Corporate Overview

JANUARY 2023

Forward Looking Statement/Safe Harbor

This slide presentation and the accompanying oral commentary contain forward-looking statements that involve risks, uncertainties and assumptions. If the risks or uncertainties ever materialize or the assumptions prove incorrect, our results may differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to, statements regarding research and clinical development plans and timelines; the timing of and future results from clinical trials, including those related to XEN1101; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101; the anticipated timing of IND, or IND-equivalent, submissions and the initiation of future clinical trials for XEN1101; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in the XEN1101; the timing and results of our interactions with regulators; and anticipated enrollment in our clinical trials and the timing thereof.

These statements are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many factors, including but not limited to: the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; promising results from pre-clinical development activities or early clinical trial results may not be replicated in later clinical trials; our assumptions regarding our planned expenditures and sufficiency of our cash to fund operations may be incorrect; our ongoing discovery and pre-clinical efforts may not yield additional product candidates; any of our or our collaborators' product candidates, including XEN1101, may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; we may not achieve additional milestones in our proprietary or partnered programs; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators' clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; impact of new or changing laws and regulations; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission and the securities commissions in British Columbia, Alberta and Ontario. Except as required by law, we assume no obligation and do not intend to update these forward-looking statements or to conform these statements to actual results or to changes in our expectations.

Xenon Overview

- Neurology-focused biopharma company; leader in small molecule, ion channel drug development with robust pipeline
- Lead program XEN1101 represents most advanced potassium channel modulator in clinical development
  - Positive Phase 2b X-TOLE data demonstrated statistically significant seizure reduction in difficult-to-treat focal onset seizure epilepsy patient population with differentiated clinical profile
  - Recently initiated Phase 3 clinical trials in focal onset seizures (X-TOLE2) and primary generalized tonic clonic seizures (X-ACKT)
  - Ongoing Phase 2 clinical trial in major depressive disorder, an important co-morbidity in epilepsy
  - Comprehensive intellectual property portfolio with patent coverage extending to 2039/40
- Strong financial position
  - $752.2 million in cash, cash equivalents and marketable securities with runway into 2026 (as of Sept. 30, 2022)

Xenon's Neurology Portfolio

	Compound	Indication		Pre-clinical	Phase 1	Phase 2	Phase 3
Potassium Channel Openers	XEN1101	Focal Onset Seizures (FOS)	X-TOLE2/3				
		Primary Generalized Tonic Clonic Seizures (PGTCS)	X-ACKT				
		Major Depressive Disorder	X-NOVA				
		Major Depressive Disorder	Mount Sinai*				
	XEN496	Orphan Pediatric Epilepsy (KCNQ2-DEE)	EPIK				
	Ion Channel Modulators	Neurological Disorders					

Partnered Programs

Sodium Channel Modulators	NBI-921352	Focal Onset Seizures	Neurocrine				
		Orphan Pediatric Epilepsy (SCN8A-DEE)	Neurocrine				

*Investigator Sponsored Phase 2 Proof-of-Concept Study

XEN1101 Summary

Novel Mechanism

- Differentiated “next generation” K_V7 potassium channel opener being developed for the treatment of epilepsy and other neurological disorders
- Preclinical models and clinical studies suggest K_V7 channel openers and may have broad anti-seizure activity in patients with focal and generalized epilepsy

XEN1101 Clinical Experience

- Phase 2b X-TOLE trial demonstrated statistically significant seizure reduction in a difficult-to-treat FOS patient population with AEs in line with other ASMs
- Alignment with FDA on use of X-TOLE and Phase 3 X-TOLE2 in FOS to support NDA submission
- Phase 3 program underway with X-TOLE2 in FOS and X-ACKT in PGTCS

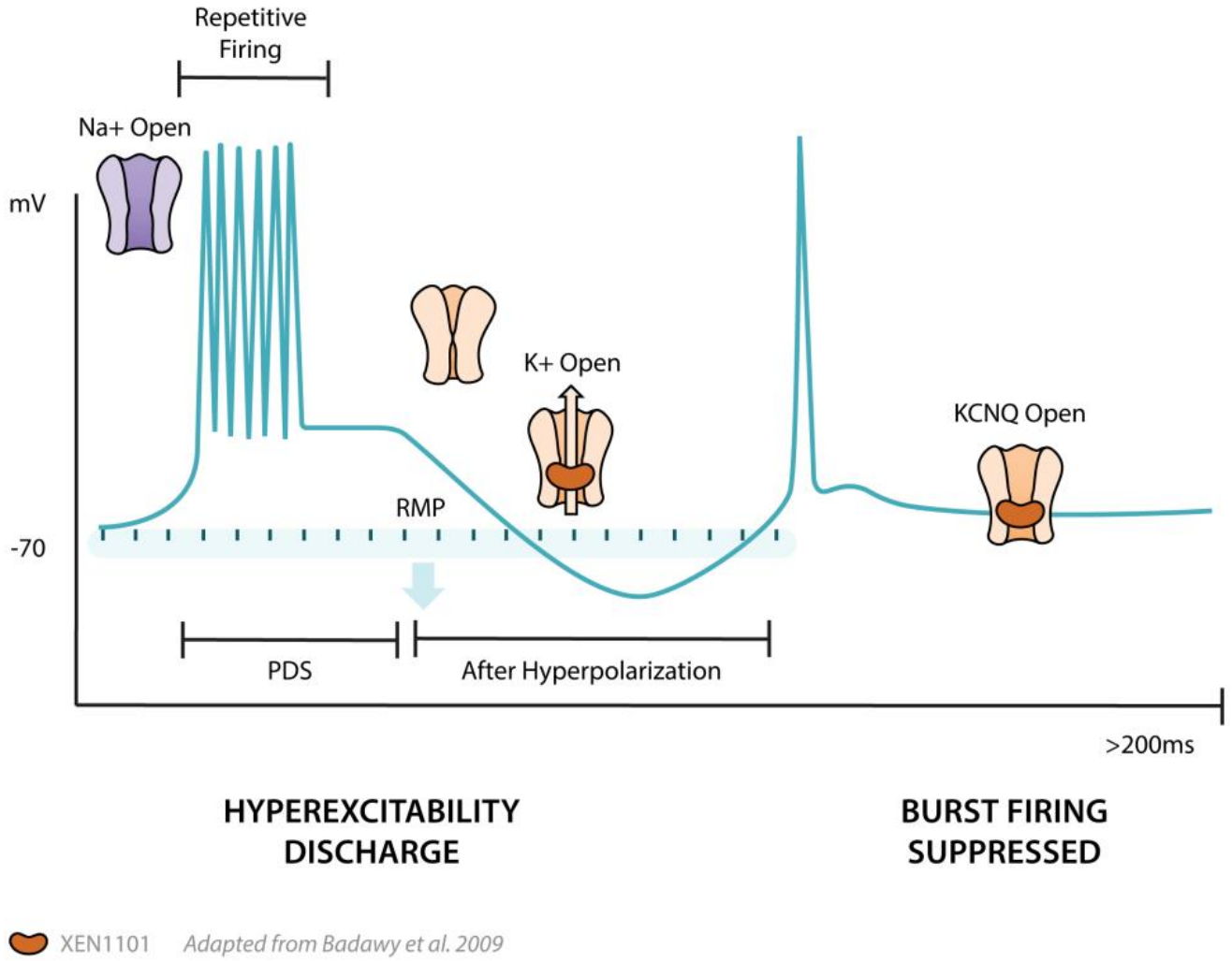
XEN1101 Opportunity

- Substantial medical need remains for new ASMs to treat patients with difficult to control seizures
- In market research, physicians reacted positively to the XEN1101 profile:
  - Broad spectrum benefits with rapid onset, no titration, QD dosing and compelling efficacy
  - Novel MOA that can be used in rational polypharmacy

XEN1101 Expansion Opportunities

- PGTCS are life-threatening seizures, with fewer ASMs available resulting in significant unmet need (Phase 3 X-ACKT clinical trial underway)
- Depression represents a key co-morbidity associated with epilepsy (Phase 2 X-NOVA clinical trial underway)

K_V7 Channels have a Critical Role in Neuronal Firing

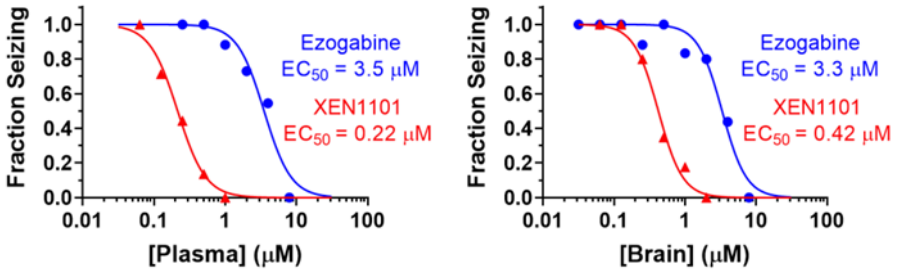


- K+ channels repolarize membranes to end the action potential
- K_V7 channels are translated from the KCNQ gene family (Q1 – Q5)
- Exert important inhibitory control over neuronal firing
- Control unwanted burst and spontaneous firing that can lead to seizures

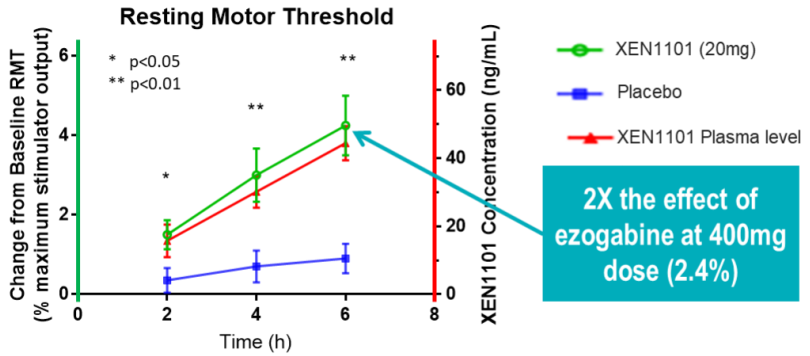
Strong Scientific Rationale and Early-Stage Data for XEN1101

- Solid scientific rationale based on validated MOA (ezogabine)
- XEN1101 demonstrated pre-clinical efficacy across various seizure models
- Strong PK/PD relationship demonstrated in Ph1b TMS study informing Phase 2 dose selection

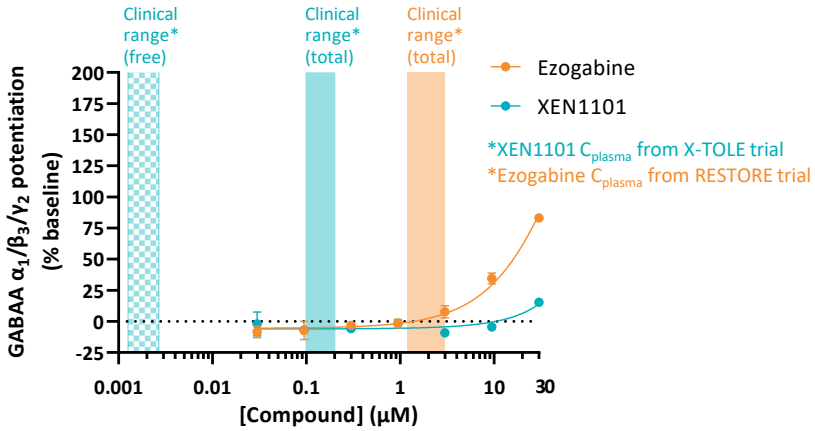
XEN1101 demonstrates activity in the mouse MES assay and compares favorably to ezogabine[1]



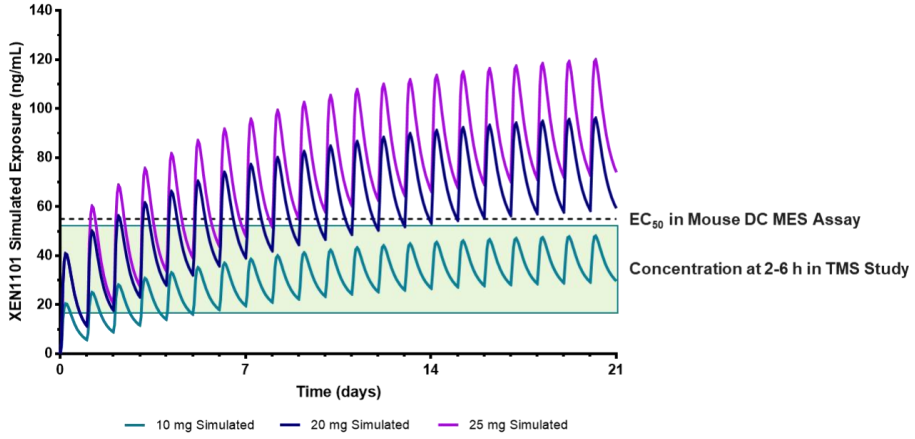
XEN1101 induced changes in corticospinal excitability as assessed using Transcranial Magnetic Stimulation (TMS)[2]



XEN1101 does not positively modulate $GABA_A$ at up to 50x clinically relevant therapeutic concentrations[3]

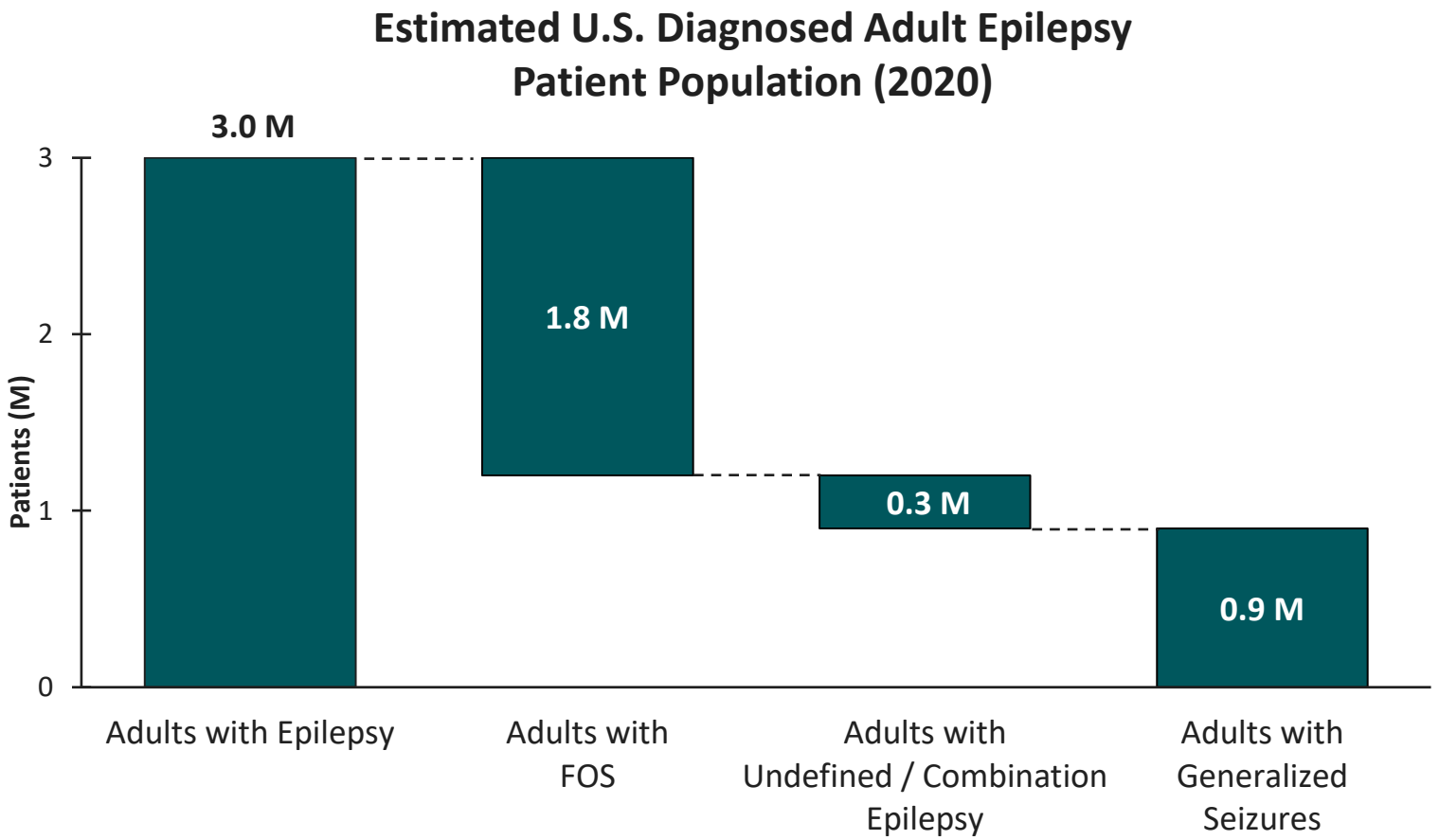


Projected XEN1101 plasma levels (based upon PK parameters in Phase 1) informed Phase 2 dose selection[2]



[1]Company Poster. 2020 AES Annual Meeting: "Preclinical In Vitro and In Vivo Comparison of the KV7 Activator XEN1101 with Ezogabine." Dec. 2020
[2]Company Poster. 2019 AES Annual Meeting: "Use of Transcranial Magnetic Stimulation Data in the Design of a Dose Ranging Finding Efficacy, Safety, Tolerability and Pharmacokinetics Study of XEN1101 in Patients with Focal Epilepsy." Dec. 2019
[3]Company Research (unpublished)

Adult Epilepsy Epidemiology

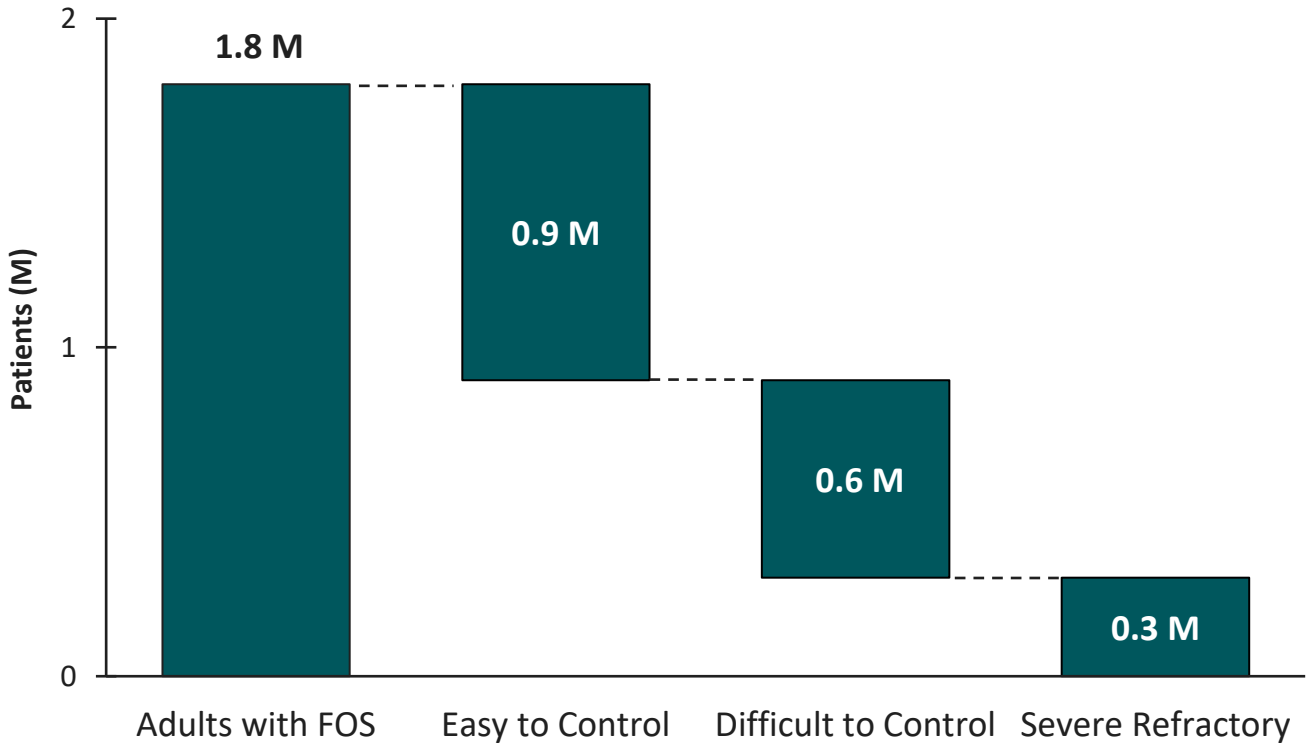


- Focal onset seizures (FOS) represent the largest segment of the epilepsy population in the U.S.
- Generalized epilepsy is the next most common form; the majority of adult patients with generalized epilepsy experience PGTCS (~80%)
- Despite the availability of multiple antiseizure medications (ASMs), a substantial unmet medical need exists for novel therapeutic options that can reduce seizure burden in patients who experience consistent seizures

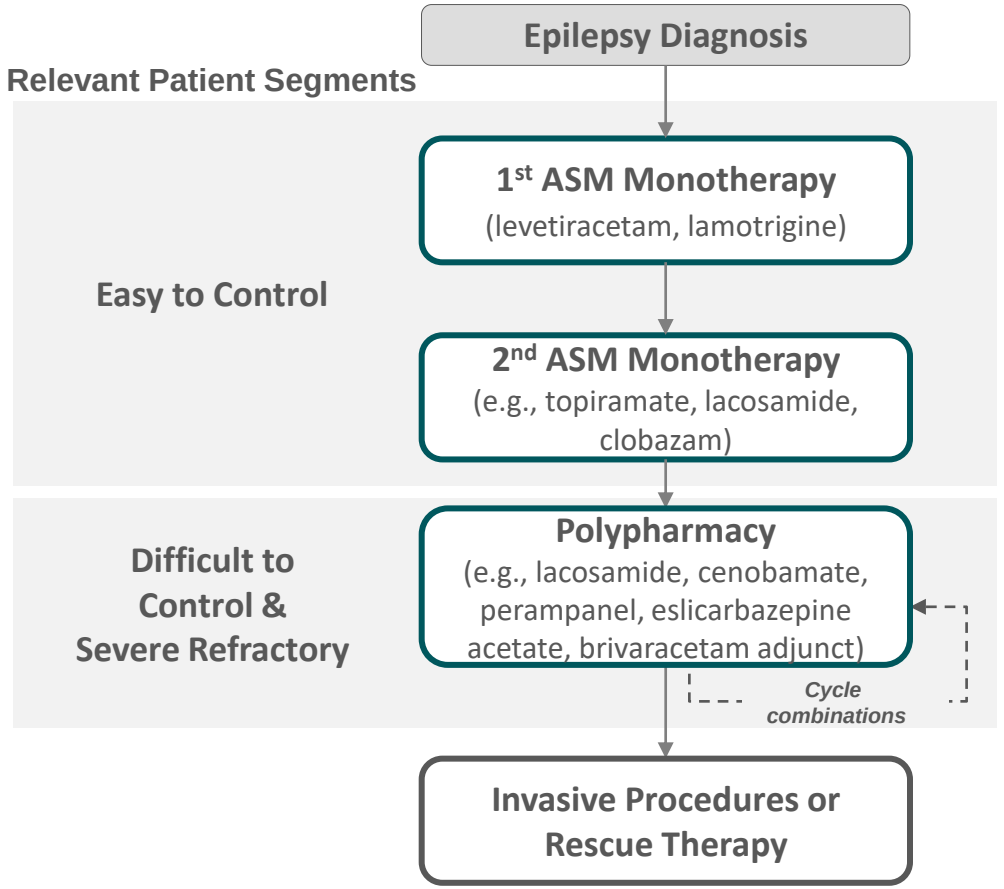
Source: Xenon sponsored market research

Adult Focal Onset Seizure Landscape

Estimated U.S. Diagnosed Adult FOS Patient Population (2020)



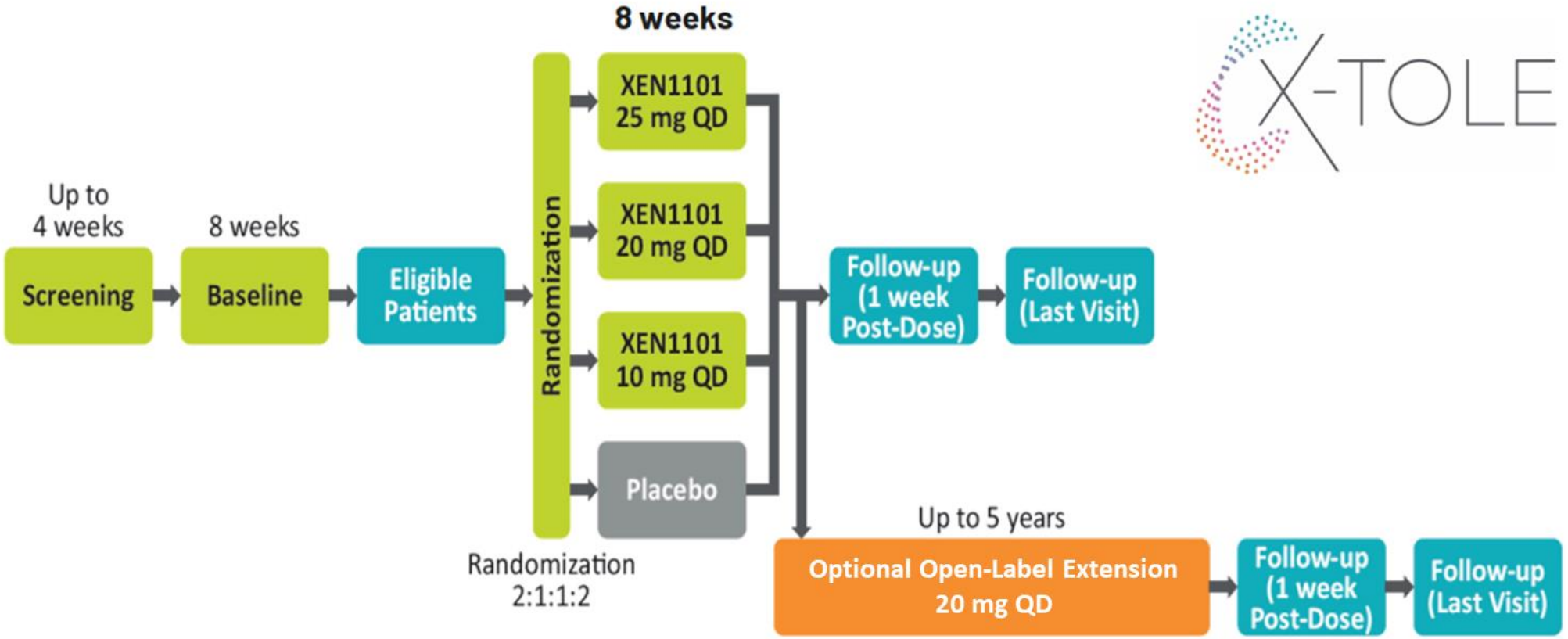
Treatment goal is to optimize efficacy while managing comorbidities and maximizing quality of life



Source: Xenon sponsored market research

XEN1101 X-TOLE Phase 2b Trial

Topline results reported in October 2021 with additional OLE data presented at AES in December 2022



Demographics and Baseline Characteristics (Safety Population)

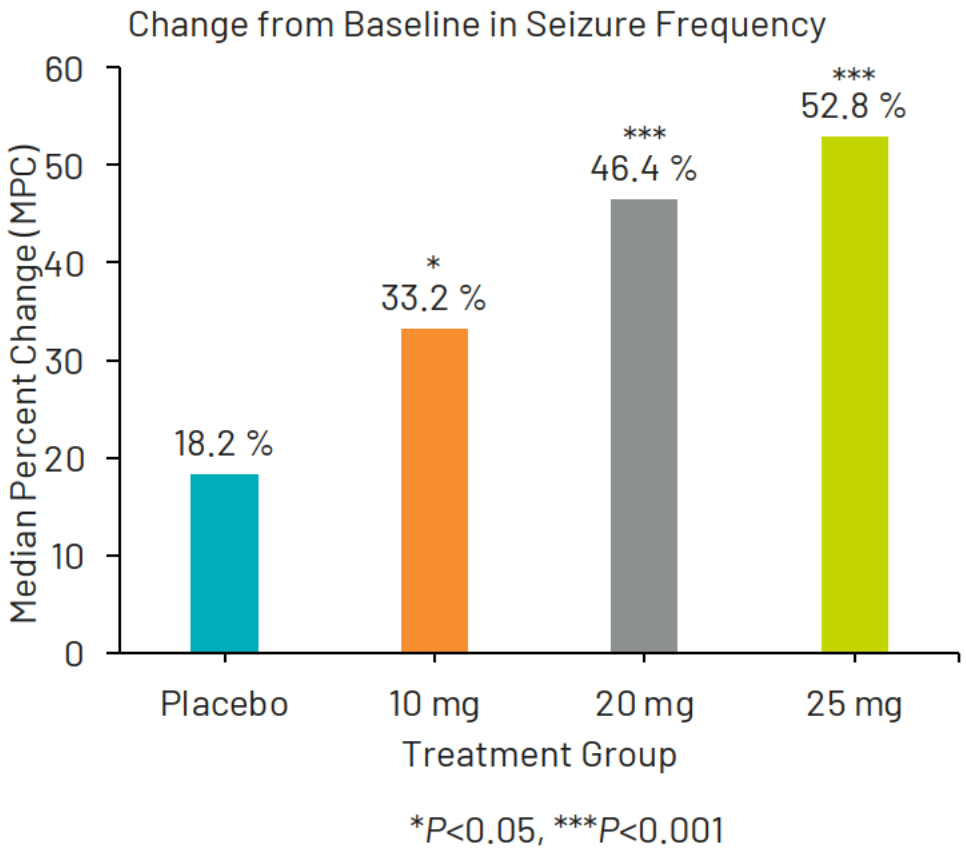
- Subjects had an average age of 40.8 ± 13.3 years
- 8.9%, 40.3%, or 50.8% of the subjects were on and continued taking 1, 2, or 3 stable background ASMs, respectively, throughout the trial
- Subjects failed a median of 6 previous ASMs prior to trial entry
- Median baseline seizure frequency across the trial groups was approximately 13.5 per month

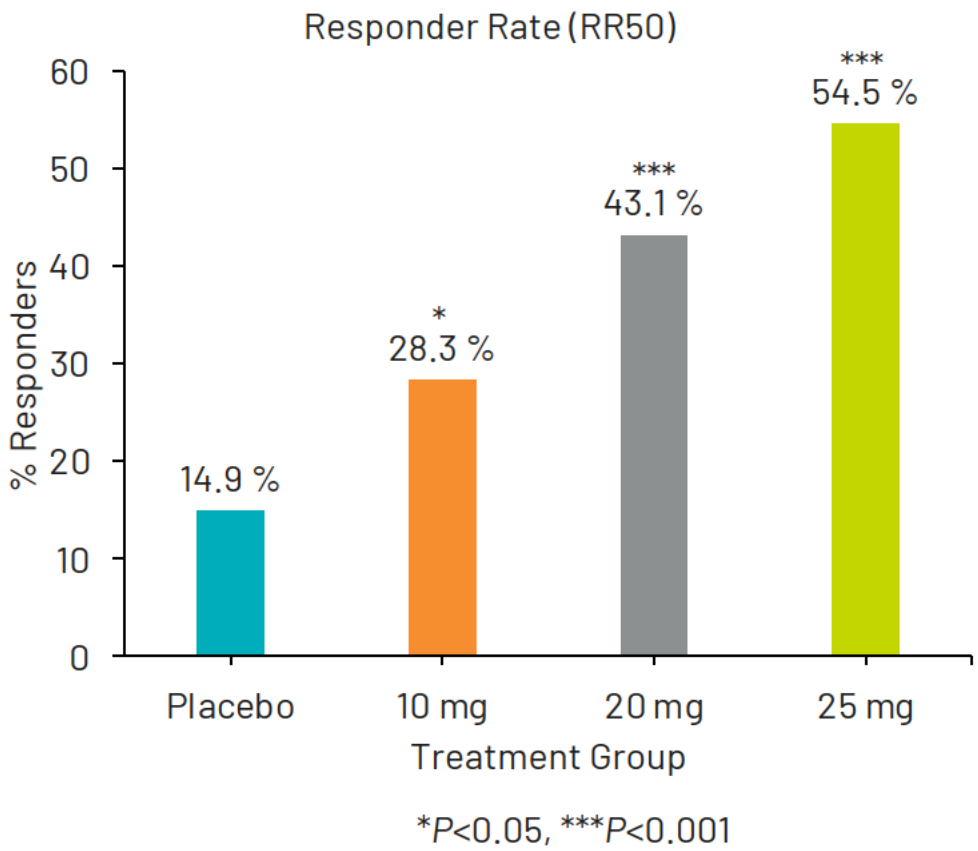
	Placebo (N=114)	XEN1101 10 mg (N=46)	XEN1101 20 mg (N=51)	XEN1101 25 mg (N=114)	TOTAL (N=325)
Age in years, Mean (SD)	42.9 (13.7)	40.0 (12.1)	41.7 (13.6)	38.7 (13.1)	40.8 (13.3)
Age at study entry category					
≥ 65, n (%)	5 (4.4)	2 (4.3)	4 (7.8)	1 (0.9)	12 (3.7)
< 65, n (%)	109 (95.6)	44 (95.7)	47 (92.2)	113 (99.1)	313 (96.3)
Gender					
Female, n (%)	61 (53.5)	27 (58.7)	26 (51.0)	54 (47.4)	168 (51.7)
Male, n (%)	53 (46.5)	19 (41.3)	25 (49.0)	60 (52.6)	157 (48.3)
Region					
Europe, n (%)	67 (58.8)	31 (67.4)	32 (62.7)	68 (59.6)	198 (60.9)
North America, n (%)	47 (41.2)	15 (32.6)	19 (37.3)	46 (40.4)	127 (39.1)
CYP3A4 Inducer Use					
No, n (%)	45 (39.5)	21 (45.7)	22 (43.1)	49 (43.0)	137 (42.2)
Yes, n (%)	69 (60.5)	25 (54.3)	29 (56.9)	65 (57.0)	188 (57.8)
Background ASM Use					
1, n (%)	12 (10.5)	4 (8.7)	2 (3.9)	11 (9.6)	29 (8.9)
2, n (%)	46 (40.4)	18 (39.1)	20 (39.2)	47 (41.2)	131 (40.3)
3, n (%)	56 (49.1)	24 (52.2)	29 (56.9)	56 (49.1)	165 (50.8)
Number of Pre-study ASMs failed					
Median [Q1, Q3]	6.0 [3.0, 8.0]	5.0 [4.0, 9.0]	6.0 [4.0, 9.0]	5.5 [3.0, 9.0]	6.0 [4.0, 9.0]

Subjects were randomized for an 8-week double-blind phase to placebo or one of three active treatment groups in a 2:1:1:2 ratio

Arms well balanced and representative of a difficult-to-treat adult FOS patient population

Compelling Phase 2b Efficacy Results



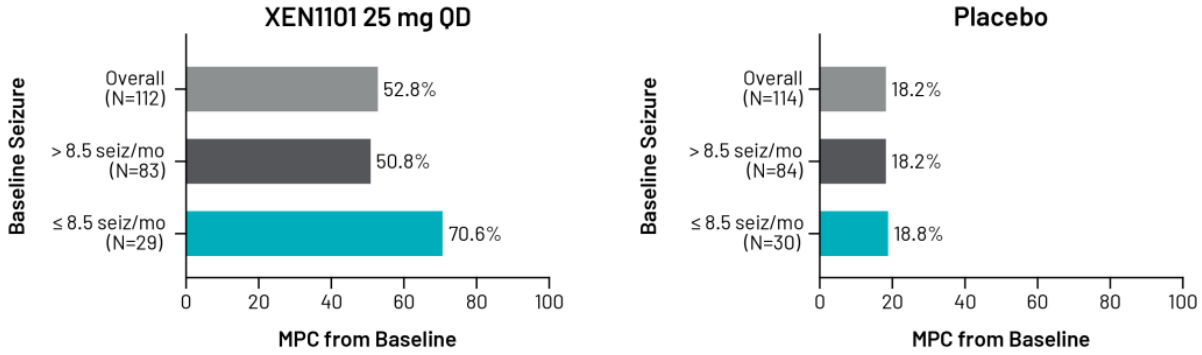


Highly significant and dose dependent reduction in seizures

X-TOLE Sub-Group Analyses – Double Blind Period

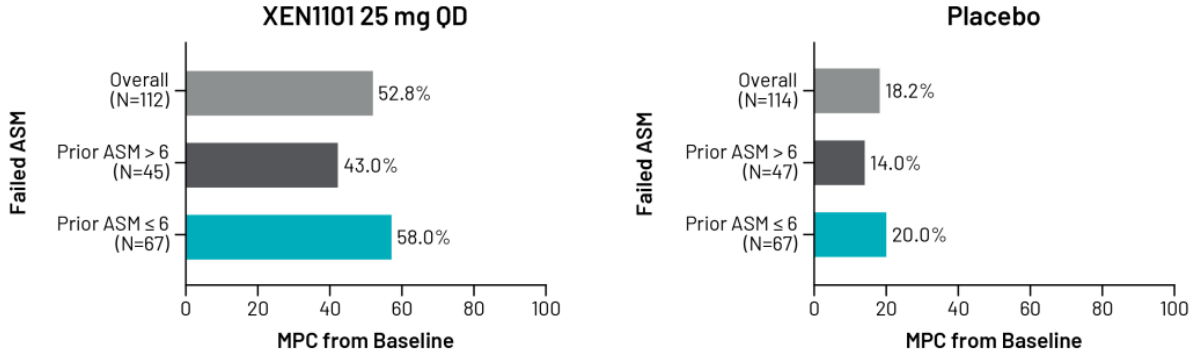
Baseline Seizure Sub-Group Analysis

- Seizure reduction was 70.6% for subjects with ≤ 8.5 seizures/month at baseline compared to 50.8% for those with > 8.5 seizures/month



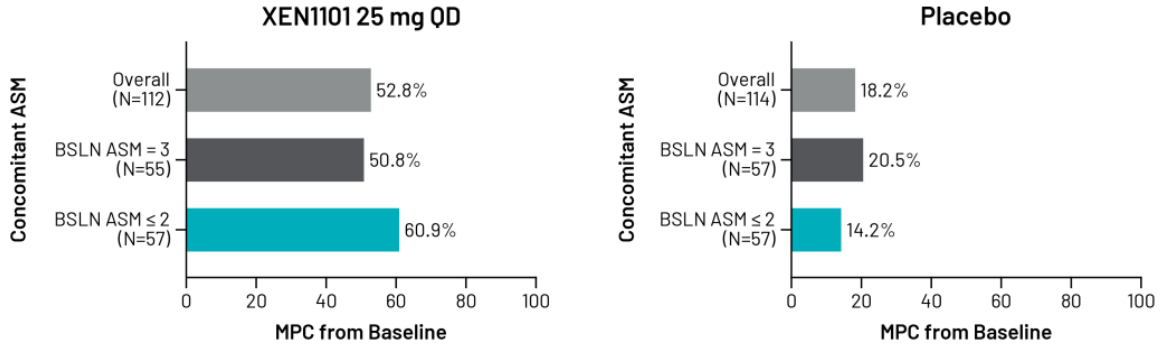
Prior Failed ASMs Sub-Group Analysis

- Median monthly FOS reduction was 58.0% in subjects who failed ≤ 6 ASMs at baseline and 43.0% in subjects who failed > 6 ASMs



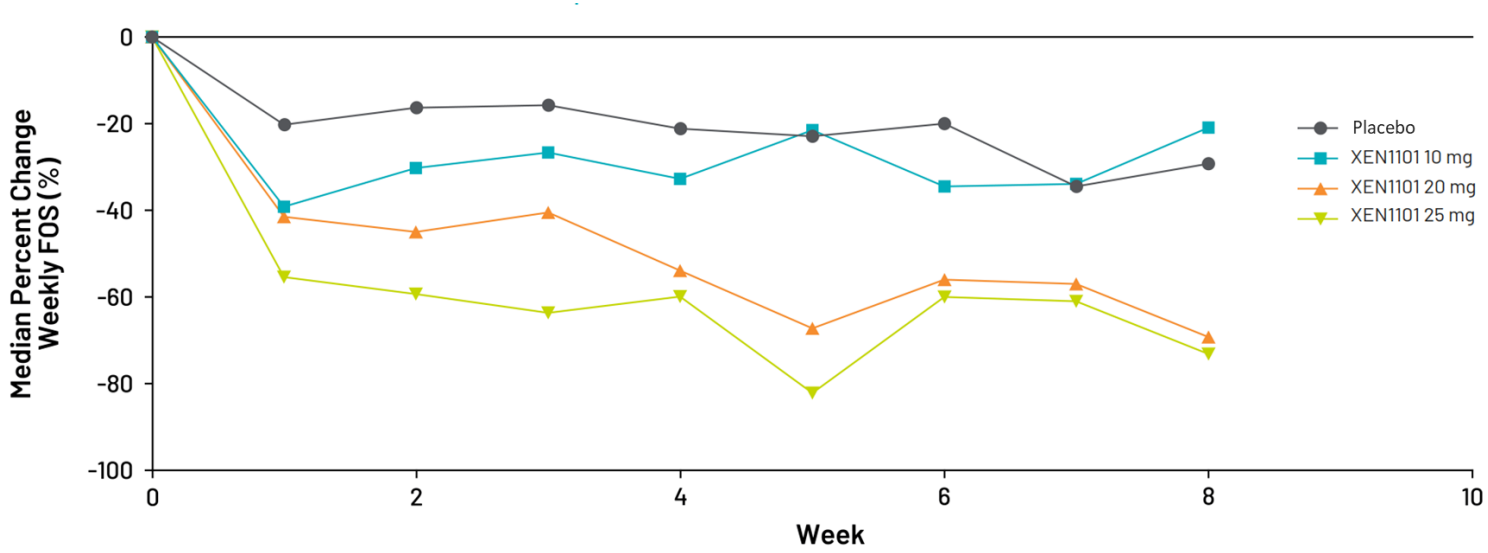
Concomitant ASMs Sub-Group Analysis

- Median monthly FOS reduction was 60.9% for subjects with 1-2 concomitant ASMs and 50.8% for subjects with 3 concomitant ASMs

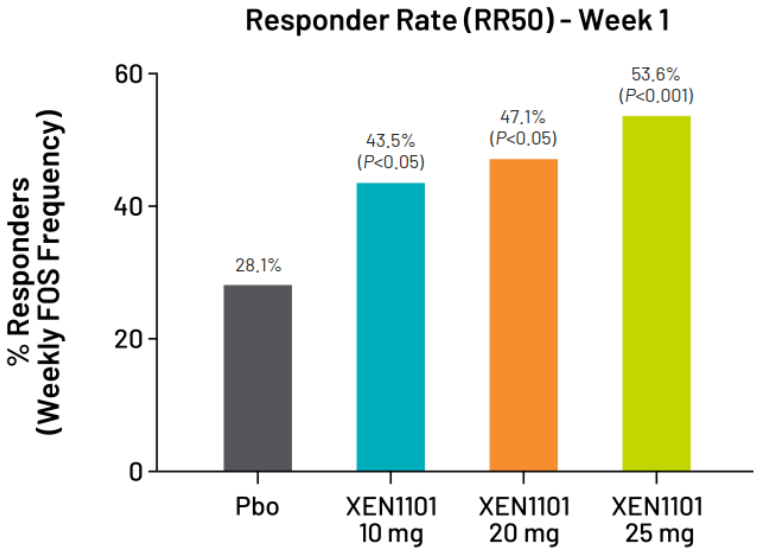


Rapid Onset of Efficacy for XEN1101 – Double Blind Period

Median Percent Change from Baseline in Weekly Focal Onset Seizure (FOS) Frequency for the Double-Blind Period



Responders (RR50) Based on Percent Change from Baseline for Week 1 in Weekly FOS Frequency in DBP



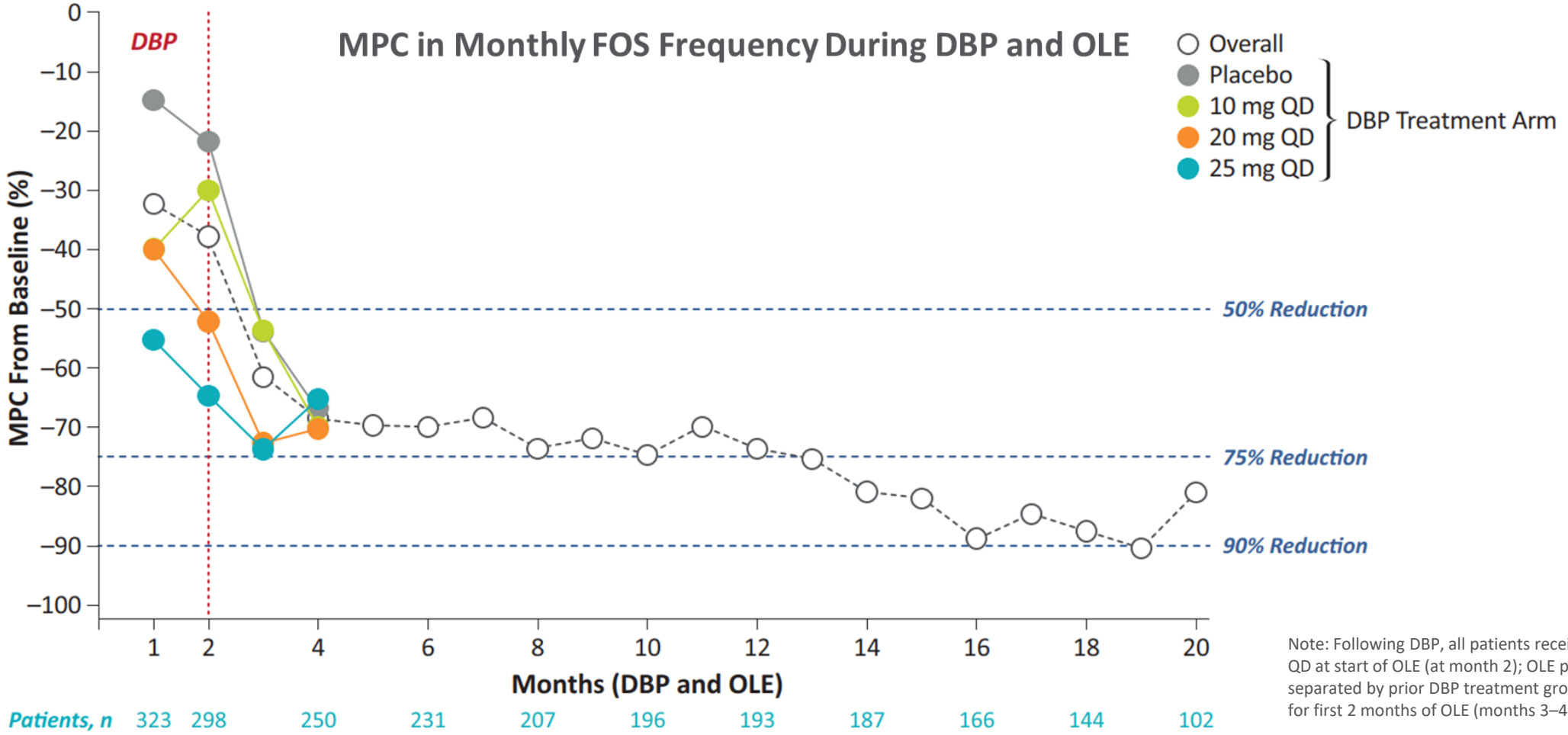
Marked reduction in median FOS frequency at Week 1 for all doses compared with placebo

XEN1101 OLE Data Continue to Support Clinical Profile

- During the OLE, there was a sustained monthly reduction in seizure frequency (80%–90% seizure reduction as measured by MPC) from the double-blind period (DBP) baseline (as of the analysis cut-off date of September 22, 2022)
- Seizure freedom for ≥6-month and ≥12-month consecutive durations was achieved in 17.5% and 10.5% of patients, respectively
- XEN1101 continues to be generally well-tolerated in the OLE with adverse events AEs consistent with prior results in the double-blind period and other anti-seizure medications (ASMs)
  - At the end of the first year in the OLE, patients recorded a mean (SD) weight gain of 1.1 (5.9) kg
  - To date, two AEs of urinary retention occurred in the OLE possibly related to study drug; both patients continued in the study without requiring intervention
  - Although not seen to date, Xenon continues to monitor for the emergence of the tissue discoloration that was associated with long-term exposure to ezogabine

Continued seizure reduction in OLE and safety and tolerability consistent with prior results

X-TOLE and X-TOLE OLE: Continued Reduction of Seizure Frequency

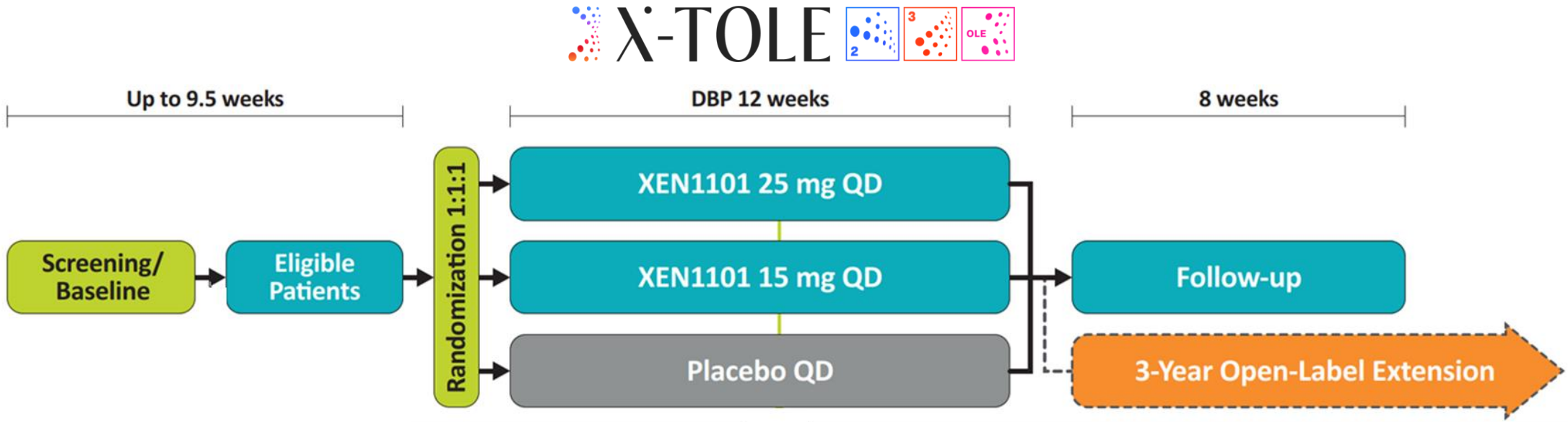


Note: Following DBP, all patients received 20 mg QD at start of OLE (at month 2); OLE patients separated by prior DBP treatment groups shown for first 2 months of OLE (months 3–4).

Improvement in MPC Demonstrated in DBP with Continued Improvement in OLE

XEN1101 X-TOLE2 and X-TOLE3 Phase 3 Trials in FOS

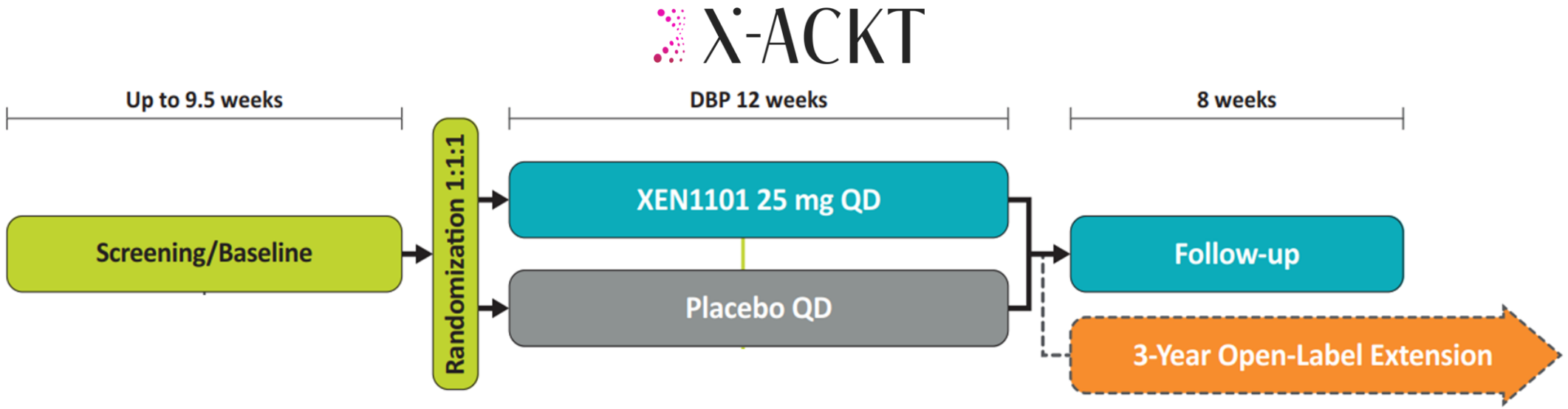
- Completed FDA EOP2 meeting and aligned on clinical program moving forward in FOS and PGTCS - with plan to submit NDA supported by efficacy data from Phase 2b study (X-TOLE) and first Phase 3 study (X-TOLE2)
- Conducting two identical multi-center, placebo-controlled Phase 3 FOS trials (N = ~360 in each study)



- **Primary Objective:**
  - Assess effect of XEN1101 vs placebo on reducing focal onset seizure frequency
- **Secondary Objectives** include assessing the effect on XEN1101 vs placebo on RR50, early treatment effect, and PGI-C

XEN1101 X-ACKT Phase 3 Trial in PGTCS

- Significant unmet need remains in PGTCS despite available treatment options and an opportunity remains for a broad-spectrum agent with activity across seizure types
- Conducting a single, multi-center, placebo-controlled Phase 3 trial to support registration (N = ~160)



- **Primary Objective:**
  - Assess effect of XEN1101 vs placebo on reducing frequency of primary generalized tonic clonic seizures
- **Secondary Objectives** include assessing the effect on XEN1101 vs placebo on RR50, seizure freedom and PGI-C

Primary Generalized Tonic-Clonic Seizures (PGTCS) Overview

Description

- Primary generalized tonic-clonic seizures (PGTCS) are a type of seizure lasting a few seconds to minutes
- PGTCS start in both hemispheres of the brain simultaneously (generalized onset) and comprised of tonic and clonic phases
  - Tonic phase: muscle stiffening, loss of consciousness
  - Clonic phase: muscle jerking, risk of inflicting self-harm
- PGTCS (formerly known as *Grand Mal* seizures) are one of the most severe forms of seizures

Disease Burden

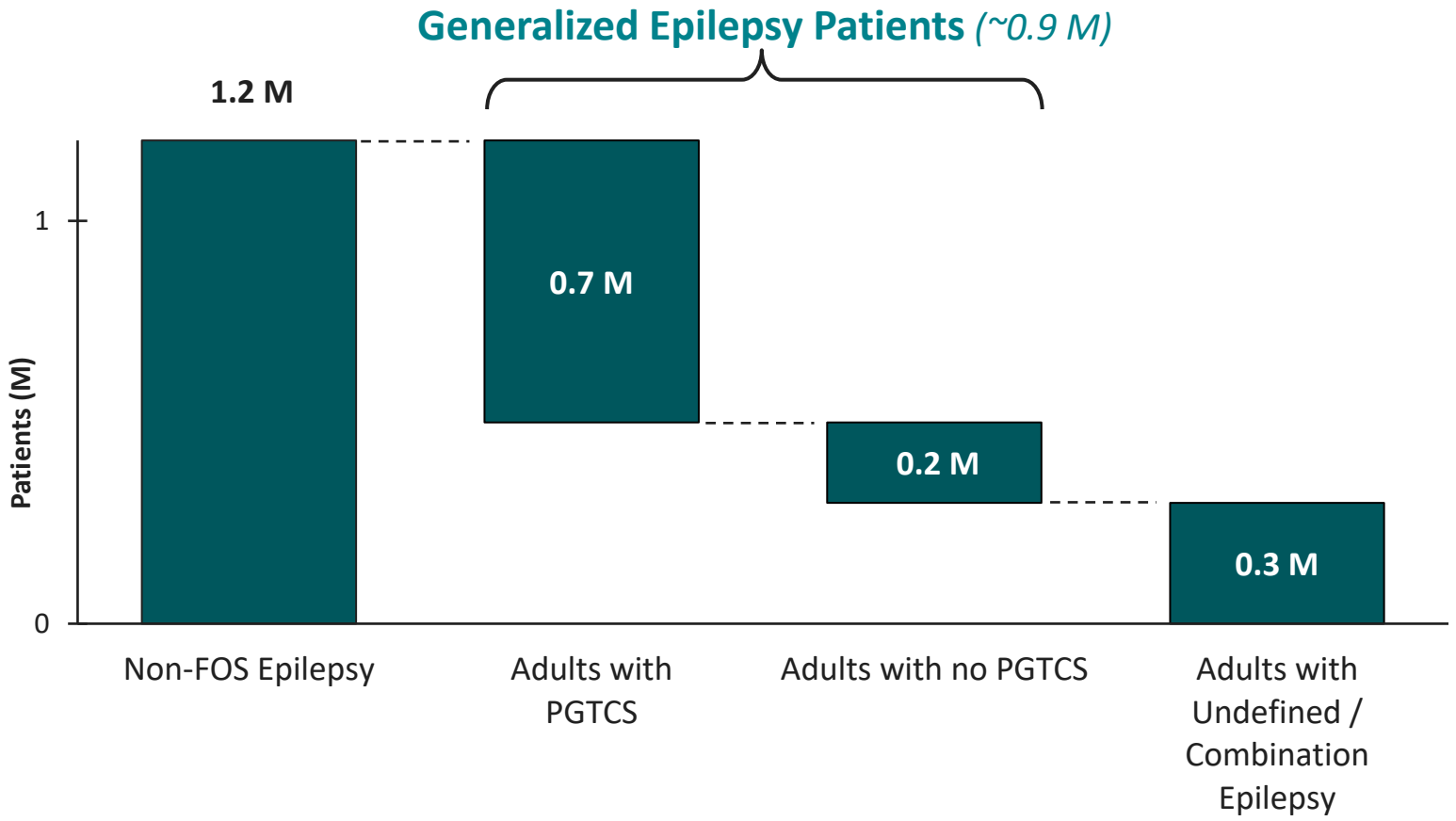
- Seizure frequency varies, usually with recurrences ranging from weeks to months, with a tendency to cluster, and can be fatal
  - 30-50% of people who have one unprovoked tonic-clonic seizure have a subsequent event
- PGTCS also has a substantial negative impact on quality of life
  - High unemployment rates (25-69%) in epilepsy patients
  - Unable to drive unless 6-12 months seizure free in most states
- Social stigma and concern of having a seizure in a public setting

Outcomes

- Given the danger and risk of death, PGTCS are generally considered more serious and dangerous than FOS
- Death can be caused by seizure injury or SUDEP (sudden unexpected death in epilepsy)
  - Tonic phase can result in falls and clonic phase can result in additional injury
  - Generalized tonic-clonic seizures increase the risk of SUDEP
  - Not well understood but involved impaired brain, heart, and lung function
- Mortality rate is 1.6-9.3x higher in epilepsy patients than the general population

Source: Xenon sponsored market research

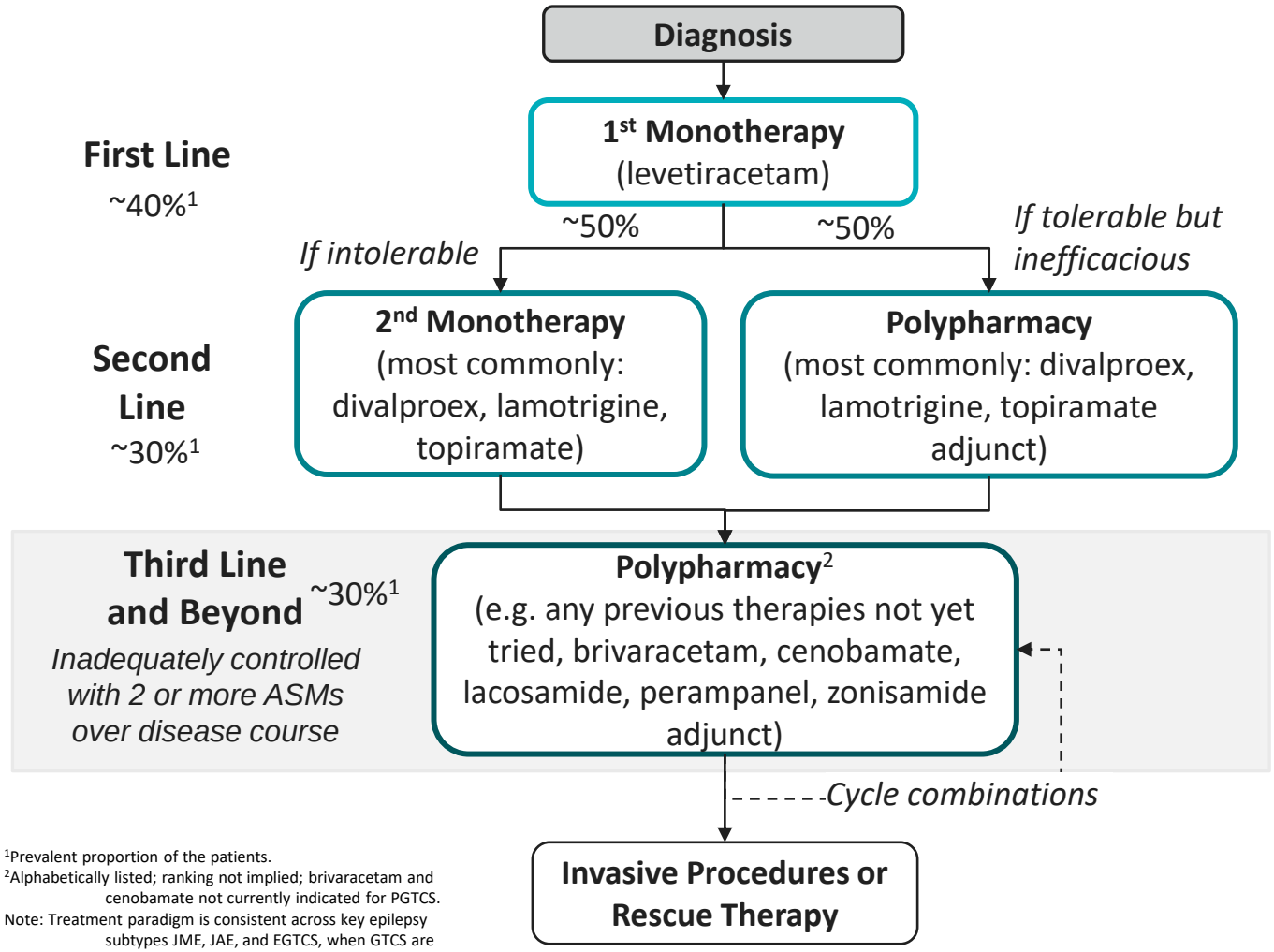
Adult Generalized Epidemiology



- The majority of adult patients with generalized epilepsy experience PGTCS (~80%)
  - While individual patients may have other seizure types as well, treating PGTCS is a key driver of treatment decisions as these can be fatal
- The generalized patient population is heterogeneous, and the underlying subtype (JME, JAE, etc.) is typically a secondary consideration influencing treatment decisions

Note:JME = juvenile myoclonic epilepsy, JAE = juvenile absence epilepsy.
Source:Xenon sponsored market research

PGTCS Treatment Paradigm



[1]Prevalent proportion of the patients.
[2]Alphabetically listed; ranking not implied; brivaracetam and cenobamate not currently indicated for PGTCS.
Note: Treatment paradigm is consistent across key epilepsy subtypes JME, JAE, and EGTCS, when GTCS are present.
Source: Xenon sponsored market research

Treatment Considerations

- Fewer ASMs are approved to treat PTGCS despite the more severe seizure phenotype
- Cycling through treatment options is common after initial monotherapy as patients seek seizure freedom
- Select ASMs, particularly sodium channel blockers and GABAergic agents, may exacerbate idiopathic generalized epilepsies (IGEs) and can provoke absence or myoclonic seizures

Rationale Supporting XEN1101 Development in PGTCS

- XEN1101 anti-seizure activity in maximum electroshock seizure and pentylenetetrazole preclinical models, both known to predict efficacy for primary generalized seizures
- ICA-105665 (Kv7 potassium channel opener) suppressed photosensitivity (EEG model) in generalized epilepsy patients[1]
- Levetiracetam, valproic acid, lamotrigine, and brivaracetam (not approved for PGTCS) suppressed photosensitivity in generalized epilepsy patients and demonstrate PGTCS efficacy[2]
- In X-TOLE, XEN1101 demonstrated broad impact across all focal seizure subtypes, including those that progressed to generalized seizures

[1]Kasteleijn-Nolst Trenité et al, Epilepsia. 2013;54(8)
[2]Verotti et al, Epileptic Disord. 2012;14(4)

Significant unmet need remains in PGTCS despite available treatment options and an opportunity remains for a broad-spectrum agent with activity across seizure types

XEN1101 Value Proposition

Efficacy

- Compelling data in difficult-to-treat adult FOS patient population in Phase 2b
- Rapid onset of action, with seizure reduction observed at Week 1
- Durable seizure reductions demonstrated in OLE
- Broad spectrum activity expected to be applicable across FOS and PGTCS

Ease of Use

- One pill, once-daily
- No titration required
- Unique and novel MOA can be leveraged in rational polypharmacy

Safety Profile / Tolerability[1]

- Well-tolerated with AE profile in line with other ASMs
- Evening dose results in C_{max} during sleep
- No drug allergic reactions observed
- No TEAEs of pigmentary abnormalities

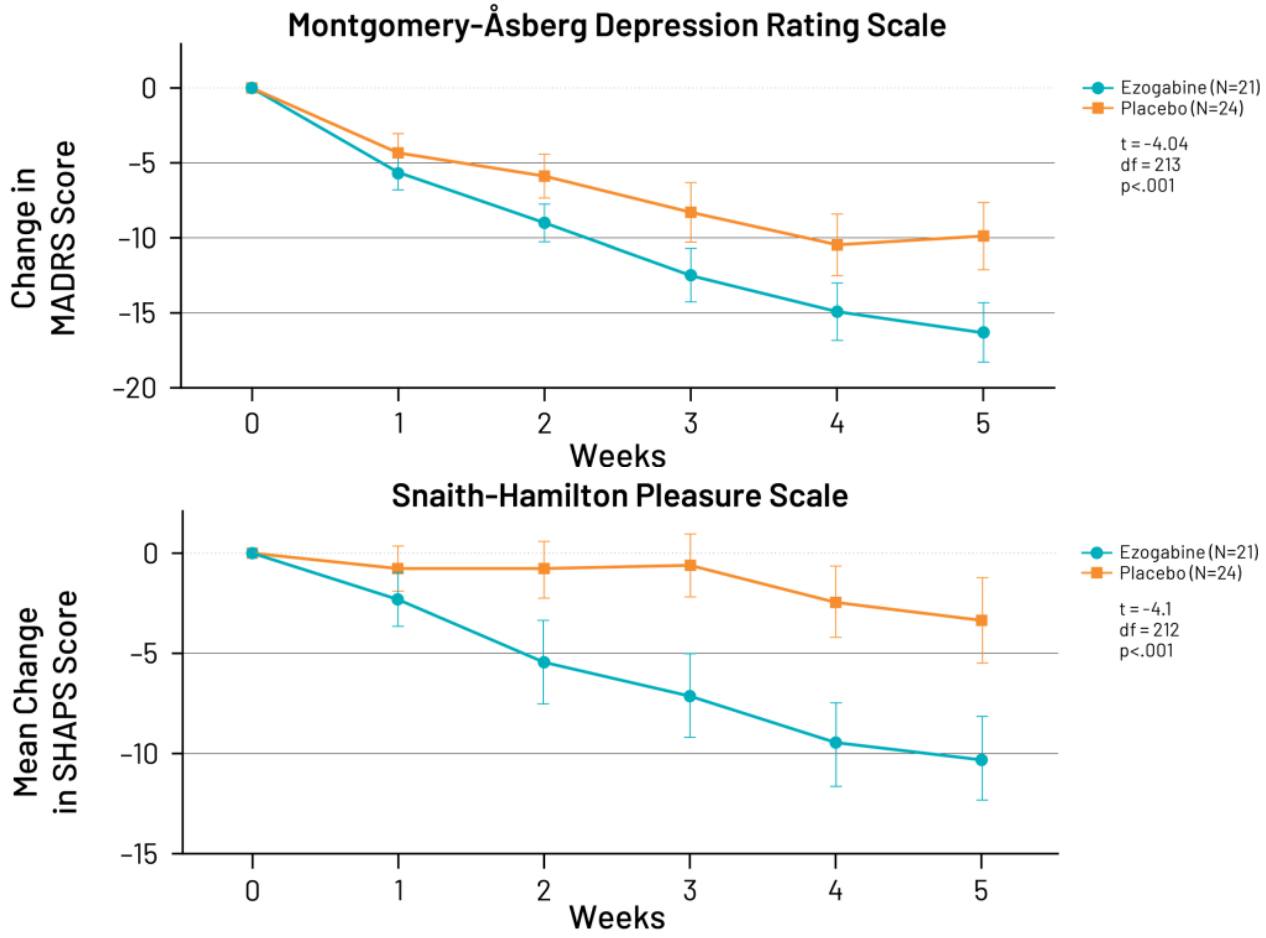
[1]Company Poster. 2018 American Epilepsy Society (AES) Annual Meeting: "A First-in-Human Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Pharmacodynamics of a Novel Small Molecule KV7.2/7.3 Positive Allosteric Modulator (XEN1101) in Healthy Subjects." December 3, 2018

We are in alignment with the FDA and have a clear path forward for clinical development for XEN1101 in FOS and PGTCS

Supportive Pre-Clinical & Clinical Data to Explore MDD

- Promising clinical results with **ezogabine** dosed 300 mg TID as a treatment for Major Depressive Disorder (MDD) and anhedonia. Ezogabine, compared with placebo, was associated with:
  - An increase in activation to reward anticipation during the flanker test from baseline to week 5 (p=0.07). Ezogabine (N=18) Placebo (N=22)
  - A large improvement in depression as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS score change from placebo: -7.9±3, p<.001)
  - A large improvement in in hedonic capacity as measured by the Snaith-Hamilton Pleasure Scale (SHAPS score change from placebo: -6.9±3.2, p<.001)
- Encouraging pre-clinical activity data with XEN1101
- Depression is one of the most common co-morbidities within the epilepsy patient population
- Patient enrollment underway in both company-sponsored and investigator sponsored Phase 2 POC studies in MDD

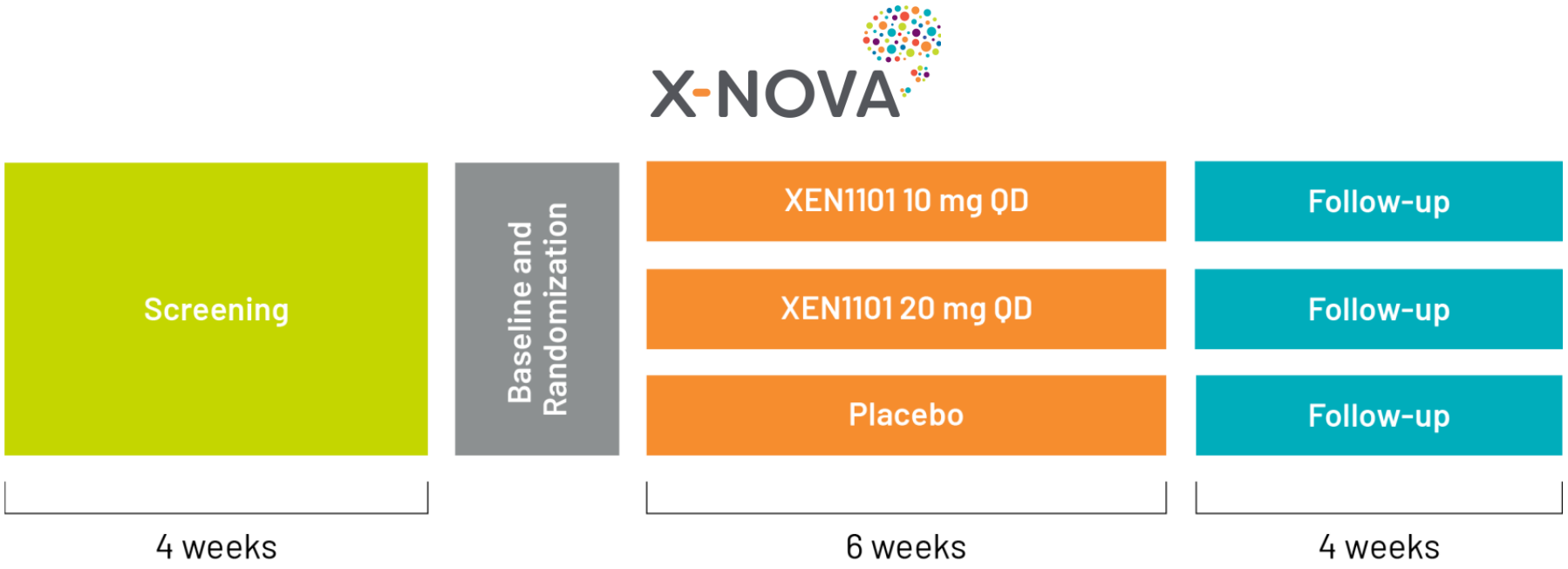
Figures reproduced from Costi et al. Depression symptoms assessed by the Montgomery-Åsberg Depression Rating Scale. Anhedonia symptoms assessed by the Snaith-Hamilton Pleasure Scale.



Costi et al, Am J Psychiatry 2021

XEN1101 Phase 2 POC Studies in Major Depressive Disorder

Company-sponsored XEN1101 X-NOVA Phase 2 Clinical Trial Underway



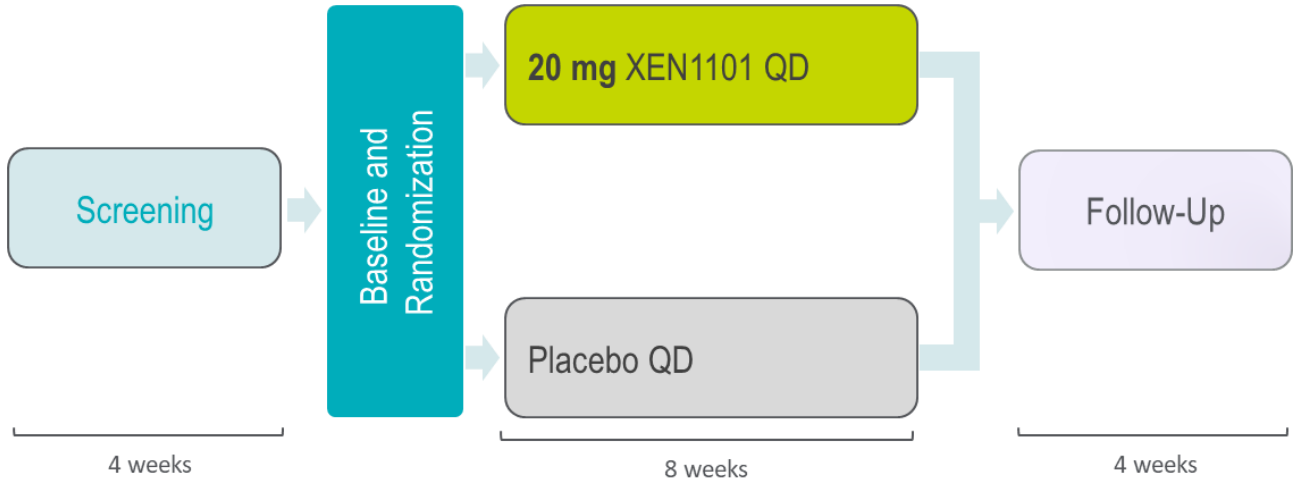
- **Primary Objective:**
  - Assess the efficacy of 10 mg and 20 mg doses of XEN1101 compared to placebo on improvement of depressive symptoms in ~150 subjects diagnosed with MDD using MADRS score change through week 6

Topline results anticipated in Q3 2023

XEN1101 Phase 2 POC Studies in Major Depressive Disorder

Mount Sinai Investigator Initiated Trial of XEN1101 for Major Depressive Disorder

- Sample size: 60 (30 per arm)
  - 2 sites (Mt Sinai and Baylor)
- Similar design to Xenon's MDD study, with some differences:
  - Primary endpoint: Change in activation within the bilateral ventral striatum, assessed through the incentive flanker task during fMRI
  - 8-week treatment duration
  - Only 20 mg dose and placebo arms
  - Subjects excluded if non-response to >4 adequate antidepressant trials in the current episode



- Investigator-initiated study
- Financed by NIMH grant
- Xenon to provide XEN1101 and matching placebo

XEN496: Potential Precision Medicine Approach for KCNQ2-DEE

Development of Proprietary XEN496

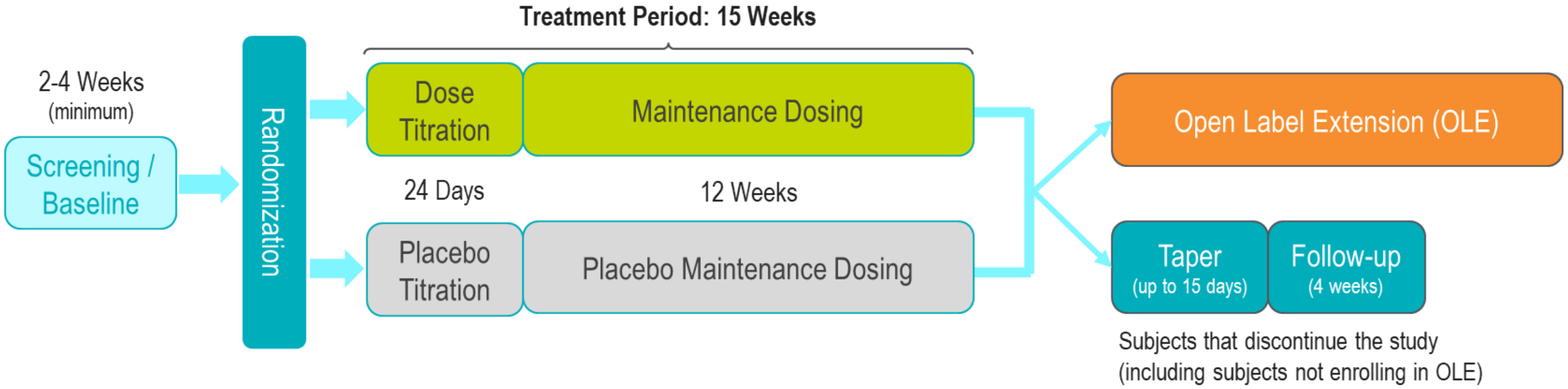
- XEN496 is pediatric-specific, granule formulation of ezogabine to be presented as sprinkle capsules
- MOA that potentiates Kv7-mediated potassium current
- Ezogabine previously approved by FDA with proven mechanism in adult focal seizures
- Potential for precision medicine approach to treat rare KCNQ2-DEE pediatric epilepsy
- Fast Track designation and Orphan Drug Designation in U.S. and Orphan Medicinal Product Designation (Europe) for KCNQ2-DEE

> "Our hope is that XEN496 could represent a genetically targeted treatment that improves the lives of children living with this debilitating disease."
>
> ***Jim Johnson, President***
> KCNQ2 Cure Alliance

EPIK Phase 3 Pediatric Clinical Trial (KCNQ2-DEE)

Primary Objective: evaluate the efficacy of XEN496 as adjunctive therapy in reducing seizure frequency from baseline, compared to placebo in pediatric subjects with KCNQ2-DEE

EPIK TRIAL DESIGN



Study completion anticipated in 2024

Summary of Potential Value-Creating Milestone Opportunities

XEN1101 (Epilepsy)

- Phase 3 clinical trial (X-TOLE2) in FOS underway with identical X-TOLE3 study to follow
- Phase 3 clinical trial (X-ACKT) in PGTCS underway to support registration in additional epilepsy indication
- NDA submission to be based on efficacy data from Phase 2b X-TOLE and first Phase 3 trial (X-TOLE2)

XEN1101 (MDD)

- Company-sponsored Phase 2 X-NOVA POC clinical trial underway; topline results anticipated in Q3 2023
- Mount Sinai investigator-sponsored Phase 2 POC underway

XEN496

- Phase 3 EPIK clinical trial in pediatric KCNQ2-DEE underway; anticipated completion in 2024

Partnered Programs

NBI-921352 (XEN901) / Neurocrine Biosciences

- Two Phase 2 clinical trials underway with NBI-921352 in adult focal-onset epilepsy (data expected in 2H:2023) and pediatric SCN8A-DEE

For more information

INVESTORS@XENON-PHARMA.COM