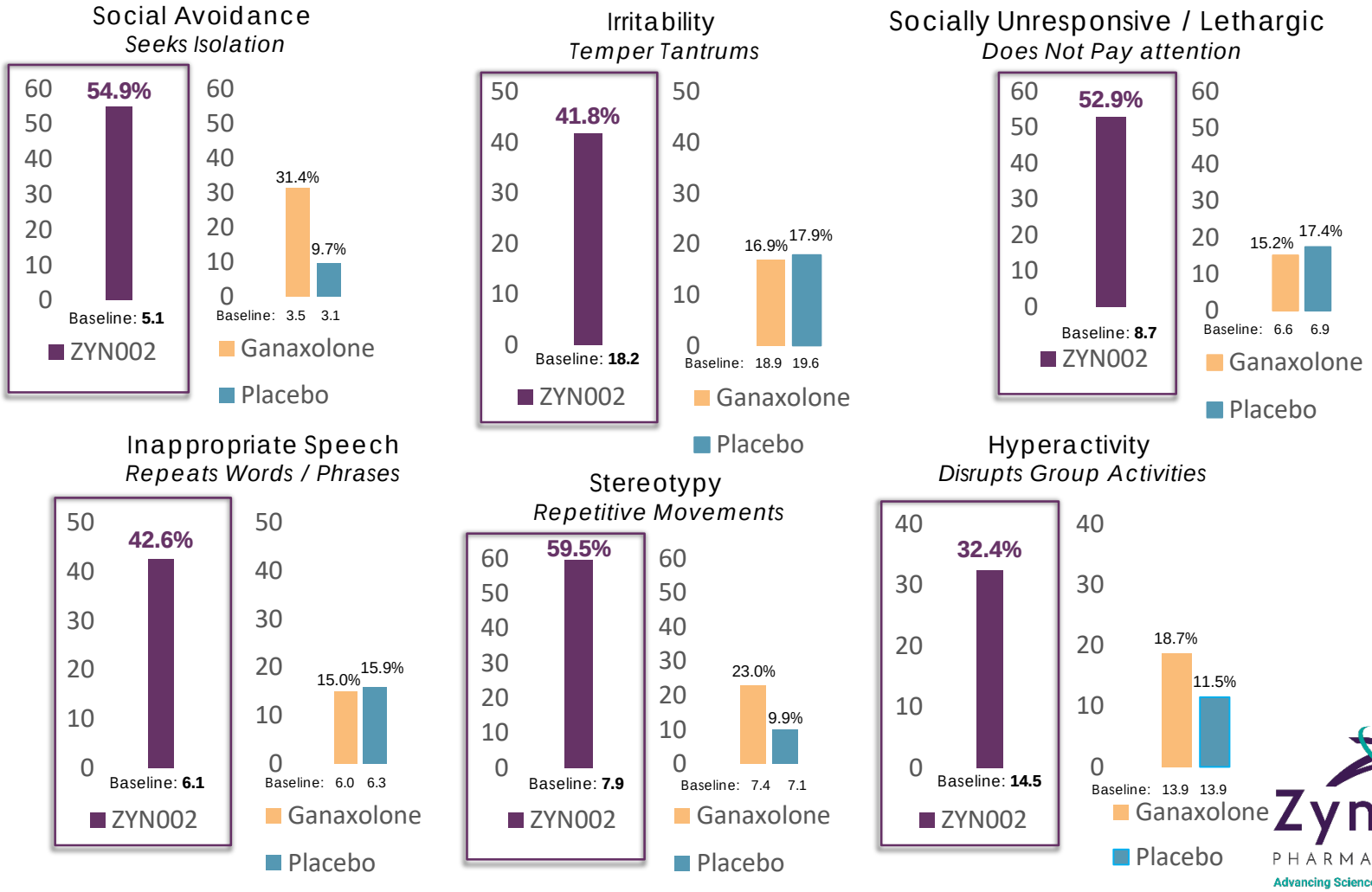
Scale: ADAMS	Baseline (n=20)	Week 12 (n=18)	Week 12 % Improvement Group Mean	P-value vs baseline
Total Score	**33.4**	**18.1**	**45.8**	**<0.0001**
General Anxiety	10.0	4.6	54.0	<0.0001
Social Avoidance	10.2	4.8	52.9	0.0002
Compulsive Behavior	2.8	1.4	50.0	0.0262
Manic/Hyperactive Behavior	9.4	6.1	35.1	0.0003
Depressed Mood	2.8	2.0	28.6	0.1417

FAB-C 12-Week Efficacy Data: ABC-C_{FXS}

Scale: ABC-C_{FXS}	Baseline (n=20)	Week 12 (n=18)	Week 12 % Improvement Group Mean	P-value vs baseline
Stereotypy	7.9	3.2	59.5	0.0006
Social Avoidance	5.1	2.3	54.9	0.0005
Socially Unresponsive/Lethargic	8.7	4.1	52.9	0.0034
Inappropriate Speech	6.1	3.5	42.6	0.0018
Irritability	18.2	10.6	41.8	0.0096
Hyperactivity	14.5	9.8	32.4	0.0237

FAB-C ABC-C_{FXS} Subscales

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



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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.

FAB-C Open Label Phase 2
New Data Presented at NFXF International FX Conference

- **Treatment with ZYN002 improved core behavioral symptoms of Fragile X syndrome with statistical significance versus baseline across multiple measures of efficacy at week 12**
- **Improvements sustained through 38 weeks of treatment**
- **ZYN002 is well tolerated**
  - **No serious adverse events were reported**
  - **No clinically meaningful trends in vital signs, ECG, or clinical safety laboratories, including liver function tests (LFTs) were observed**
  - **No THC detected in the plasma**

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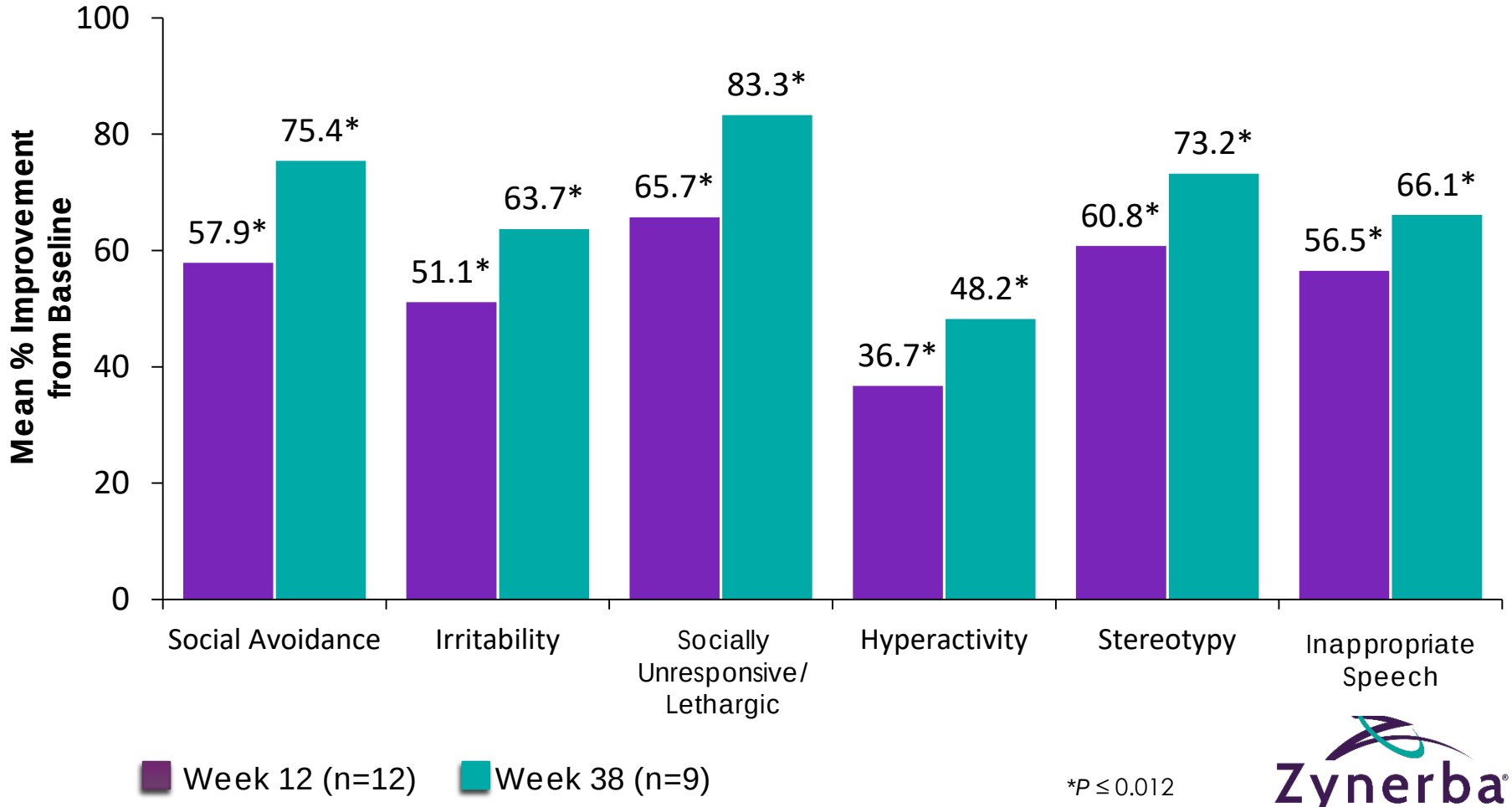
FAB-C Open Label Phase 2
Additional 12-Week Efficacy Data

Scale	Baseline (n=20)	Week 12 (n=18)	Week 12 % Improvement Group Mean	P-value vs baseline	Assessor
CGI Improvement (7 point scale)	n/a	2.5*	n/a	n/a	Clinician
Pediatric Anxiety Rating Scale – Revised (5-item used for Clinical Trials)	15.6	10.6	32.1	0.0006	Clinician
Pediatric Quality of Life Inventory: Total	57.3	67.7	18.2	0.0100	Caregiver
VAS Hyperactivity/Impulsivity	6.2	3.6	41.9	0.0002	Caregiver
VAS Tantrum/Mood Lability	5.0	3.2	36.0	0.0023	Caregiver
VAS Anxiety	6.2	3.8	38.7	0.0005	Caregiver
Vineland III: Overall Adaptive Behavior	48.3	48.9	1.2	0.0472	Clinician

* N=17 at week 12

FAB-C Open Label Phase 2
ABC-C_{FXS} Mean Score: 38 Weeks



*$P \leq 0.012$

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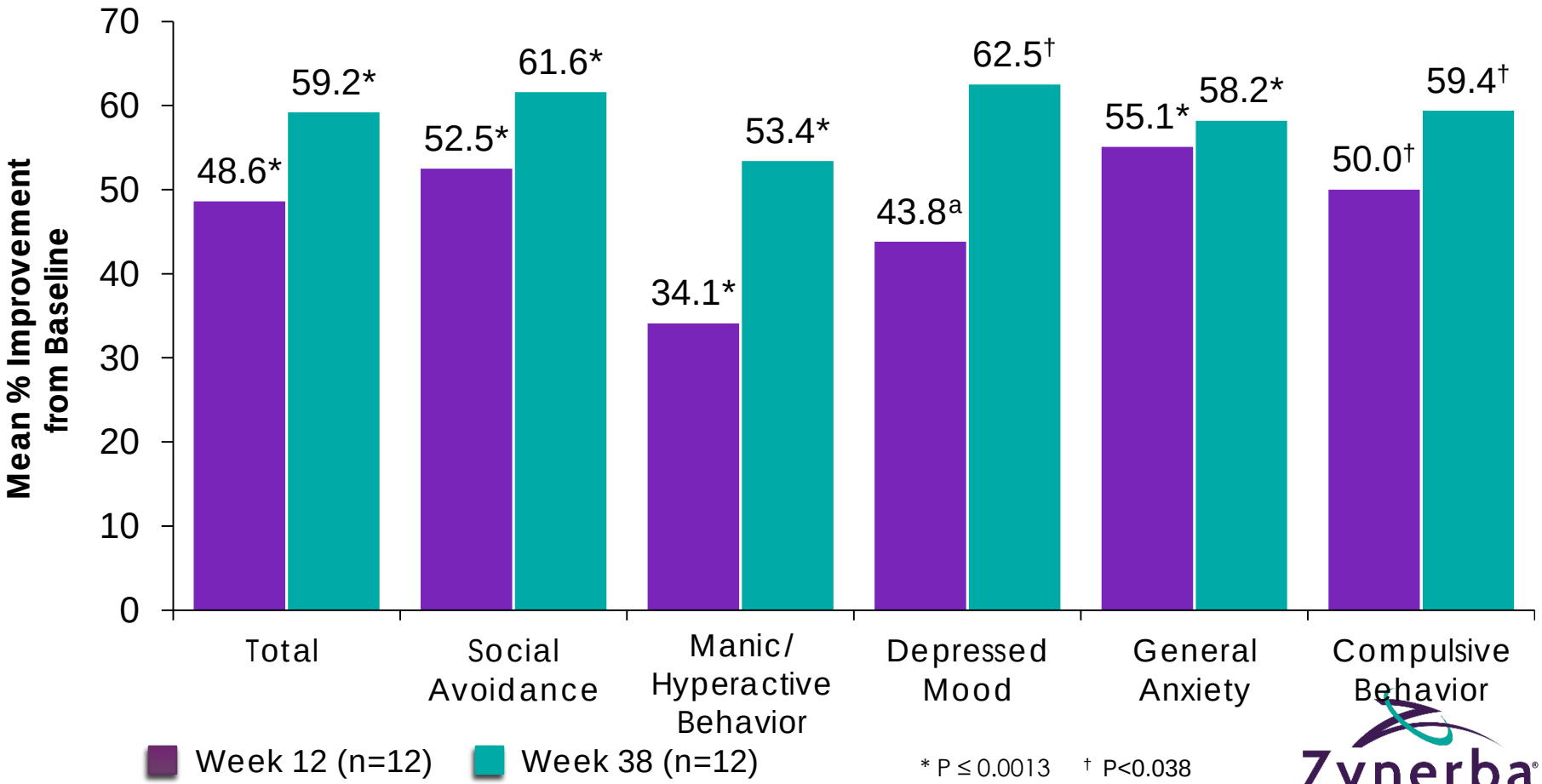
FAB-C Open Label Phase 2

ADAMS Mean Score: Week 38



* P ≤ 0.0013 † P<0.038

[a] P = 0.083

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FAB-C Open Label Phase 2
Safety Summary

ZYN002

- **Overall safety database across all studies comprised of 570 volunteers and patients**
  - **Single dose to 24 months of exposure to ZYN002**

FAB-C (Through 38 Weeks)

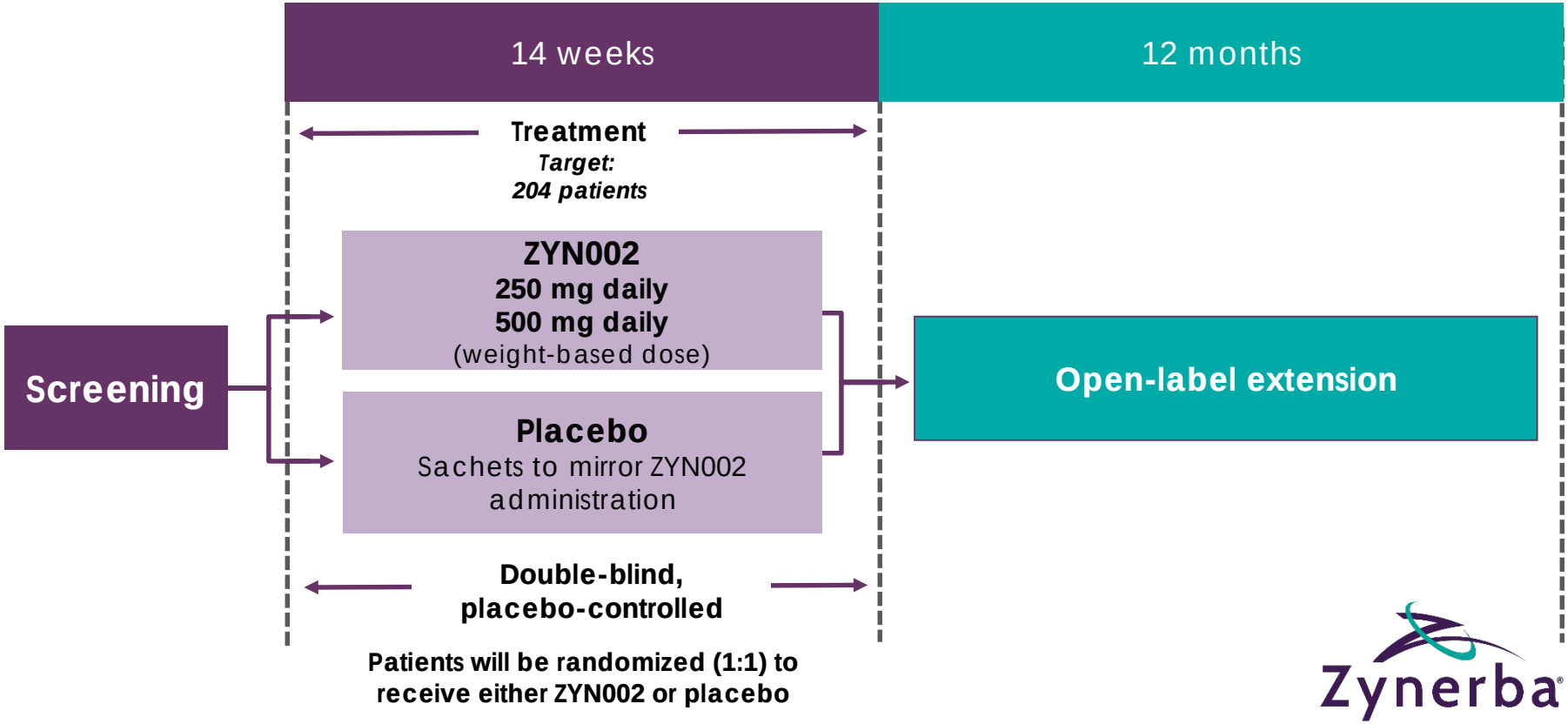
- **Well tolerated, consistent with previously reported clinical data; no SAEs**
- **No clinically meaningful trends in vital signs, ECG, or clinical safety laboratories, including liver function tests (LFTs)**
- **No THC was detected in the plasma**
- **Two sibling patients discontinued in Period 1 of study**
  - **One patient for worsening of pre-existing eczema (not considered treatment related)**
  - **One patient (sibling of the patient with eczema) discontinued due to administrative reasons**
- **Application site assessment scores showed little to no redness in most patients**
  - **One patient developed moderate application site rash, which resolved and did not recur; patient remains in the study**

FAB-C Open Label Phase 2
Treatment-Emergent Adverse Events

- **Through Week 38, patients have reported 43 treatment-emergent adverse events (TEAEs)**
  - **TEAEs were mild or moderate and most unrelated to treatment with CBD**
- **Most common TEAEs (all considered not related and resolved during study period):**
  - **Gastroenteritis (14%)**
  - **Upper respiratory tract infection (12%)**
- **One patient developed moderate application site rash – resolved**

CONNECT-FX: A Pivotal Trial in FXS Patients

Clinical study of Cannabidiol (CBD) in Children and Adolescents with Fragile X (CONNECT-FX)



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CONNECT-FX - Multi-national, randomized, double-blind, placebo-controlled, 14-week study

- 204 patients with FXS, three to 17 years of age
- Primary endpoint:
  - Change from baseline to end of treatment in ABC-C_{FXS} Social avoidance subscale
- Key secondary endpoints:
  - Change from baseline to the end of the treatment period in
    - ABC-C_{FXS} Irritability subscale score
    - ABC-C_{FXS} Socially Unresponsive/Lethargic subscale score
  - Improvement in CGI-I at the end of the treatment period.
- Study will anchor the CGI-I to behavioral symptoms of FXS
- Additional qualitative data on the clinical relevance of FXS behaviors to caregivers and patients will be collected
  - Based on FDA's Voice of the Patient Guidance

CONNECT-FX
Top Line Results Expected in 2H2019

- **With positive results from this trial, Zynerba intends to request a meeting with the FDA to:**
  - **Determine the acceptability of these data as the basis for an NDA filing**
  - **Seek advice on preparation of our marketing authorization**
- **We believe ZYN002 indication may include the treatment of behavioral symptoms associated with Fragile X syndrome**
- **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

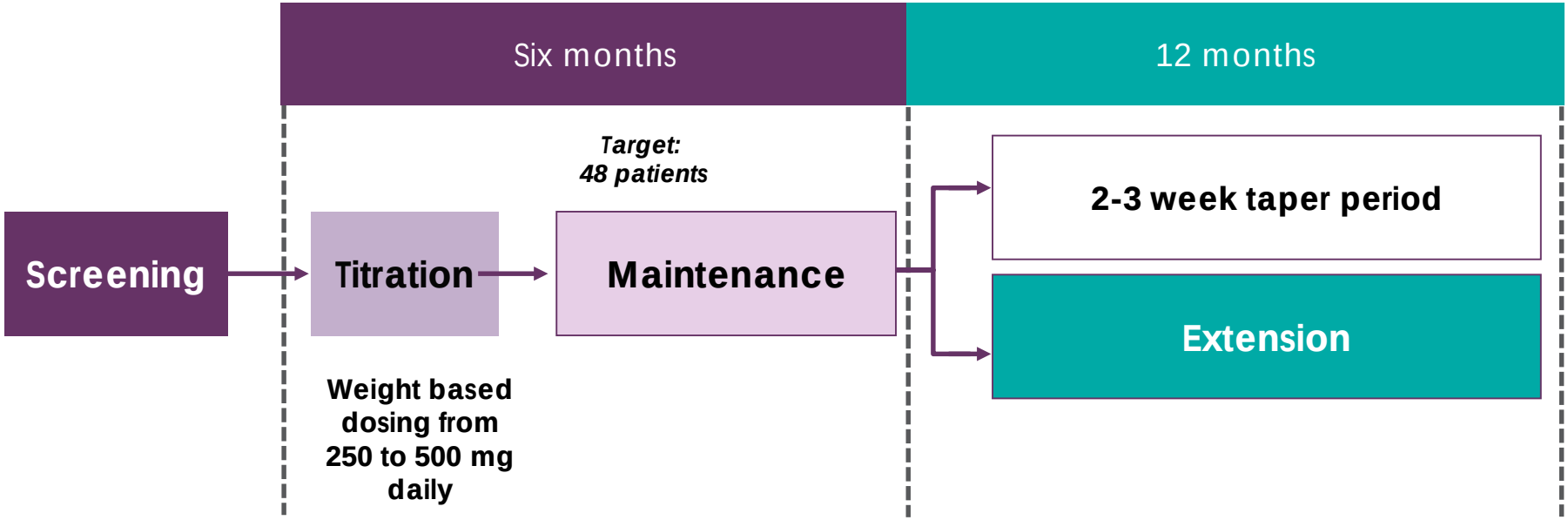
- **Heterogeneous group of rare and ultra rare epilepsy syndromes associated with severe cognitive impairment and behavioral disturbances**
- **~45,000 U.S. children and adolescents with DEE**
- **Syndromes involve:**
  - **Significant developmental impairment (*developmental* encephalopathies)**
  - **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**

Developmental & Epileptic Encephalopathies
BELIEVE 1 New Phase 2 Program Initiated April 2018

- Third party clinical data show impact of CBD on seizures and behavioral issues in children
- DEE classified by the International League Against Epilepsy (ILAE) (Scheffer et al. 2017)
- Patient enrollment in BELIEVE 1 Phase 2 study underway
  - Six month multi-dose study in ~50 DEE patients (3 to <18 years)
  - Approximately half may have either Dravet or Lennox-Gastaut syndrome
  - Primary efficacy assessment: change in seizure frequency
- Results expected in 2019

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; enrollment ongoing

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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 Study Initiation Anticipated in 2H2018

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 continued improvement in seizure control in adult refractory focal seizure patients receiving ZYN002 through 12 months of open label exposure
  - Presented in Late Breaking poster session 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

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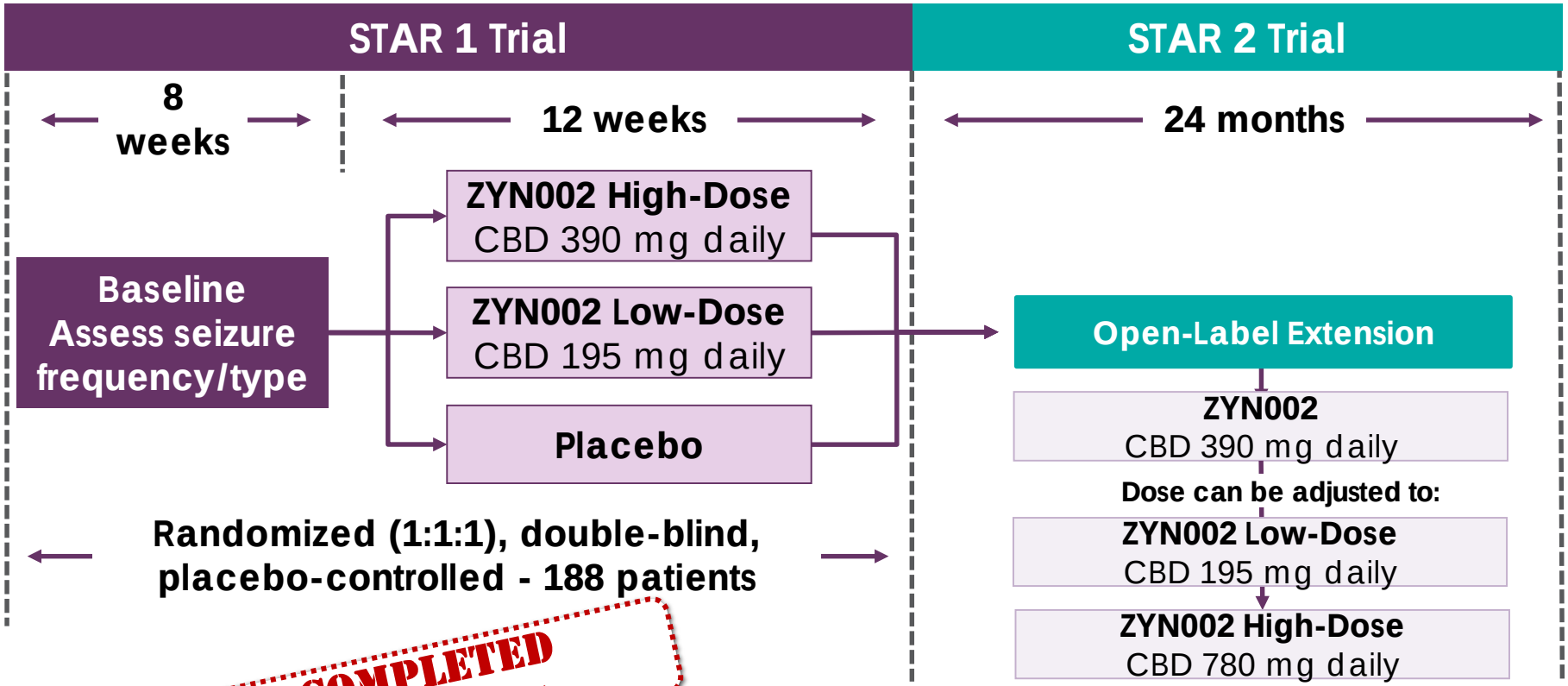
Epilepsy Phase 2 Clinical Study
Trial Design

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

- **98 patients have reached 9 mo. of total drug exposure; 84 have reached 12 months***
- **Excellent tolerability**
- **Data suggest continued improvement in seizure control with longer term use**

Learnings provide input into revised Phase 2B clinical trial design

Twelve Month STAR 2 data presented during Emerging Science (Late Breaker) poster session at the 2018 American Academy of Neurology (AAN) meeting

*As of July 9, 2018

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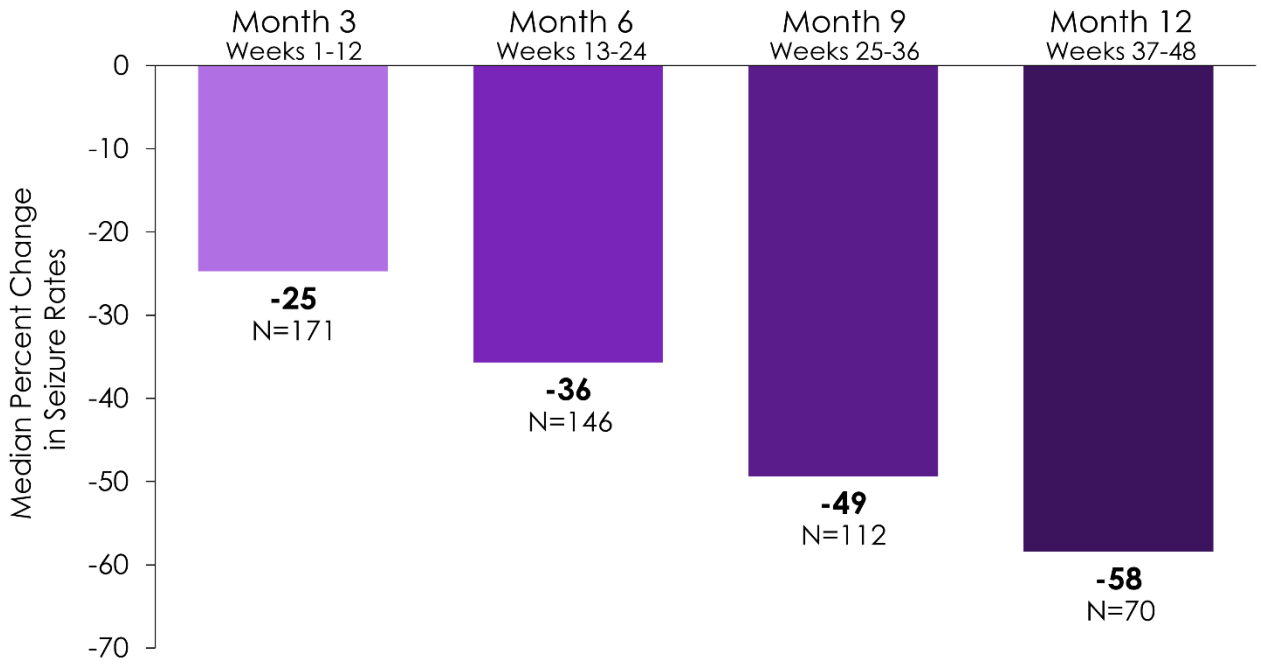
Data Presented at 2018 AAN

STAR 2 Efficacy Data

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

All ZYN002-Treated Patients in STAR 2



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

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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 2H2018

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 March 31, 2018

- **Cash and cash equivalent position of $52.1 million**
- **Well capitalized, expect cash to fund operations into 2H2019**

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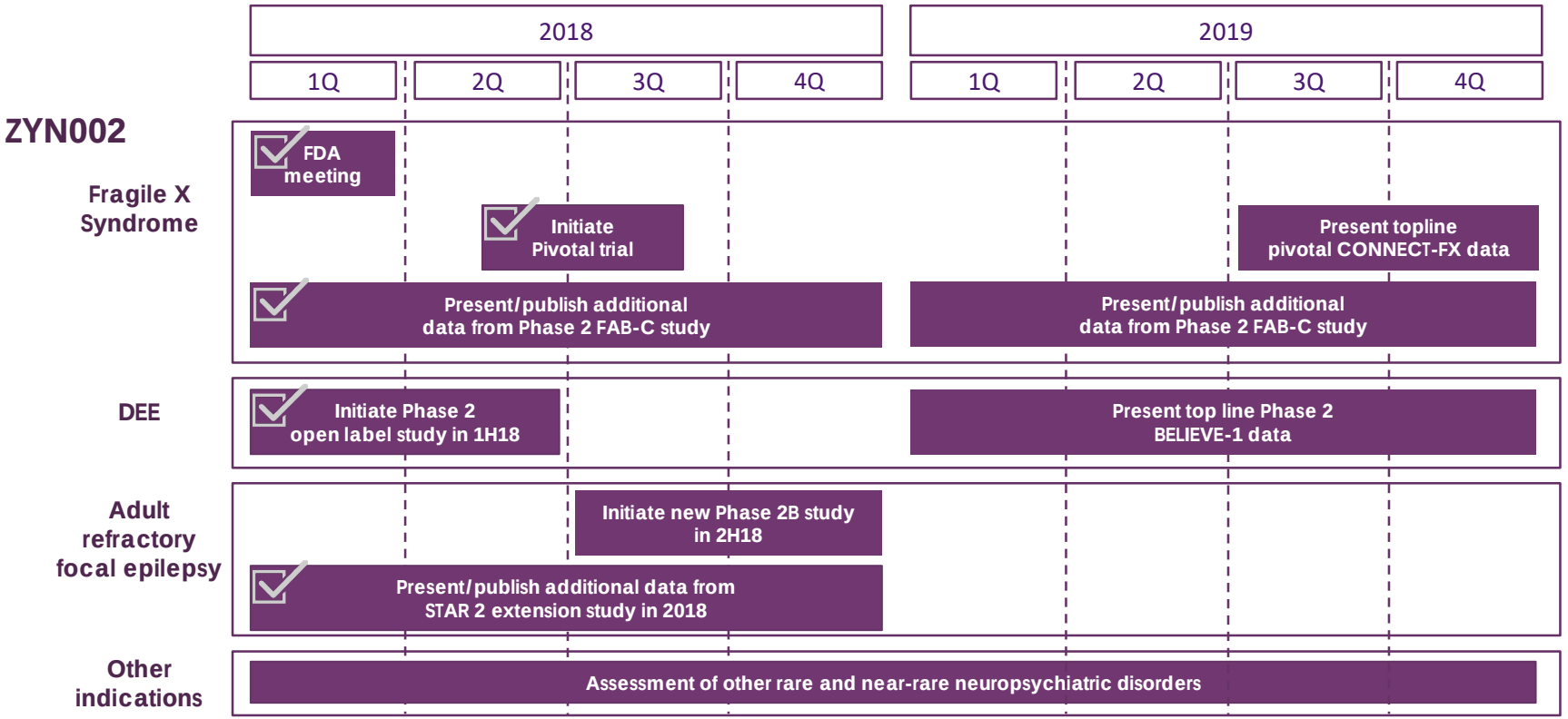
Expected 2018 and 2019 Milestones



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Fragile X Syndrome Epilepsy

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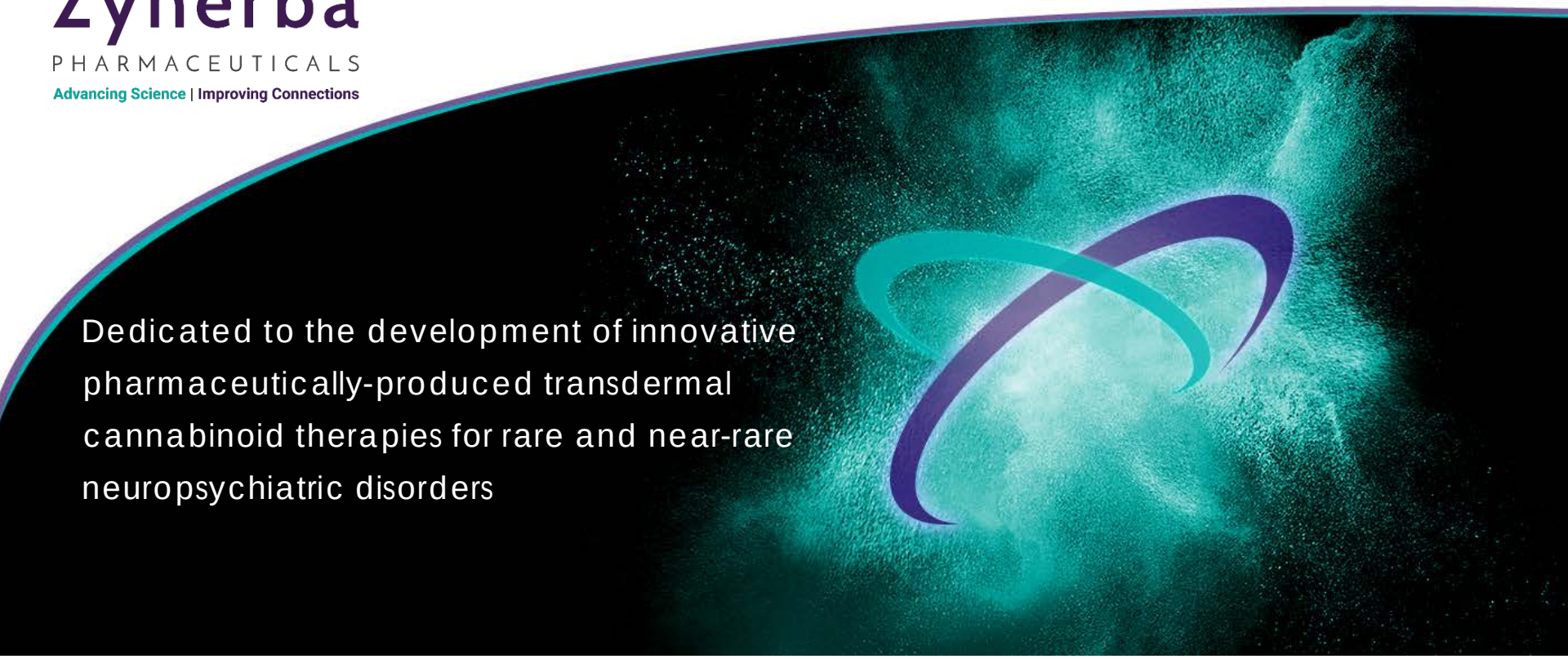

Dedicated to the development of innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders

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