Corporate Overview

AUGUST 2022

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
  - A leader in small molecule, ion channel drug development
- Multiple mid- to late-stage clinical trials underway
  - Announced positive topline data from XEN1101 Phase 2b X-TOLE clinical trial (Oct. 2021)
  - XEN1101 Phase 3 program expected to be initiated 2H2022, starting in focal onset seizures (FOS) (X-TOLE2)
  - EOP2 meeting with FDA supports NDA submission based on Phase 2b X-TOLE and first Phase 3 (X-TOLE2) efficacy data
  - Expansion into primary generalized tonic-clonic seizures (PGTCS), also known as grand mal seizures
  - XEN1101 Phase 2 trial in MDD with data expected in 2023
- Strong financial position
  - $788.2 million in cash, cash equivalents and marketable securities (as of June 30, 2022)

Xenon's Neurology Portfolio

	Compound	Indication		Pre-clinical	Phase 1	Phase 2	Phase 3
Potassium Channel Openers	**XEN496**	Orphan Pediatric Epilepsy (KCNQ2-DEE)	EPIK				
	XEN1101	Focal Onset Seizures (FOS)	X-TOLE2 X-TOLE3				
		Primary Generalized Tonic-Clonic Seizures (PGTCS)	X-ACKT				
		Major Depressive Disorder	X-NOVA				
		Major Depressive Disorder	Mount Sinai*				
	Ion Channel Modulators	Neurological Disorders					

Partnered Programs

Sodium Channel Modulators	**NBI-921352**	Orphan Pediatric Epilepsy (SCN8A-DEE)	Neurocrine				
		Focal Onset Seizures	Neurocrine				
	PCRX301	Post-Operative Pain	Pacira				

*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 may have broad anti-seizure activity in patients with focal and generalized epilepsy

XEN1101 Clinical Experience

Positive results from the Phase 2b X-TOLE trial demonstrate statistically significant seizure reduction in a difficult-to-treat FOS patient population

Additional X-TOLE and X-TOLE OLE analyses support differentiated clinical profile

Alignment with FDA regarding use of X-TOLE to support NDA submission and planned Phase 3 program in FOS

XEN1101 Commercial Opportunity

In market research, physicians reacted positively to the XEN1101 profile:

- Broad spectrum benefits with rapid onset and no titration
- Novel MOA that can be used in polypharmacy
- QD dosing

XEN1101 Expansion Opportunities

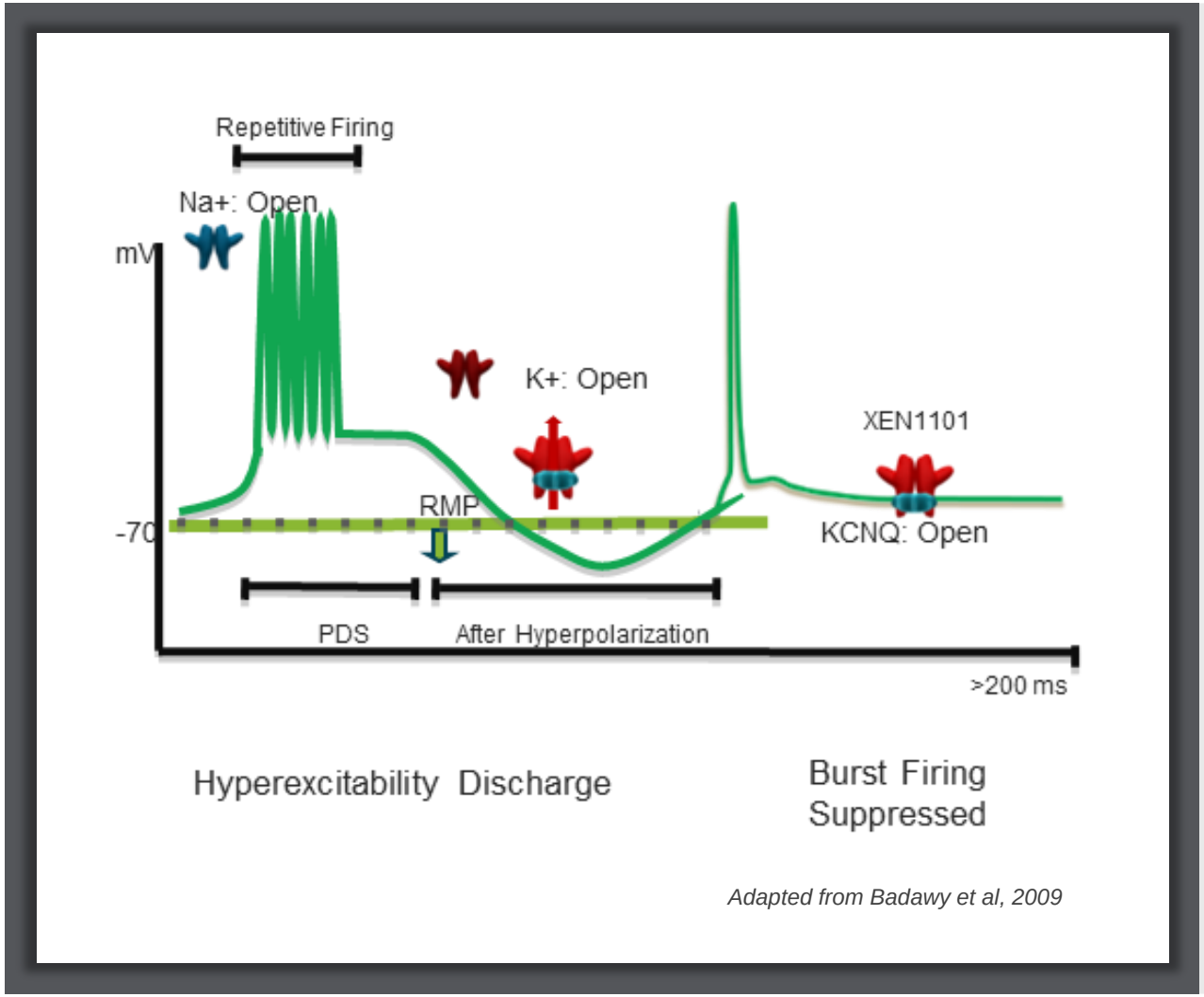
PGTCS are life-threatening seizures, with fewer ASMs available resulting in significant unmet need

- Single Phase 3 X-ACKT clinical trial; a randomized, placebo-controlled, double-blind trial in PGTCS

Depression represents a key co-morbidity associated with FOS

- Phase 2 X-NOVA POC clinical trial ongoing in MDD to understand impact on depression and anhedonia

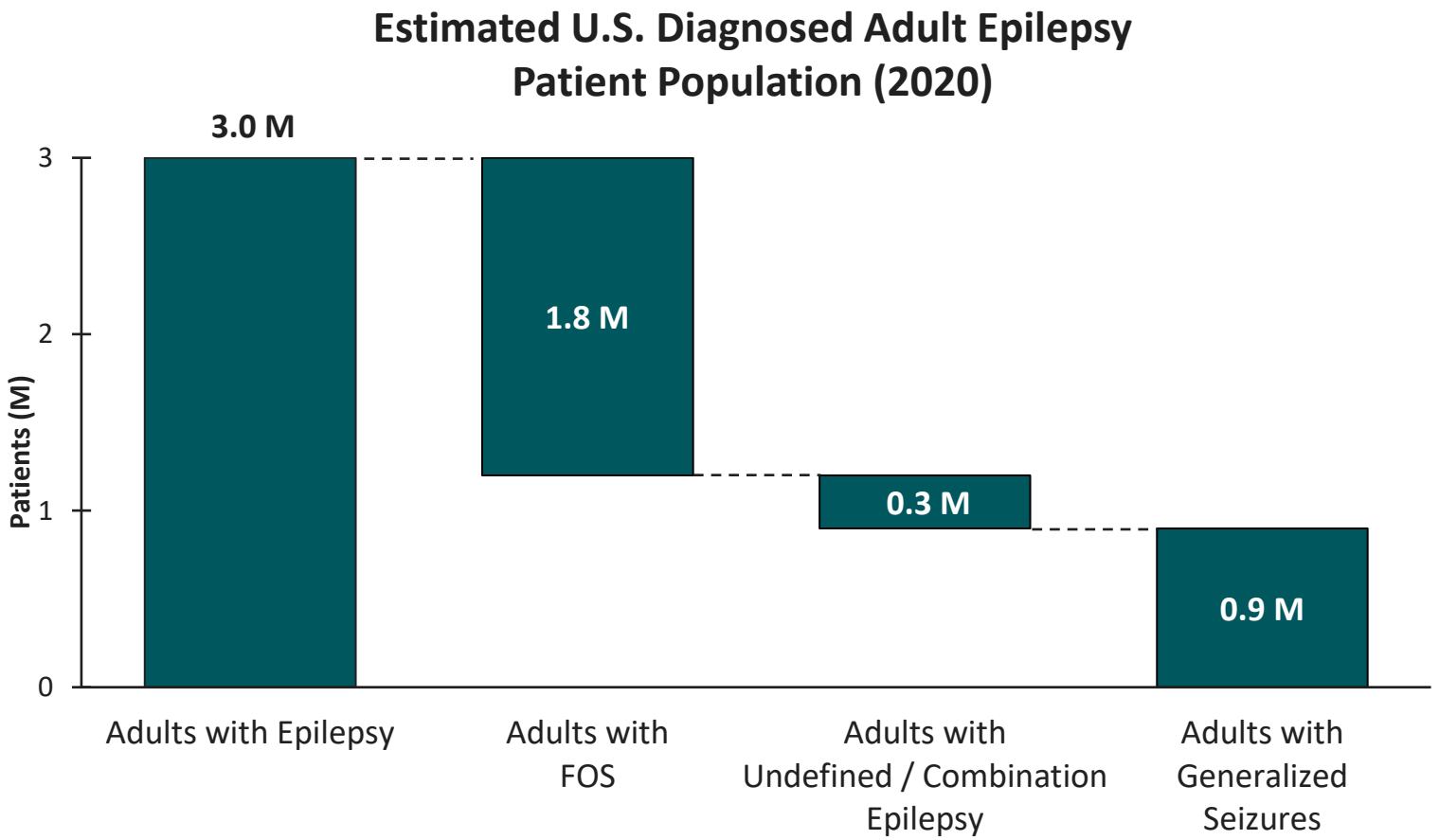
K_V7 Channels have a Critical Role in Neuronal Firing



Adapted from Badawy et al, 2009

- 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

Adult Epilepsy Epidemiology

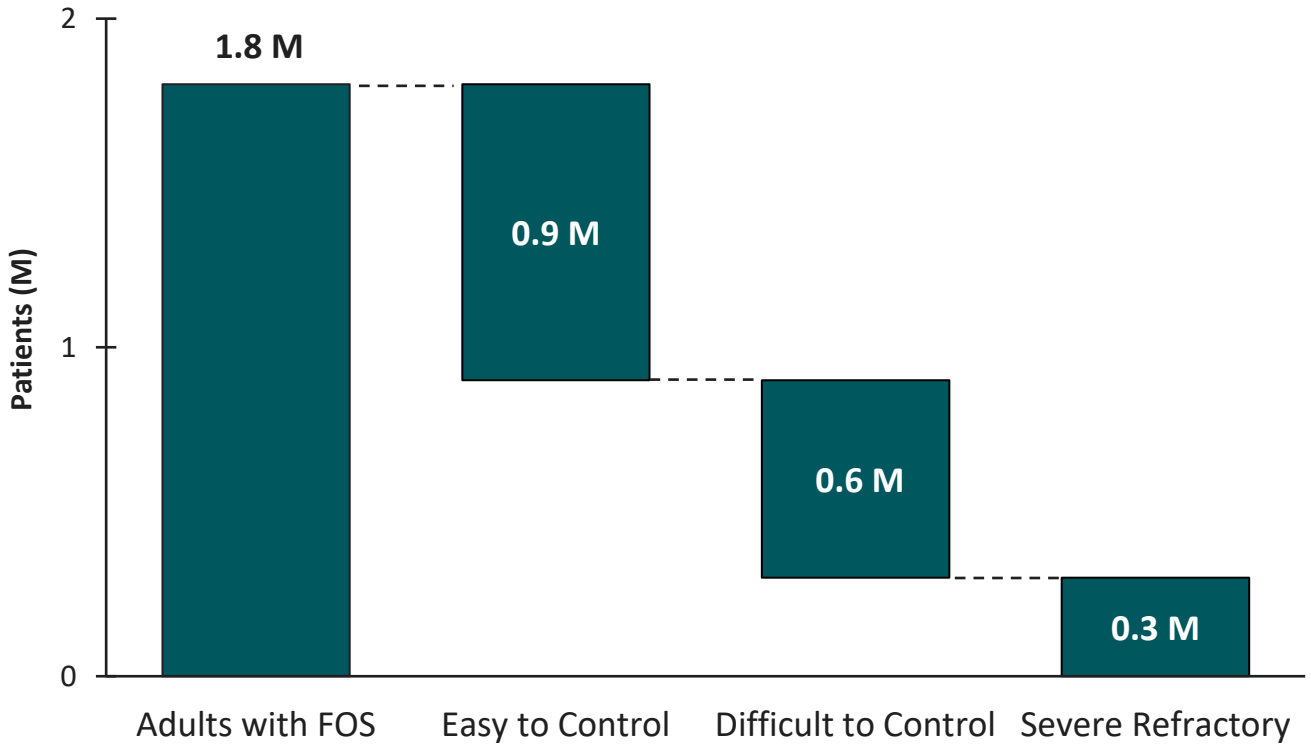


- Focal onset seizures (FOS) represent the largest segment of the epilepsy population in the U.S.
- Generalized epilepsy is the next most common form; the majority of adult patients with generalized epilepsy experience PGTCS (~80%)
- Despite the availability of multiple antiseizure medications (ASMs),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

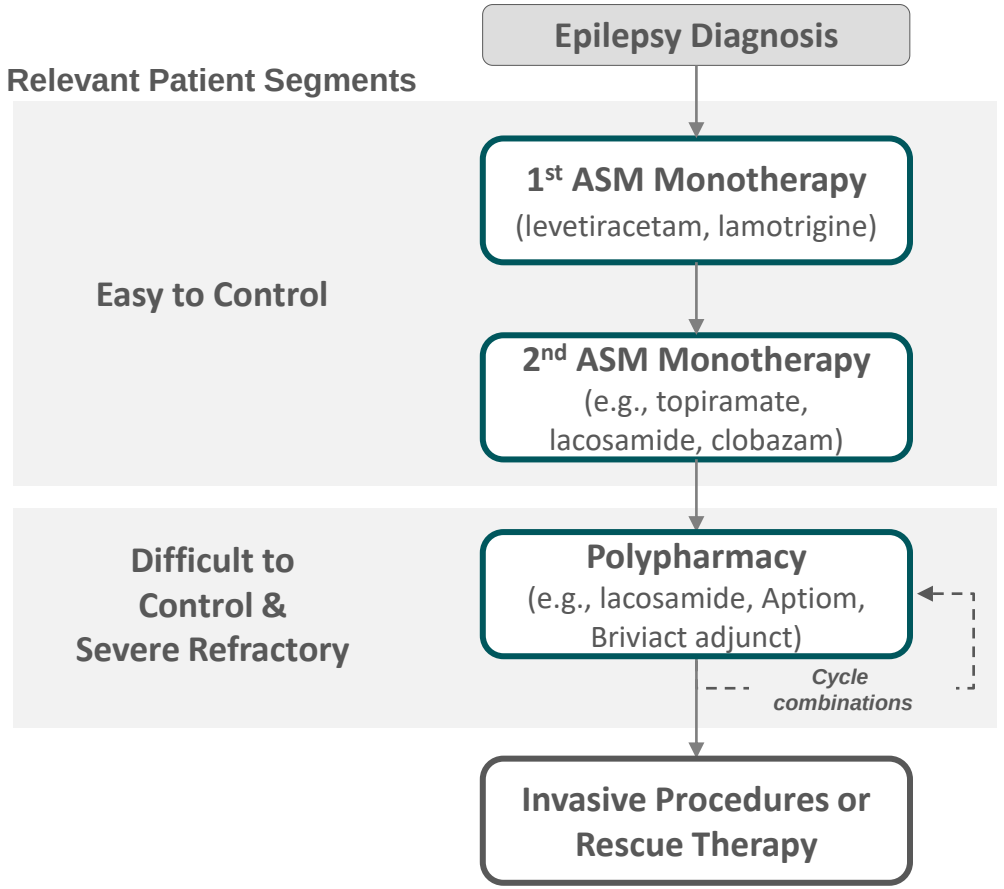
Source: Xenon sponsored market research

Adult Focal Onset Seizure Landscape

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

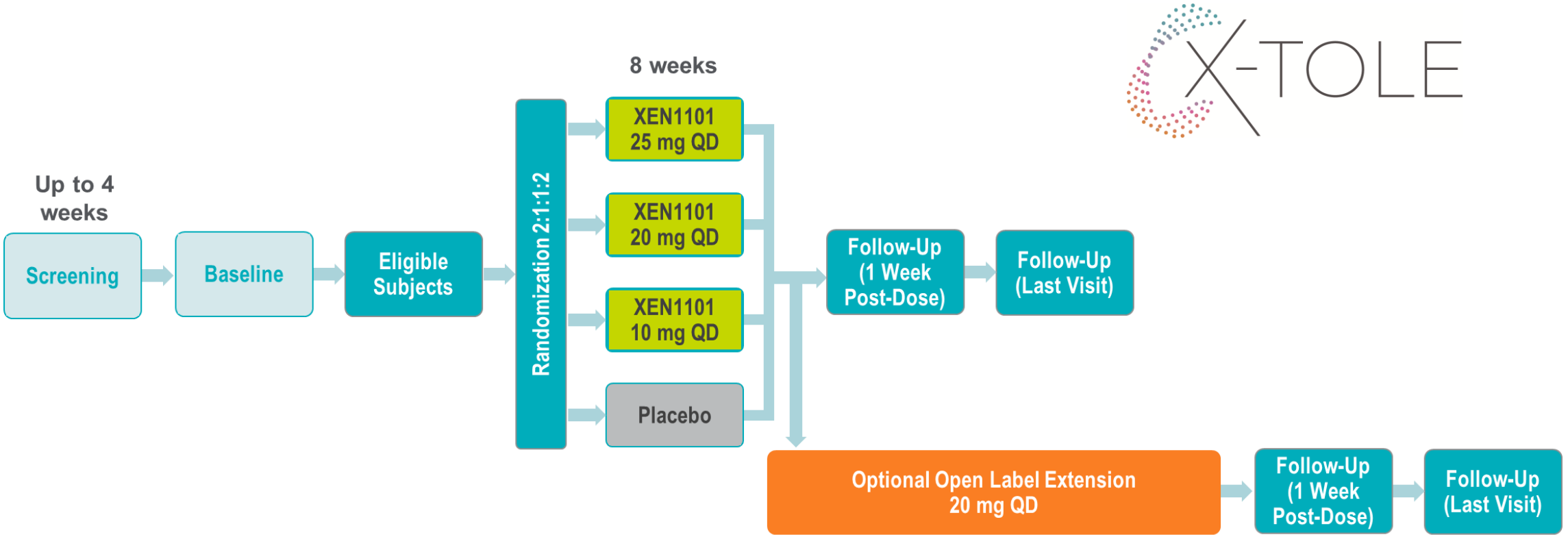


Treatment goal is to optimize efficacy while managing comorbidities and maximizing quality of life



Source: Xenon sponsored market research

XEN1101 “X-TOLE” Phase 2b Trial Design



Topline results reported in October 2021

Additional sub-analyses presented at AES in December 2021

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

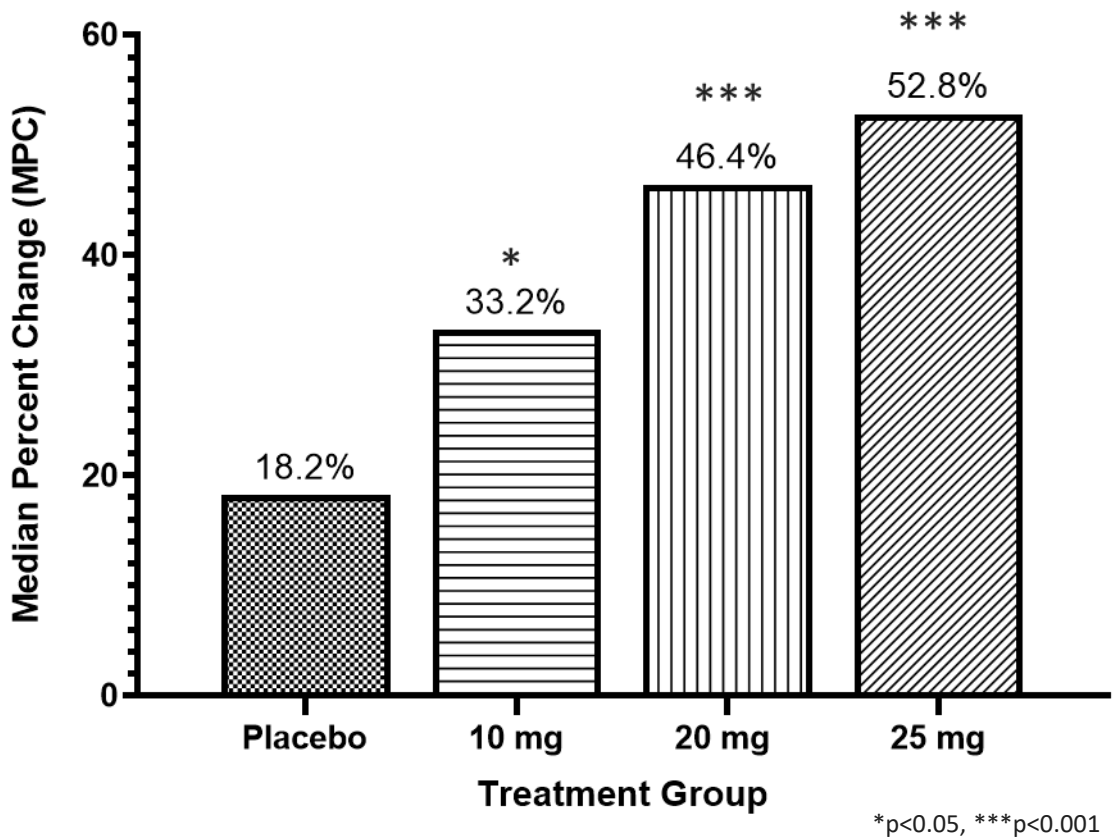
	Placebo (N=114)	XEN1101 10mg (N=46)	XEN1101 20mg (N=51)	XEN1101 25mg (N=114)	TOTAL (N=325)
Age in years, Mean (SD)	**42.9 (13.7)**	**40.0 (12.1)**	**41.7 (13.6)**	**38.7 (13.1)**	**40.8 (13.3)**
Age at study entry category					
≥ 65, n (%)	**5 (4.4)**	**2 (4.3)**	**4 (7.8)**	**1 (0.9)**	**12 (3.7)**
< 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)**
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

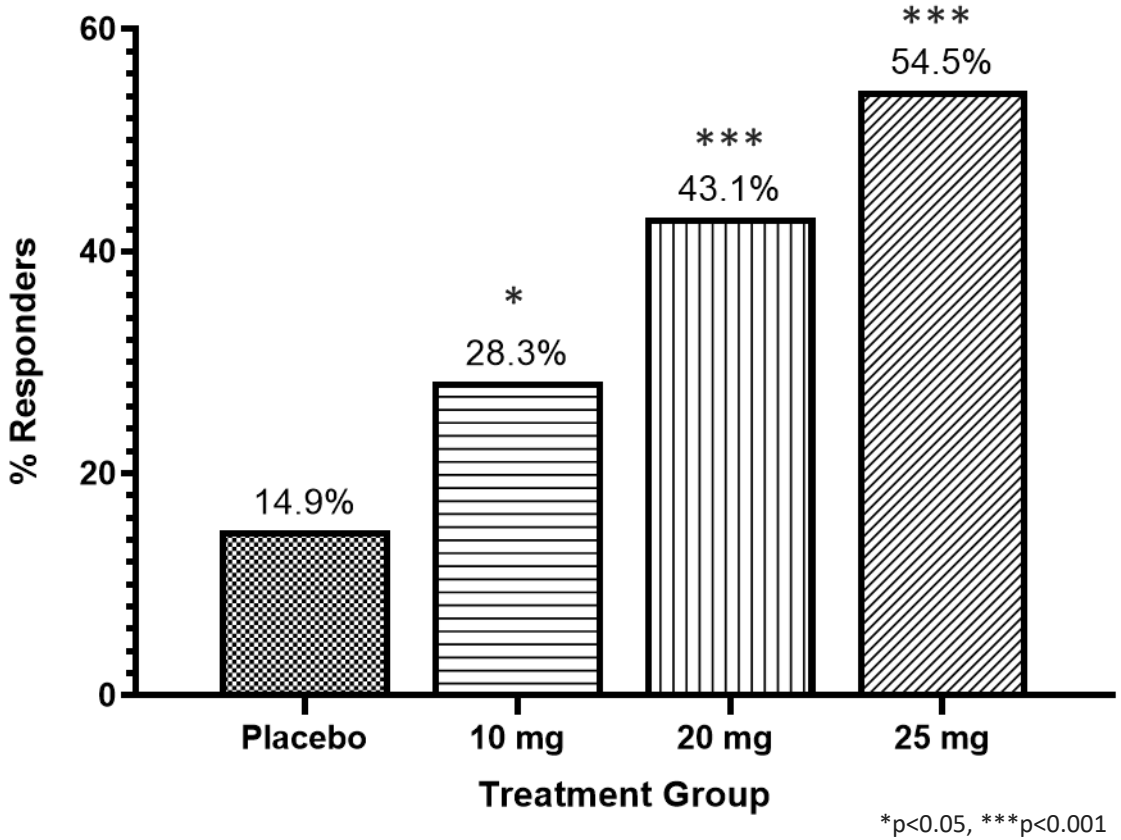
Compelling Phase 2b Efficacy Results

Change from Baseline in Seizure Frequency



*p<0.05, ***p<0.001

Responder Rate (RR50)



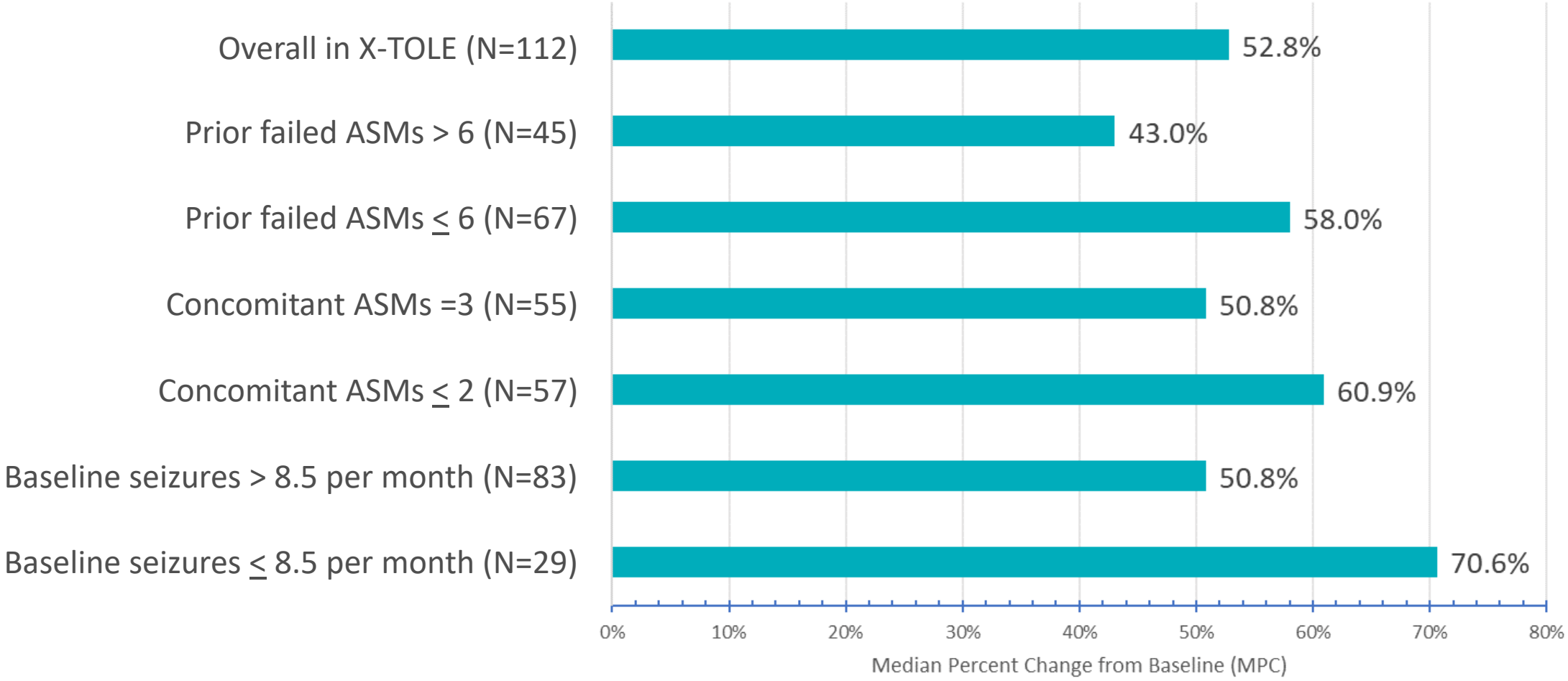
*p<0.05, ***p<0.001

Highly significant and dose dependent reduction in seizures

X-TOLE Sub-Group Analysis

Increased Seizure Reduction in Patients with Less Disease Severity at Baseline

25 mg QD: Reduction in Seizures (MPC) Subgroup Analyses



Safety and Tolerability Profile

- XEN1101 was generally well-tolerated in this study with AEs consistent with other commonly prescribed ASMs
  - The most common treatment emergent adverse events across all XEN1101 dose groups were dizziness (n=52, 24.6%), somnolence (n=33, 15.6%), fatigue (n=23, 10.9%), and headache (n=21, 10.0%)
  - Two TEAEs of urinary retention were reported in the active treatment groups, one of which required a dose reduction, and both subjects remained on drug with no other changes or intervention
  - There have been no TEAEs of pigmentary abnormalities reported during the double-blind phase of the study or in preliminary analysis during the ongoing OLE to date
  - Electrocardiogram changes were evenly balanced between placebo and active treatment groups

Safety and tolerability profile in line with commonly used ASMs

XEN1101 Additional Data Continue to Support Clinical Profile

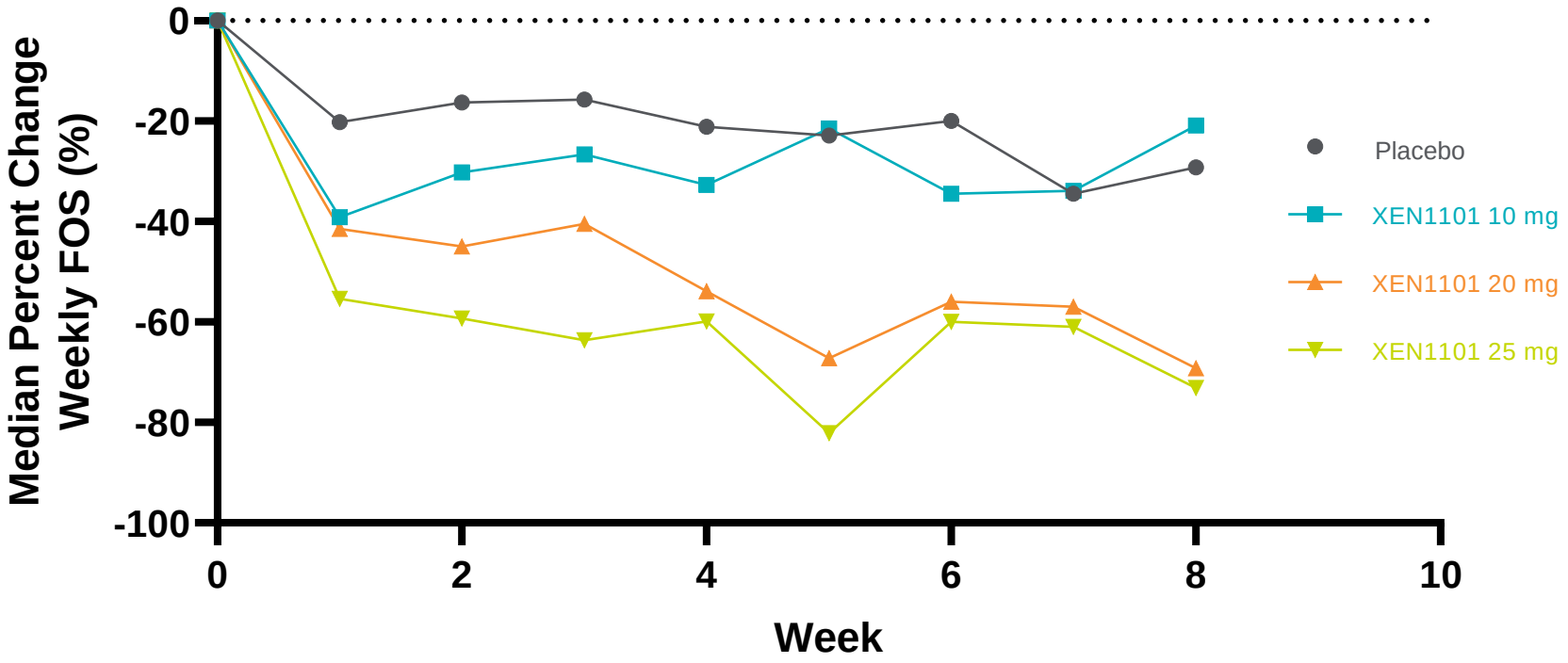
1. Rapid onset of action with statistically significant efficacy endpoints in all treatment arms at Week 1
2. Continued seizure reduction during OLE
   - Subjects remaining in the X-TOLE OLE for at least 3 months and 12 months experienced a greater than 70% and 80% reduction, respectively, in MPC compared to baseline
   - 19.6% and 9.5% of subjects in the OLE experienced a ≥6 and a ≥12 consecutive months of seizure freedom, respectively
3. As of June 2022, OLE safety data consistent with profile observed in double blind period (DBP)
   - Similar CNS side effects consistent with active CNS drug
   - No TEAEs of pigmentary abnormalities have been observed
   - 2 AEs of urinary retention observed; both patients remained on study drug with no intervention required
   - Weight gain observed in OLE is consistent with the DBP (0.9 kg mean weight gain at 1 year in uncontrolled setting)

- X-TOLE OLE being extended from 3 to 5 years to continue to collect long term data

Rapid onset of seizure reduction in double blind period of X-TOLE and continued seizure reduction in OLE

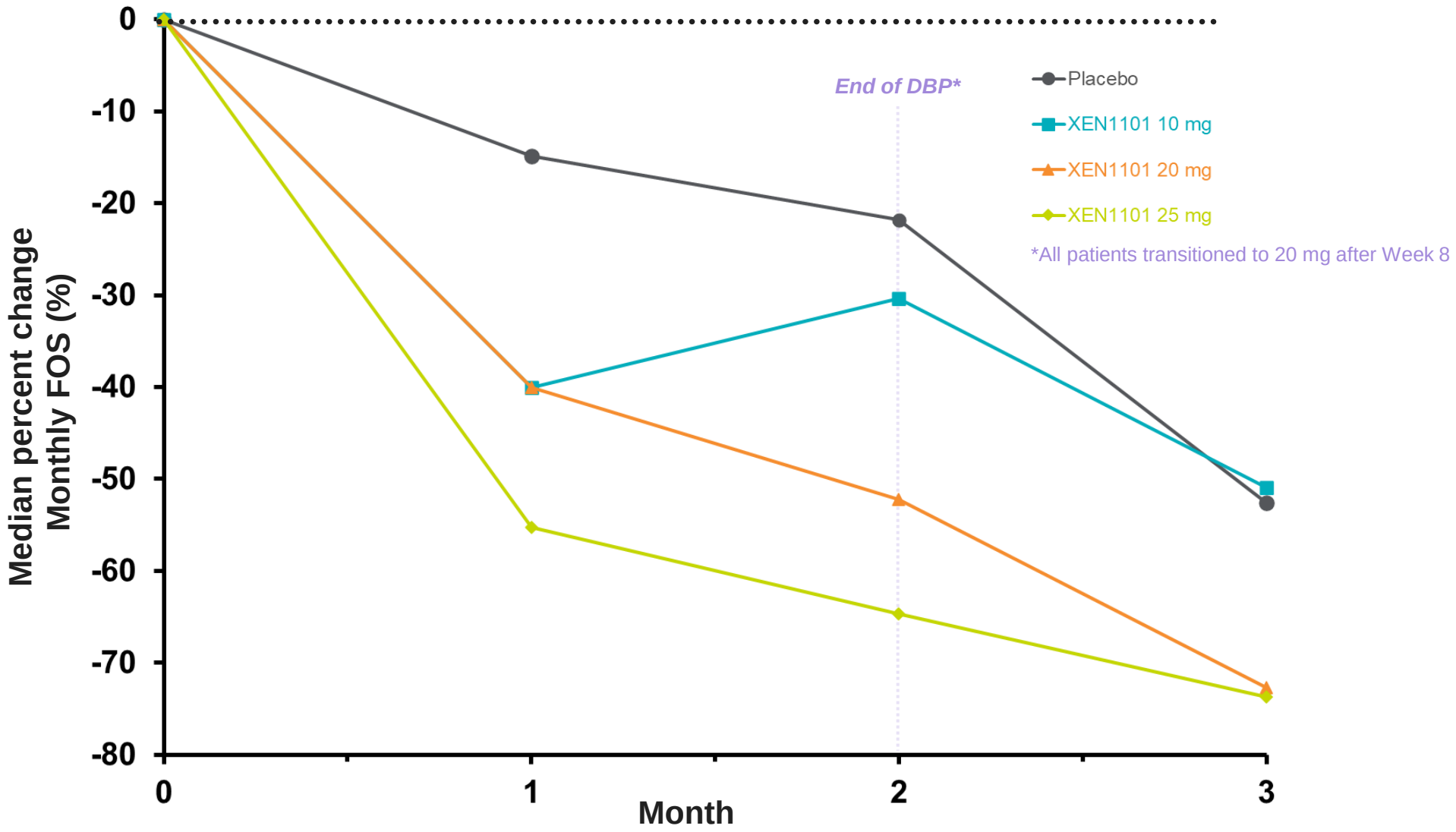
XEN1101 Rapid Reduction of Seizure Frequency

- MPC at Week 1 showed rapid seizure reduction
  - At Week 1, XEN1101 demonstrated a reduction of:
    - 39.1% (p=0.002) N=46 in 10 mg group
    - 41.5% (p=0.039) N=50 in 20 mg group
    - 55.4% (p<0.001) N=110 in the 25 mg group



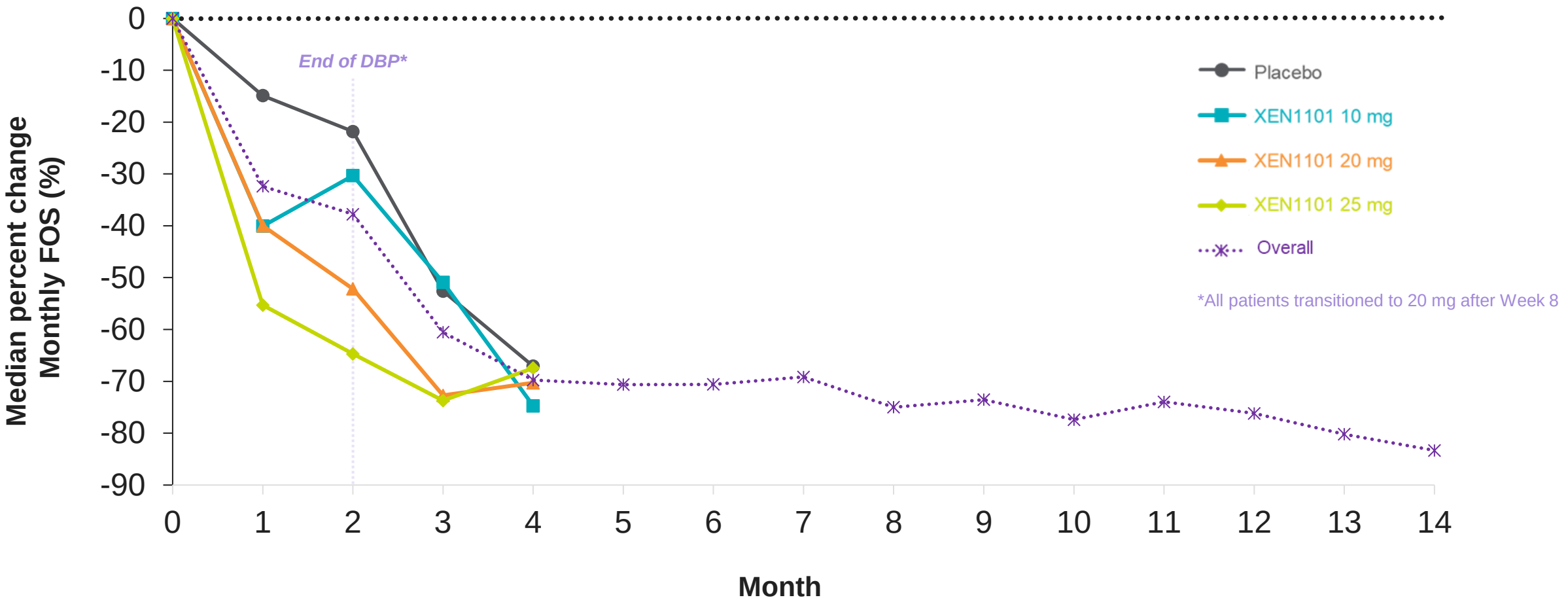
X-TOLE and X-TOLE OLE: Continued Reduction of Seizure Frequency

- Improvement in MPC demonstrated during double blind period continued from Week 8 to Week 12 (Phase 3 endpoint)
- Greater seizure reductions in placebo and 10 mg groups as they transitioned to 20 mg in OLE



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

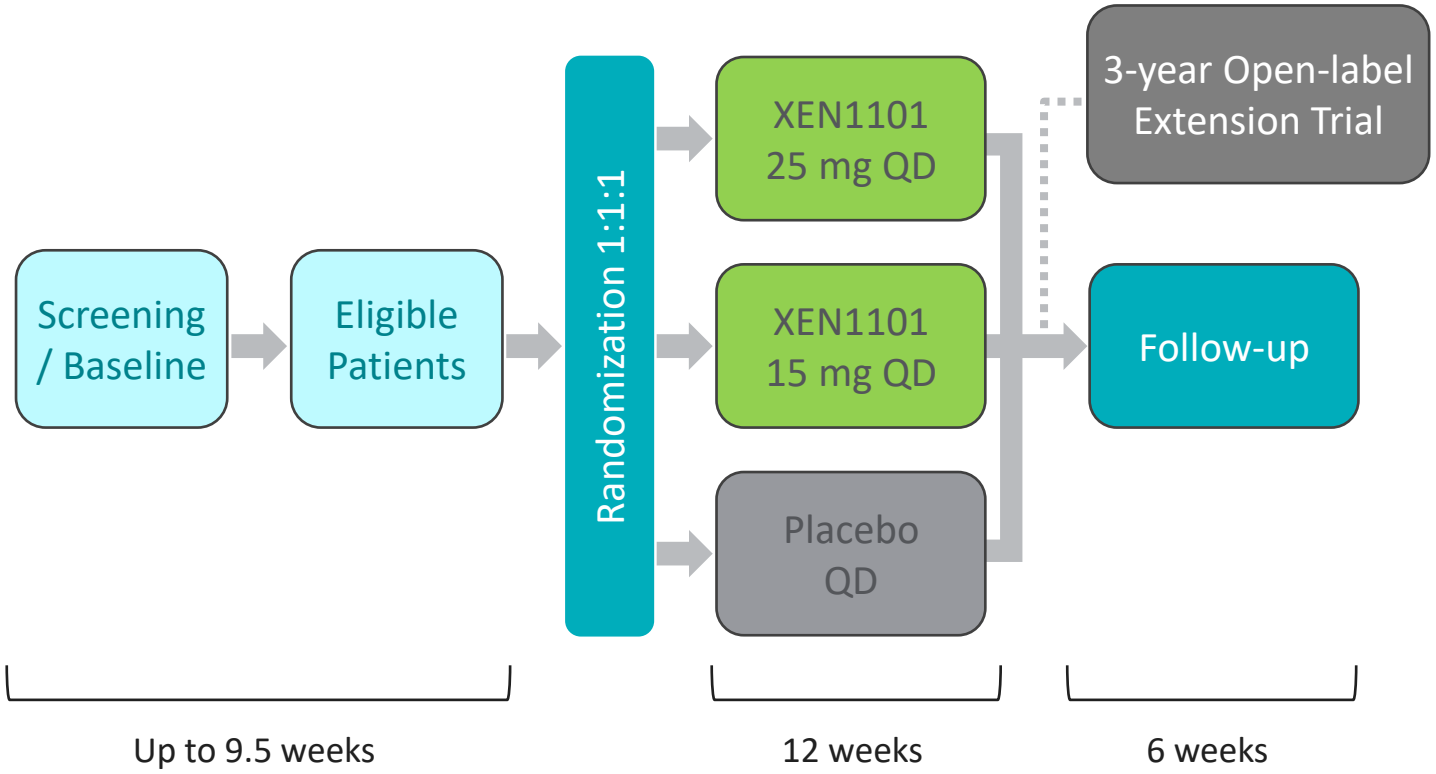
- Improvement in MPC demonstrated during DBP with continued improvement in OLE



Next Steps for XEN1101

- Completed End-of-Phase 2 meeting with the FDA, resulting in alignment on clinical programs moving forward in FOS and PGTCS
- Plan on submitting NDA supported by efficacy data from Phase 2b study and one Phase 3 study (X-TOLE2)
- Expansion into Phase 3 X-ACKT trial in PGTCS (to be initiated) and Phase 2 X-NOVA POC trial in MDD (ongoing)

X-TOLE2 and X-TOLE3 Trial Design



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

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

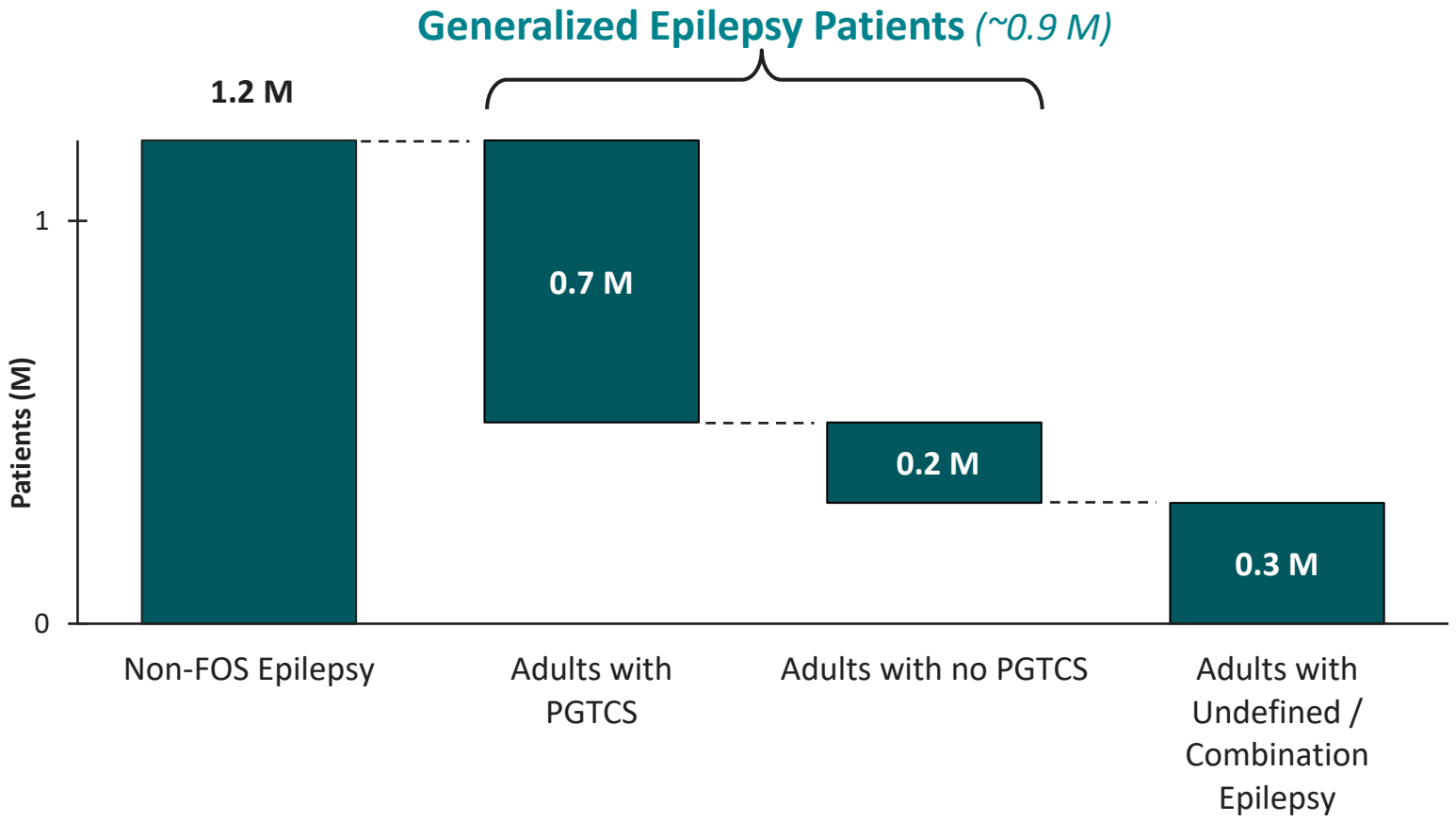
- Seizure frequency varies, usually with recurrences ranging from weeks to months, with a tendency to cluster, and can be fatal
  - 30-50% of people who have one unprovoked tonic-clonic seizure have a subsequent event
- PGTCS also has a substantial negative impact on quality of life
  - High unemployment 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

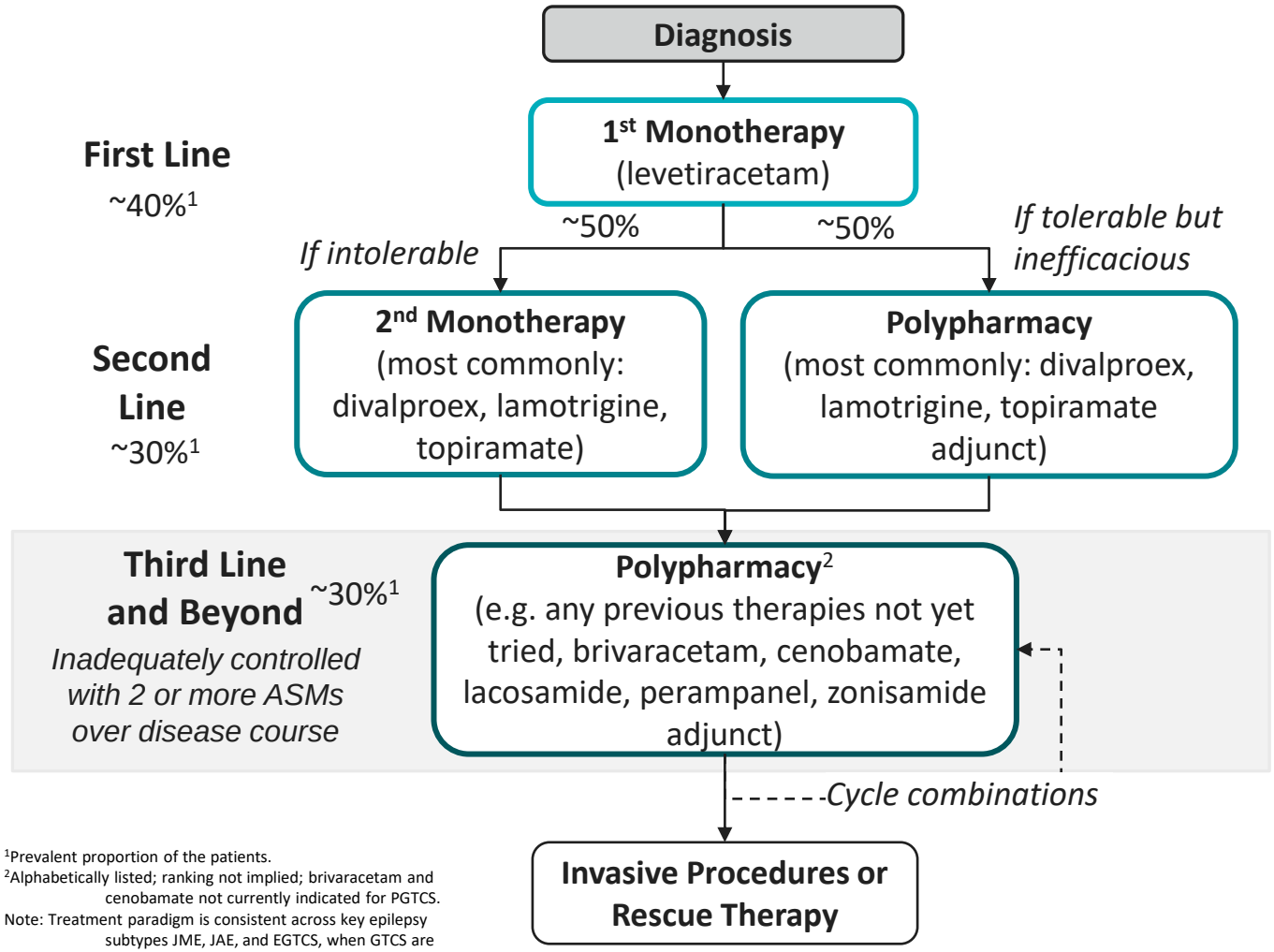
Adult Generalized Epidemiology



- 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

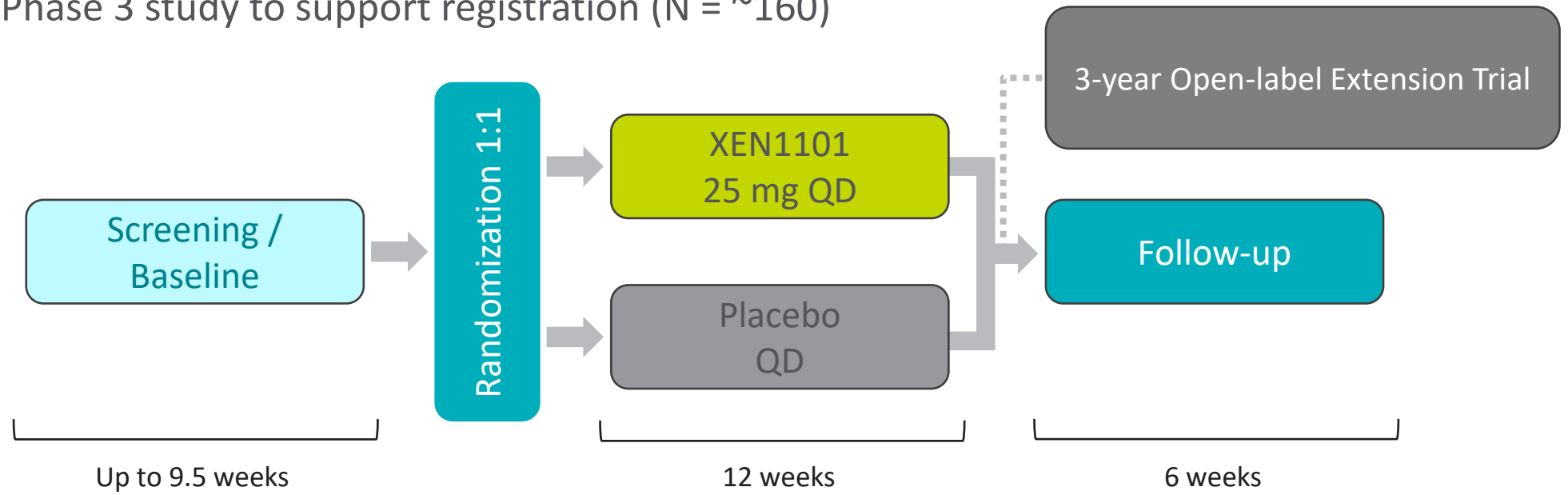
- XEN1101 anti-seizure activity in maximum electroshock seizure and pentylenetetrazole preclinical models, both known to predict efficacy for primary generalized seizures
- ICA-105665 (Kv7 potassium channel opener) suppressed photosensitivity (EEG model) in generalized epilepsy patients[1]
- Levetiracetam, 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 “X-ACKT” PGTCS Phase 3 Trial Design

- Aligned with FDA regarding clinical development plan in PGTCS to conduct a single, multi-center, placebo-controlled Phase 3 study to support registration (N = ~160)



- **Primary Objective:**
  - MPC of 25 mg dose of XEN1101 vs placebo on seizure frequency in adults with primary generalized tonic-clonic seizures (PGTCS) taking 1 to 3 ASMs in the DBP
- **Secondary Objectives** include assessing the effect on XEN1101 vs placebo on RR50, seizure freedom and PGI-C

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

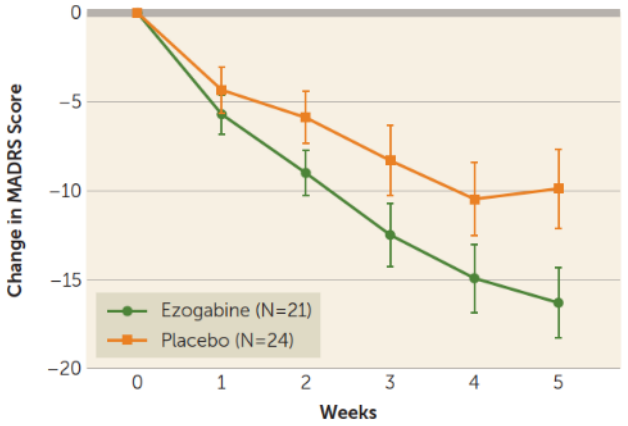
[1]Company Poster. 2018 American Epilepsy Society (AES) Annual Meeting: "A First-in-Human Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Pharmacodynamics of a Novel Small Molecule KV7.2/7.3 Positive Allosteric Modulator (XEN1101) in Healthy Subjects." December 3, 2018

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

XEN1101 Phase 2 POC Studies in Major Depressive Disorder

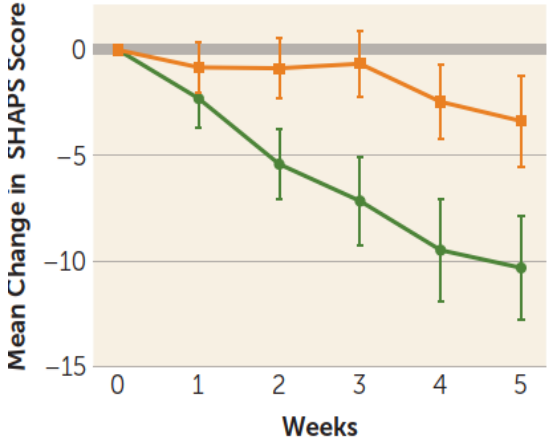
- Promising clinical results with ezogabine dosed 300 mg TID as a treatment for Major Depressive Disorder (MDD) and anhedonia
- Encouraging pre-clinical activity data with XEN1101
- Depression is one of the most common co-morbidities within the FOS patient population
- Patient enrollment underway in both company-sponsored and investigator sponsored Phase 2 POC studies in MDD

Montgomery–Åsberg Depression Rating Scale



Ezogabine, compared with placebo, was associated with a large improvement in depression as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS score change from placebo: -7.9±3, p<.001)

Snaith-Hamilton Pleasure Scale



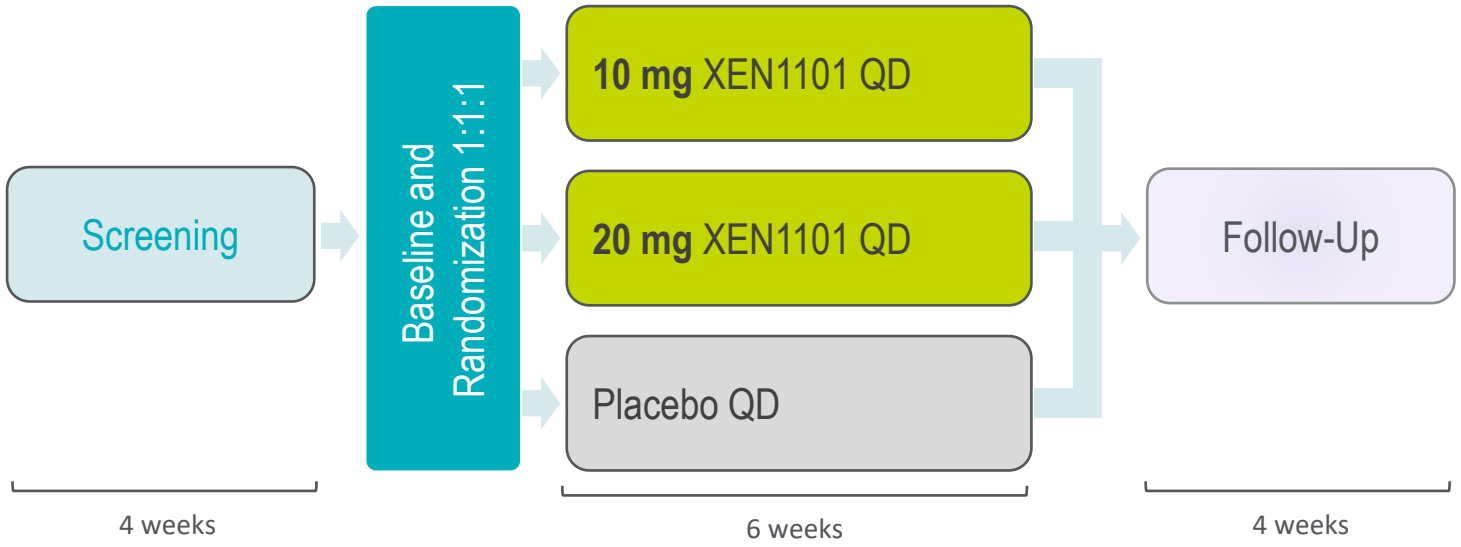
Compared with placebo, ezogabine was associated with a large improvement in hedonic capacity as measured by the Snaith-Hamilton Pleasure Scale (SHAPS score change from placebo: -6.9±3.2, p<.001)

Costi et al, Am J Psychiatry 2021

XEN1101 Phase 2 POC Studies in Major Depressive Disorder

Company-sponsored "X-NOVA" XEN1101 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 2023

XEN496: Potential Precision Medicine Approach for KCNQ2-DEE

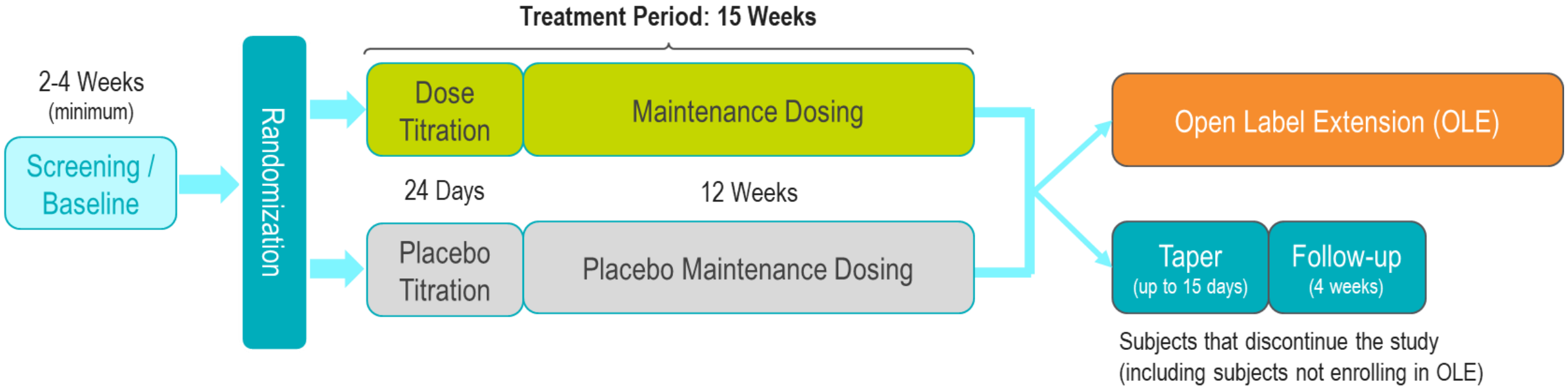
Development of Proprietary XEN496

- 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

Phase 3 Clinical Trial Underway

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



Study completion anticipated in 2023

Summary of Potential Value-Creating Milestone Opportunities

XEN1101 (Epilepsy)

- Successful Phase 2b X-TOLE clinical trial in adult focal seizures demonstrated statistical significance on primary and secondary seizure reduction endpoints, showing dose-dependent CNS activity
- Completed End-of-Phase 2 meeting with the FDA resulting in alignment on clinical program:
  - Initiation of Phase 3 clinical trial (X-TOLE2) in FOS expected in 2H:22
  - Single Phase 3 trial (X-ACKT) to support registration in PGTCS expected to be initiated shortly after initiation of X-TOLE2
  - NDA submission to be based on Phase 2b X-TOLE and first Phase 3 (X-TOLE2) efficacy data

XEN1101 (MDD)

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

XEN496

- Phase 3 EPIK clinical trial in pediatric KCNQ2-DEE underway; anticipated completion in 2023

Partnered Programs

NBI-921352 (XEN901) / Neurocrine Biosciences

- Two Phase 2 clinical trials underway with NBI-921352 in adult focal-onset epilepsy and pediatric SCN8A-DEE

PCRX301 / Pacira BioSciences

- Phase 1b POC clinical trial underway with PCRX301 in patients undergoing bunionectomy (post-operative pain)

For more information

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