Cantor 2019 Global Healthcare Conference

October 3, 2019

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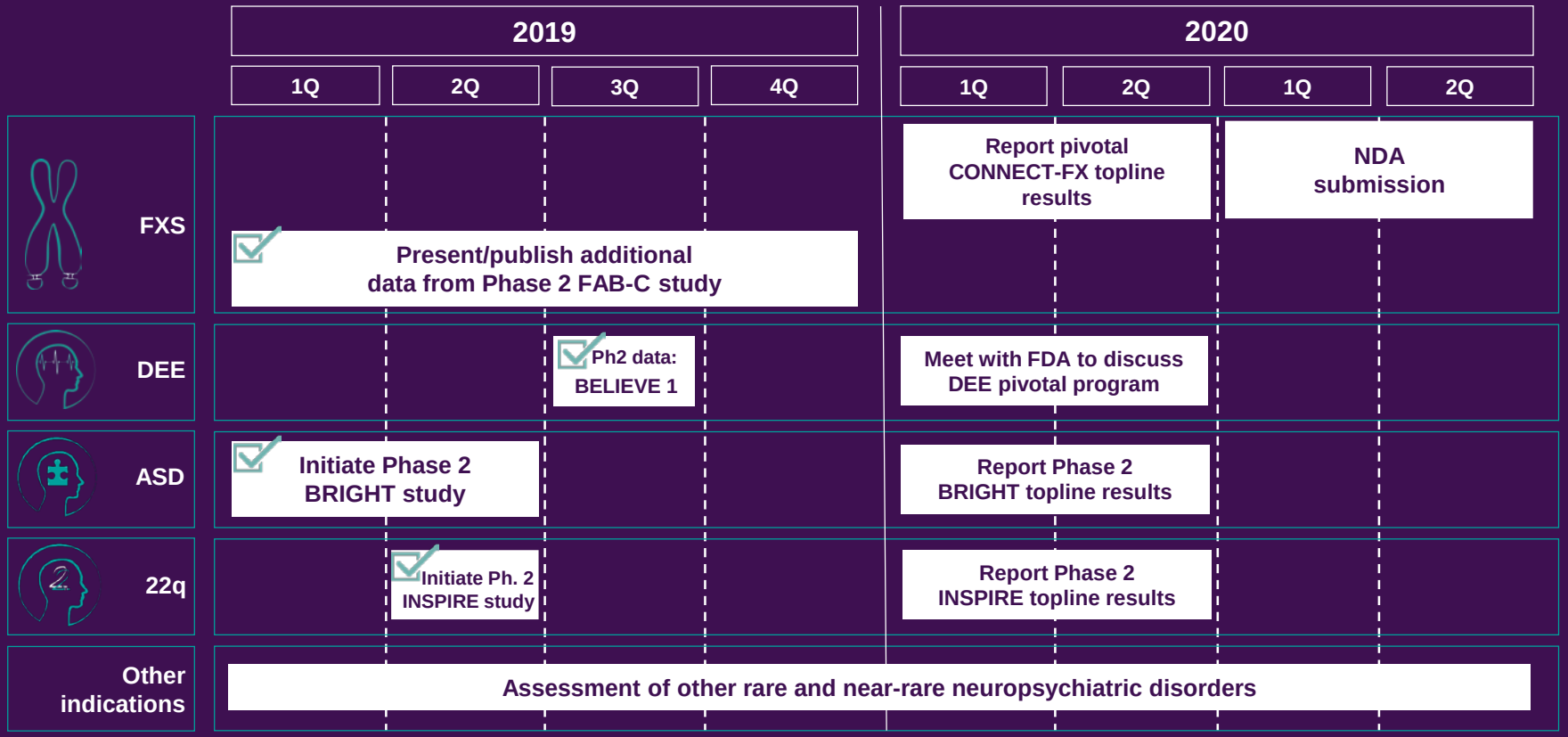
Zynerba Pharmaceuticals (NASDAQ: ZYNE)

A Rare/Near-Rare Neuropsychiatric-focused Pharmaceutical Company

- Deep pipeline focused on high unmet medical needs; translating into multi-billion dollar market opportunity with Zygel™ (CBD transdermal gel)
  - Four clinical shots on goal: FXS, DEE, ASD, 22q
  - Reported compelling safety and efficacy data in BELIEVE 1 DEE open label Phase 2 trial (September 18, 2019)
- 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

Expected Milestones into 2020



Compelling Results from the BELIEVE 1 Trial Appear to have been Misinterpreted

- DEE is a medically fragile population and adverse events are common and expected
- Safety results:
  - Zygel was well tolerated
  - Consistent with previously reported Zygel studies
  - May compare favorably to tolerability profiles of reported safety data from oral CBD solution[1] and other currently available AEDs[2]
- Zynerba approach to FDA approval will likely focus on most common and disabling seizure types in DEE, rather than patient syndromes
- Efficacy results:
  - Clinically meaningful reductions in seizures beginning in month two and sustained through six months
  - Suggest improvements on important behavioral symptoms

[1]Devinsky - *Lancet Neurol* 2016

[2]Moavero – *Expert Opin Drug Saf*, 2018

DEE Patients are Medically Fragile

- Group of rare / ultra rare childhood-onset epilepsies with impaired or regressed developmental progress
- Cognitive impairment, psychiatric problems, and behavioral disturbances are phenotypic
- Medically fragile population
  - Comorbidities include cerebral palsy, chronic respiratory infections, gait disturbances, movement disorders, scoliosis, and feeding problems
  - Many wheelchair bound with feeding tubes
- Most common and debilitating seizure types in DEEs are:
  - Focal impaired-awareness seizures (FIAS) – formerly known as complex partial
  - Focal to bilateral tonic-clonic and generalized tonic-clonic seizures – commonly known as convulsive seizures (CS)

BELIEVE 1 Safety

Well Tolerated over 6 Month Trial

- DEE is a fragile population; adverse events (AEs) common and expected
- 96% of patients experienced an AE
  - All events whether unrelated or related to study drug were reported as AEs (e.g.: influenza, runny nose, ingrown toenail, scrapes, etc.)
  - Most were mild and transient
  - Only one patient discontinued due to an AE (application site reaction)
- Ten patients experienced a serious adverse event (SAE)
  - Eight were unrelated to study drug
  - Two possibly drug-related (LRTI and status epilepticus)
- No hepatic, gastrointestinal, or lethargy-related SAEs
- Consistent with the safety database for Zygel
  - May compare favorably to tolerability profiles of reported safety data from oral CBD solution[1] and other currently available AEDs[2]

[1]Devinsky - *Lancet Neurol* 2016

[2]Moavero – *Expert Opin Drug Saf*, 2018

Planned Approach to FDA – All DEE Patients with Consciousness Impairing Seizures

Syndromes and encephalopathies

Dravet	Lennox Gastaut	West	Hypoxic-ischemic enceph.	Early myoclonic epilepsy
Doose	Ohtahara	Landau Kleffner	CDKL5 enceph.	Other Syndromes

Seizure type

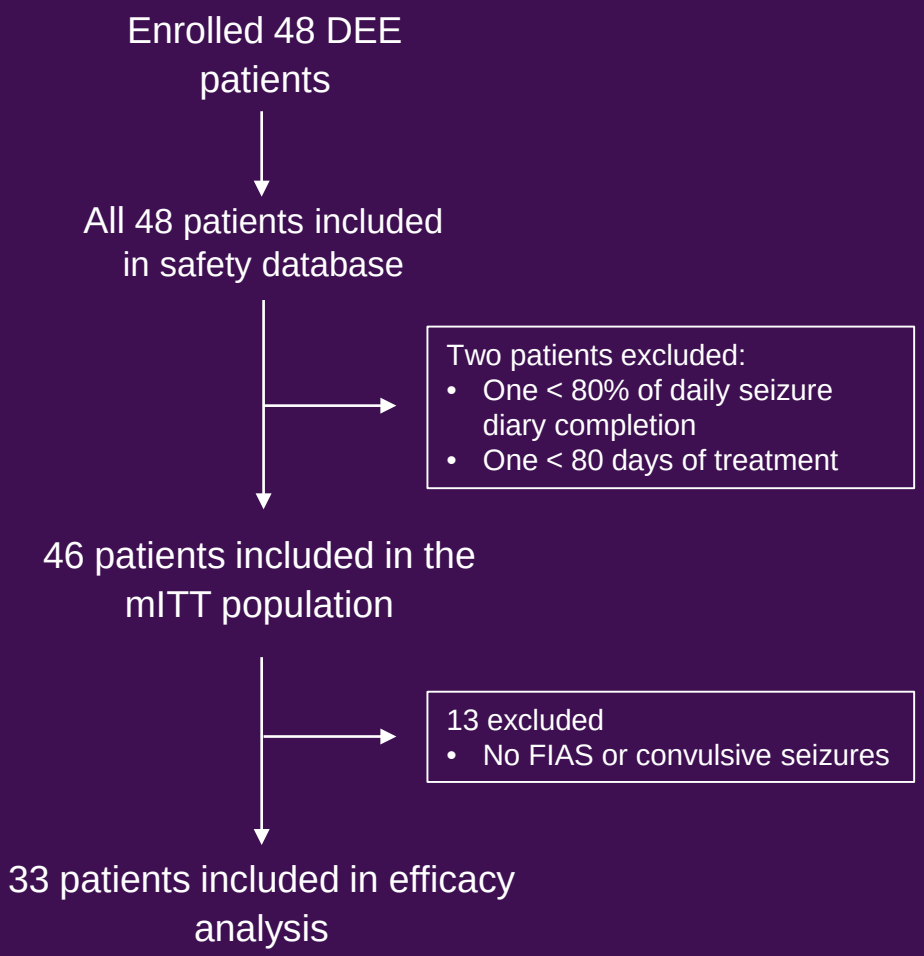
Convulsive

- Focal Impaired Awareness
- Bilateral Tonic Clonic
- Generalized Tonic Clonic

Consciousness impairing seizures

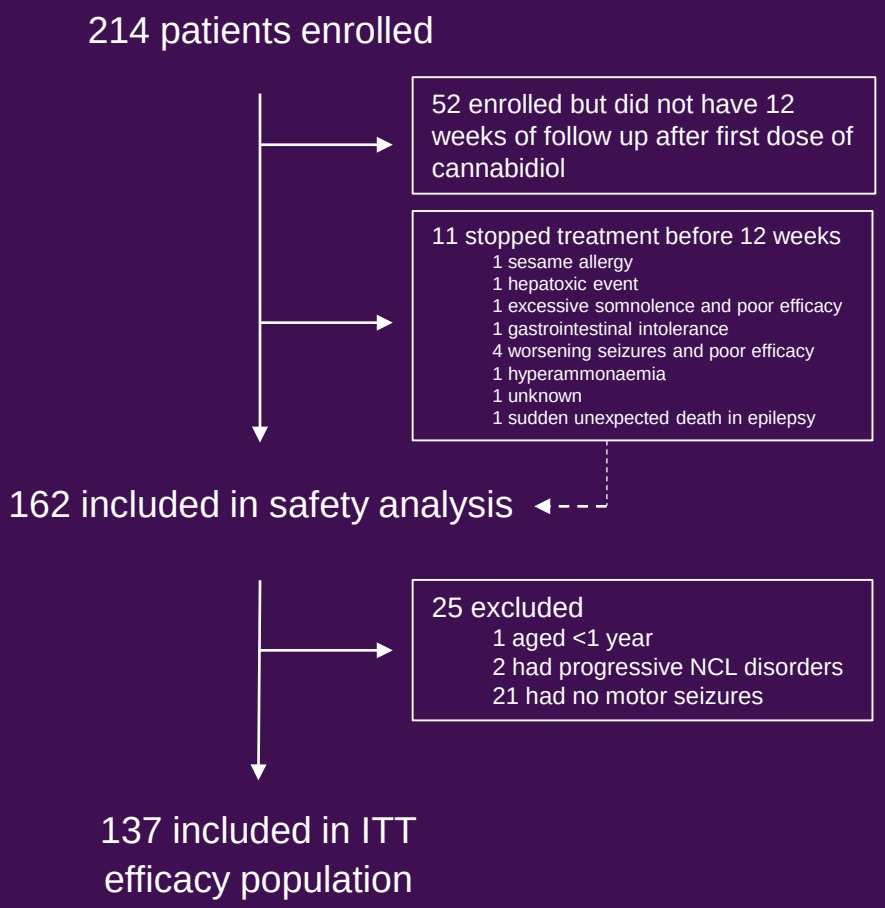
- Focal aware
- Absence
- Other Seizure types

BELIEVE 1 Patient Disposition



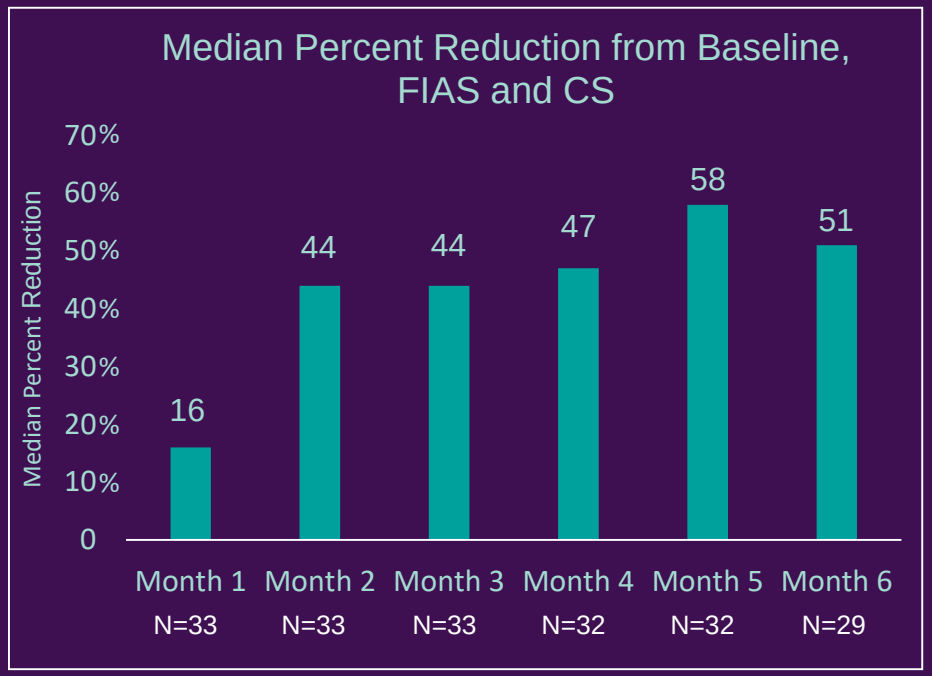
Oral CBD Solution Open Label Patient Disposition

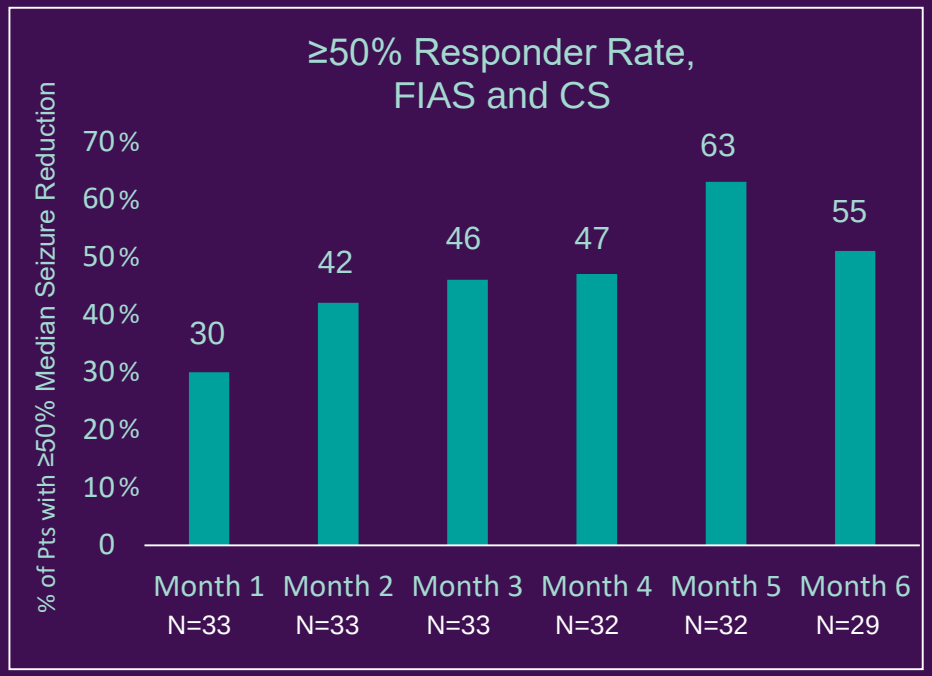
Devinsky, *Lancet Neurol* 2016



Note: Head to head clinical trials with Zygel and Epidiolex® were not undertaken and information in this slide is sourced from publicly available data.

BELIEVE 1: Clinically Meaningful Seizure Reductions from Baseline and Sustained through Six Months in DEE



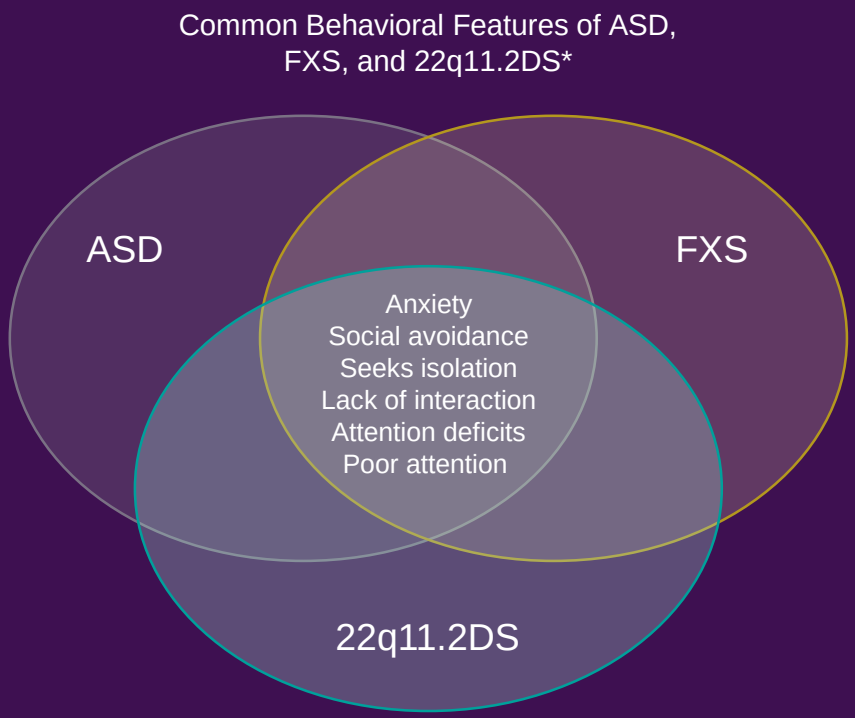


BELIEVE 1: Qualitative Assessments of Behavioral and Cognitive Improvements

- Parents and caregivers provided qualitative assessment on their child's overall experiences with Zygel
- Improvements were seen in seizure intensity and duration, and socio-behavioral and cognitive impairments
- Improvements in >25% of children:
  - 58% reported improved vitality (e.g. alertness / awareness, energy)
  - 51% reported improvement in seizures
  - 47% reported improved cognition and concentration
  - 44% reported improved socially avoidant behaviors
  - 28% reported that their child attended school on time / more often
- Improvements in socio-behavioral and cognitive impairments provide additional confidence in design of FXS, ASD and 22q11.2DS (22q) studies

Improvements in Behavior May Provide a Read-Through to Other Zygel Studies

- Presented data at SSBP* showing constellation of shared socio-behavioral symptoms in ASD, FXS, and 22q
- These include anxiety leading to:
  - Isolation and social avoidant behaviors
  - Irritability
  - Attention deficits
  - Poor communication
- Qualitative data from BELIEVE 1 suggest improvements in overlapping behaviors in ASD, FXS, and 22q



Common Behavioral Features of Autism, Fragile X Syndrome, and 22q11.2 Deletion Syndrome, SSBP, 2019

Compelling Results Suggest a Pathway to Pivotal Trials – Anticipate Meeting with FDA in 1H2020

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