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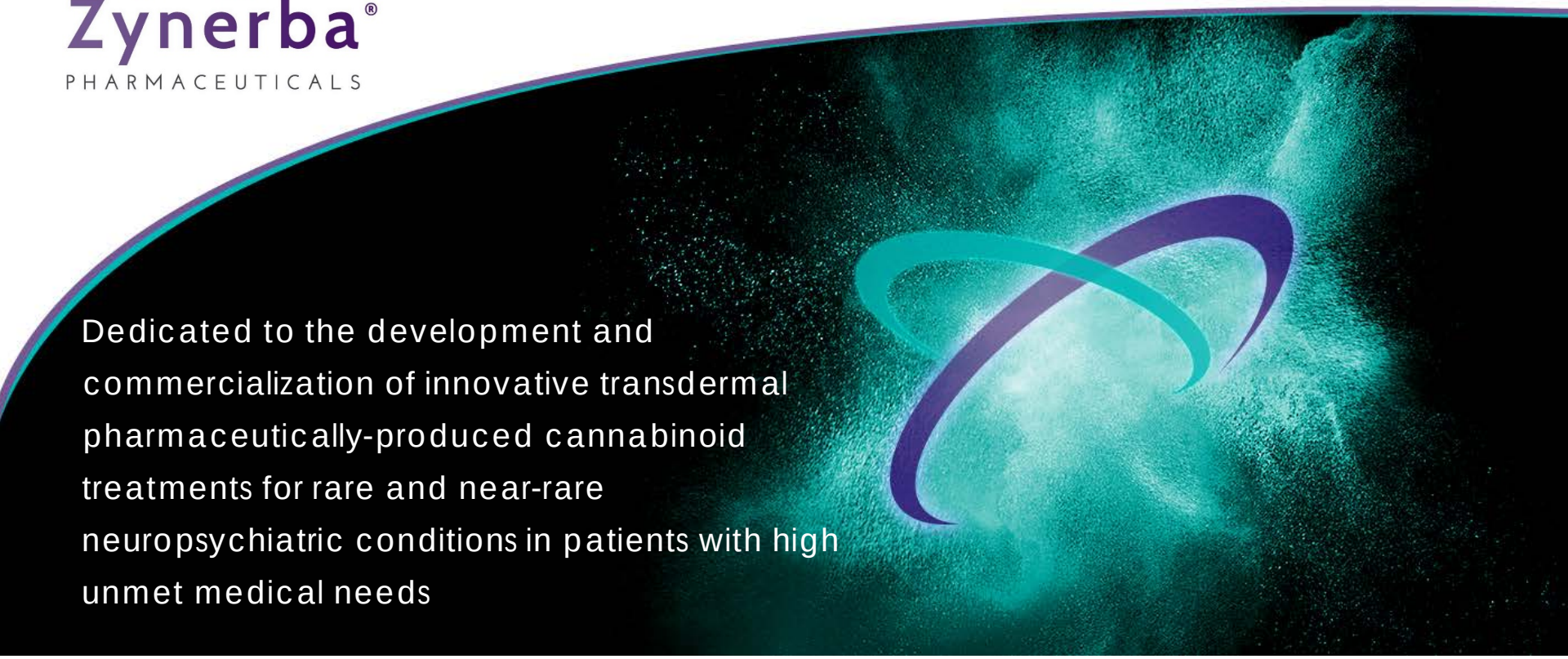

Strategy Focused on Rare and Near-Rare Neuropsychiatric Disorders
January 4, 2018

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Rare/Near-Rare Neuropsychiatric Strategy

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

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Rare/Near-Rare Neuropsychiatric Strategy

- **Concentrating on rare (orphan; <200K patients) and near-rare (<1 million patients) neuropsychiatric diseases:**
  - **ZYN002 (CBD gel)**
    - **Fragile X Syndrome: 1Q18 meeting with FDA; plan to initiate pivotal program mid-year 2018**
    - **Developmental and epileptic encephalopathies (DEE): Plan to initiate pediatric/adolescent trial in 1H18**
    - **Adult refractory focal epilepsy: Plan to initiate Phase 2B trial in 2H18**
    - **Assessing other potential neuropsychiatric indications**
  - **ZYN001 (THC prodrug patch)**
    - **Expect to complete ongoing Phase 1 trials in 1H18**
    - **Tourette Syndrome: Plan to initiate Phase 2 trial in late 2H18**
    - **Assessing other potential neuropsychiatric indications**
- **Discontinuing investment in capital-intensive pain programs**
  - **ZYN002 in osteoarthritis**
  - **ZYN001 in fibromyalgia and PNP**

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Rare/Near-Rare Neuropsychiatric Strategy

- **High unmet medical needs and significant market opportunities**
  - **Fragile X Syndrome: ~71K US patients; no approved products**
  - **DEE: Category of rare and ultra rare, severe brain disorders manifesting with seizures, including Lennox-Gastaut and Dravet syndromes**
  - **Refractory focal epilepsy: AEDs fail in ~500K US patients**
  - **Tourette Syndrome: ~200K US patients with most severe form of TS**
- **Opportunities for efficient development and commercialization strategy**
  - **Orphan drug designation provides opportunity for rapid development/approval**
  - **FDA Breakthrough Therapy Designation, Fast Track Status, Accelerated Approval or Priority Review Designation, if granted, can accelerate approval of drugs that meet respective criteria**
  - **Targeted physician audience = modest commercial investment**
  - **Potential for consistent pricing across indications**
- **Expected reduction in long term capital requirements by discontinuing pain programs**

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

- **Inherited autism spectrum disorder with 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

ZYN002 in Fragile X Syndrome

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

FAB-C Secondary Endpoint: 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)*

- **Primary endpoints achieved in FAB-C 12 week Phase 2 open label study**
  - **46% improvement (p<0.0001) in the ADAMS total score at week 12 vs baseline**
  - **Results of secondary endpoints reinforce the results demonstrated in ADAMS**
- **Meeting scheduled with FDA in 1Q18 to discuss development strategy including clinical pivotal program**
- **Expect to initiate Phase 2/3 pivotal program in mid-year 2018**
- **Evaluating opportunities for FDA fast-track status, breakthrough therapy designation, and/or accelerated approval**
- **Assessing opportunity to present / publish full data set as soon as possible in 2018**

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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

- Category of rare and ultra-rare severe brain disorders that manifest with seizures or EEG abnormalities that can directly worsen cognition or behavior
- Often progressive; highly resistant to treatment
- Treatment of seizures or EEG abnormalities expected to improve the cognitive or behavioral deficits and reduce the seizures
- Third party clinical data show impact of CBD on seizures and behavioral issues

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Proposed Phase 2 Study of ZYN002 in DEE
Trial Design*

- **Expect to initiate open label study in 1H18**
- **48 pediatric and adolescent patients (3 to <18 years old)**
- **24 week, multi-dose trial ranging from 195 mg/day to 780 mg/day**
- **Primary endpoints: reduction in seizures at 12 weeks and 24 weeks**
- **Results will determine next steps**
- **Twelve month extension trial to follow**

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

Refractory Focal Epilepsy
STAR 1 and STAR 2 Findings

- Learnings provide input to a revised Phase 2b clinical trial design
- Company believes that 12 week STAR 1 Phase 2 study missed primary endpoint due to bimodal distribution of placebo patient responses
- Response to ZYN002 correlated to baseline seizure severity
  - Patients with severe epilepsy (>15 seizures/month) receiving ZYN002 had greater percent seizure reduction than patients with less severe epilepsy (<15 seizures/month)
- ZYN002 was very well tolerated in STAR 1 and STAR 2
- STAR 2 data suggest clinically meaningful response with longer term use of ZYN002

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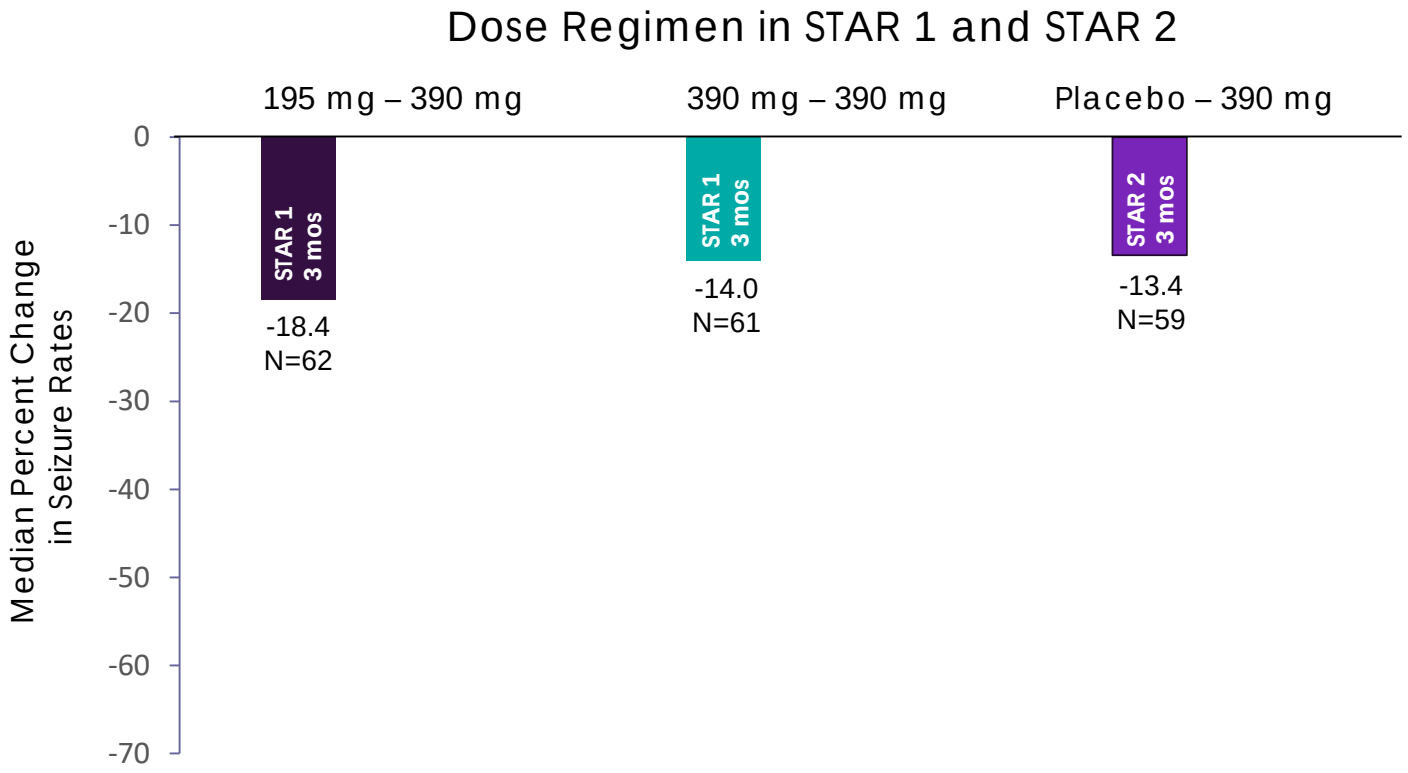
Consistent Results at Various Timeframes

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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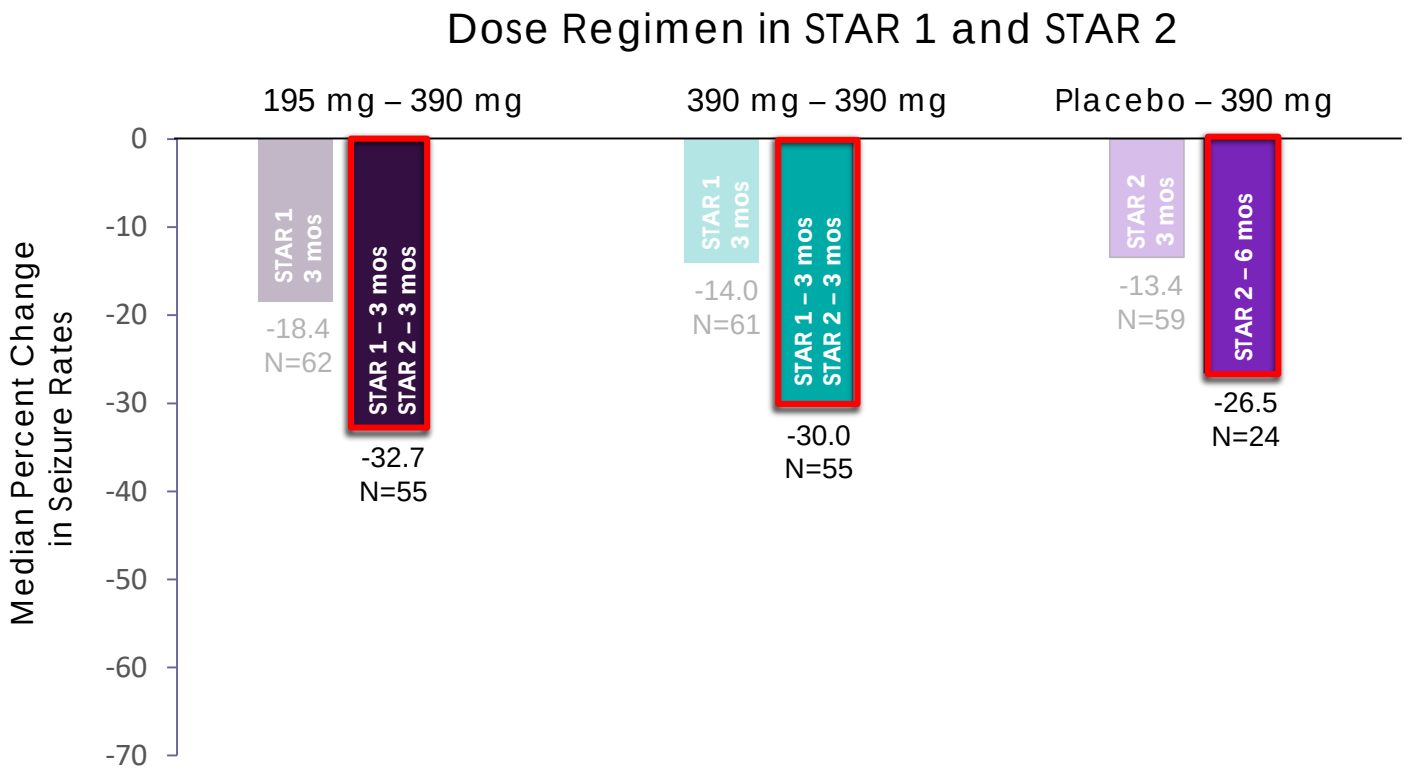
Consistent Results at Various Timeframes

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.

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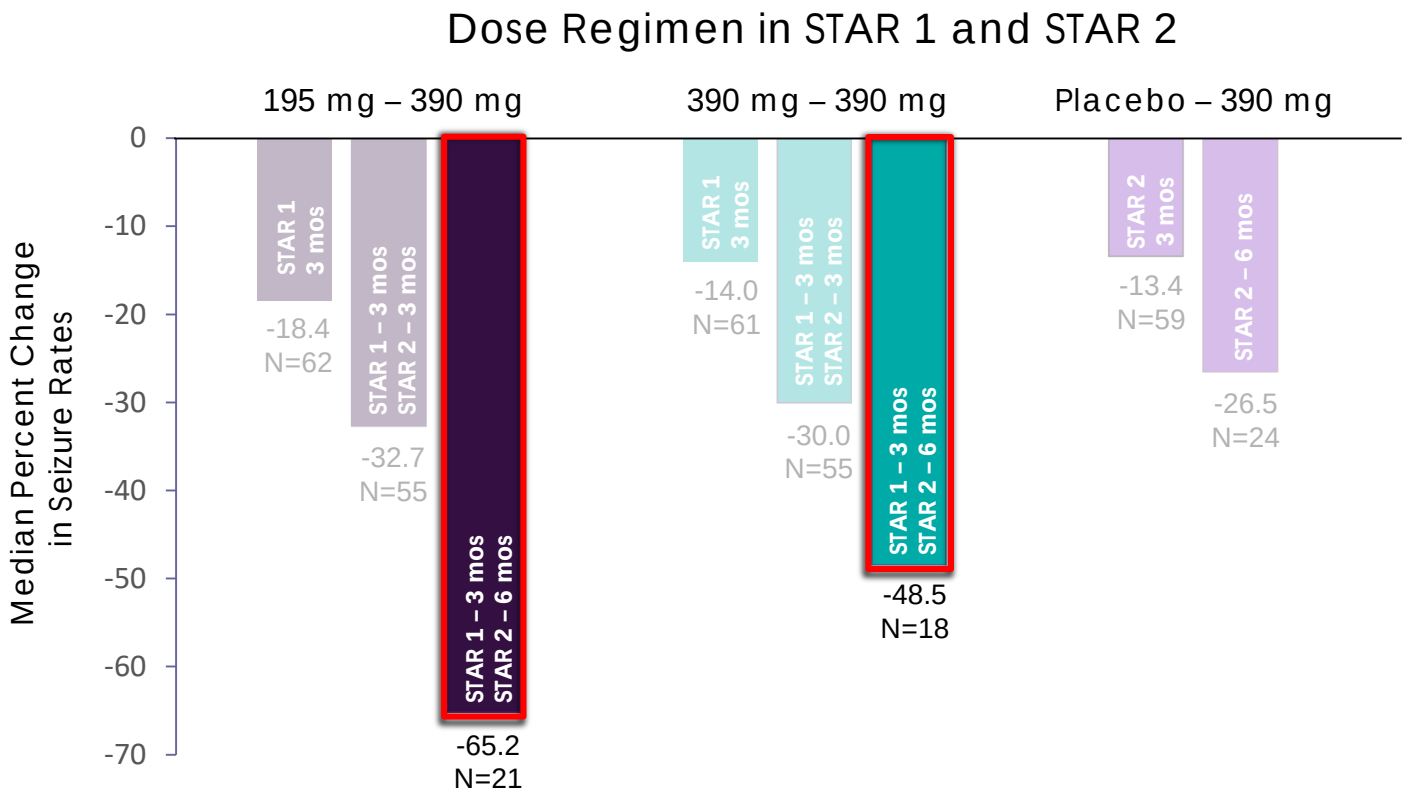
Consistent Results at Various Timeframes
Nine Months on ZYN002



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Proposed Phase 2b Study
Adult Refractory Focal Epilepsy

Design*

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

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

Expected to initiate in 2H18

Open label extension to follow

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

Potential for THC in Tourette Syndrome (TS)

Overview

- Neurodevelopmental disorder characterized by motor / vocal tics
  - Evident in early childhood
  - ~200K US pts have most severe form according to the National Institute of Neurological Disorders and Stroke
  - Up to 1:100 exhibit milder and less complex symptoms

Rationale

- Central cannabinoid receptor system believed to play role in Tourette Syndrome pathology
- Two third party double blind, placebo controlled studies show activity of THC in TS
  - Assessments included self- and examiner-rated scales validated in TS (TSSL, TS-CGI, YGTSS, others)
  - Statistical significance achieved vs placebo in tic severity and obsessive compulsive behavior

Phase 2 study expected to initiate in late 2H18

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Liza Squires, MD
Newly Created Role of Chief Medical Officer

- **Responsibilities will include clinical strategy and execution, clinical research, medical affairs, regulatory affairs, and drug safety and surveillance**
- **25 years of experience in rare and neuropsychiatric disorders**
  - **Vice President, Therapeutic Area Head, Neuroscience for Aevi Genomic Medicine**
    - **Led neuroscience product strategy and development**
  - **Chief Medical Officer for Lumos Pharma**
    - **Developed an accelerated development strategy for an ultra-orphan population**
  - **10 years at Shire Pharmaceuticals, culminating as Vice President of R&D and Product General Manager of CNS Early Pipeline**
  - **Director of Pediatric Neurology for DeVos Children's Hospital**
- **Board certified in Neurology and Psychiatry, and Pediatrics**

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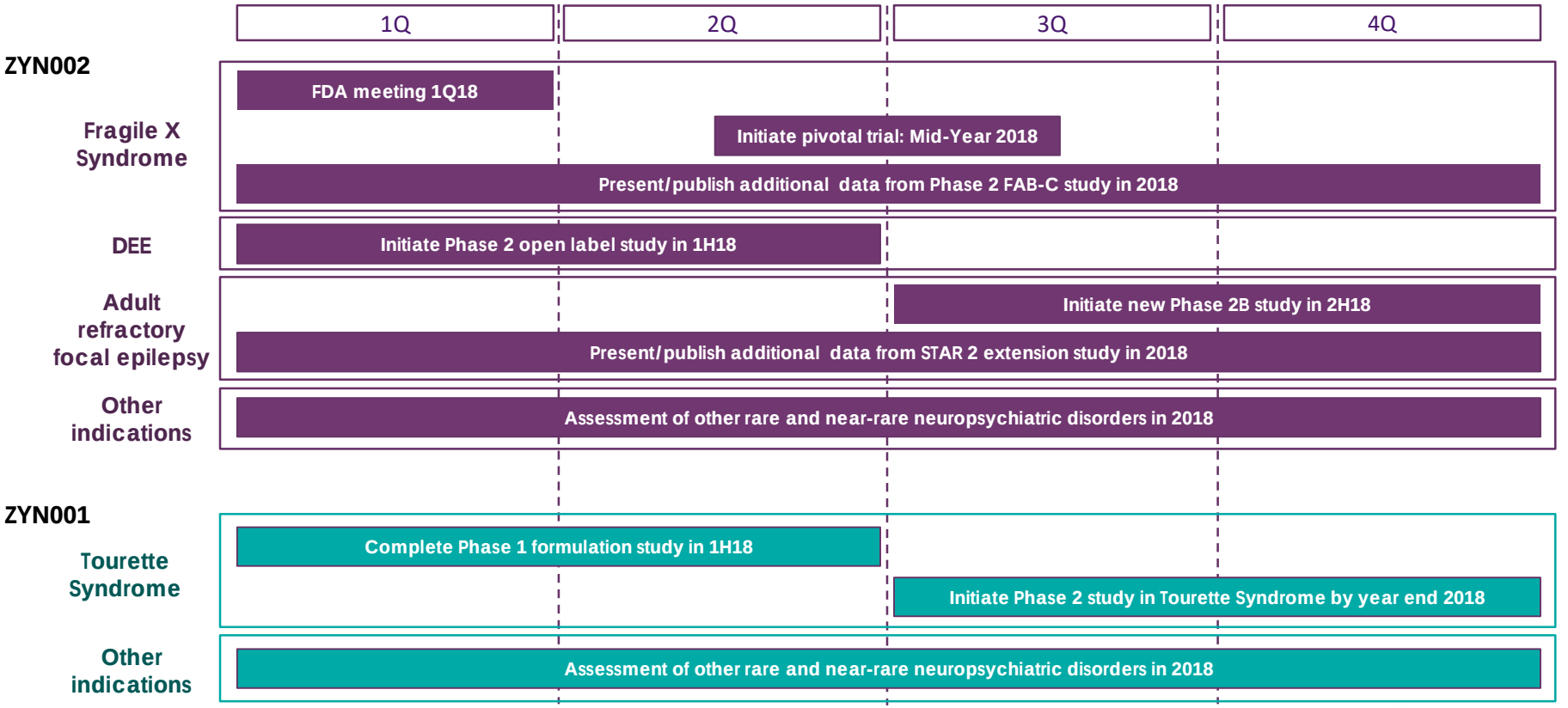
Expected 2018 Milestones



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Zynerba Is Well Positioned to Execute on Neuropsychiatric Focused Strategy

- **Experienced team with proven development and commercialization track record in transdermal delivery, orphan diseases, neurology, and psychiatry**
- **Global ownership of two proprietary product candidates with potential applicability to numerous neuropsychiatric disorders**
- **Capital efficient development and commercialization strategy anticipated**
- **Multiple expected milestones in 2018**
- **Well capitalized with cash runway well into 2019**

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Question & Answer Session

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