Corporate Overview

MARCH 2024

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 and include statements regarding the timing of and potential results from clinical trials; the potential efficacy, safety profile, future development plans in current and anticipated indications, addressable market, regulatory success and commercial potential of our and our partners' product candidates; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in our XEN1101 and other pipeline and development programs; the timing and results of our interactions with regulators; our ability to successfully develop and obtain regulatory approval of XEN1101 and our other product candidates; anticipated enrollment in our clinical trials of XEN1101 and the timing thereof; and our expectation that we will have sufficient cash to fund operations into 2027.

These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause the actual results, events, or developments to be materially different from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: 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; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; the impact of new or changing laws and regulations; the impact of pandemics, epidemics and other public health crises on our research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, regulatory agencies and related review times, and contractors who act for or on our behalf; the impact of unstable economic conditions in the general domestic and global economic markets; adverse conditions from geopolitical events; 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. These forward-looking statements speak only as of the date hereof and we assume no obligation to update these forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

About Xenon Pharmaceuticals

- Neuroscience-focused biopharma company
- Leader in small molecule, ion channel drug discovery and development
- XEN1101 represents most advanced potassium channel modulator currently in clinical development for multiple indications
  - Comprehensive intellectual property portfolio with patent coverage extending to at least 2040, absent any extensions of patent term
- Robust pipeline of therapeutic candidates
- Strong financial position
  - $930.9 million in cash, cash equivalents and marketable securities (as of Dec. 31, 2023)
  - Anticipated cash runway to fund operations into 2027

Xenon's Neuroscience-Focused Pipeline

	Clinical Trial/Partner	Pre-Clinical	Phase 1	Phase 2	Phase 3
XEN1101 (Potassium Channel Opener)					
Focal Onset Seizures (FOS)	X-TOLE2				
Focal Onset Seizures (FOS)	X-TOLE3				
Primary Generalized Tonic-Clonic Seizures (PGTCS)	X-ACKT				
Major Depressive Disorder (MDD)	X-NOVA				
Major Depressive Disorder (MDD)*	Mount Sinai				
Other Ion Channel Modulators					
Kv7 (Potassium Channel) Openers					
Nav 1.7 (Sodium Channel) Inhibitors					
Nav 1.1 (Sodium Channel) Openers					
NBI-921352 (Partnered Program - Sodium Channel Inhibitor)					
Orphan Pediatric Epilepsy (SCN8A-DEE)	Neurocrine				

*Investigator Sponsored Phase 2 Proof-of-Concept Study

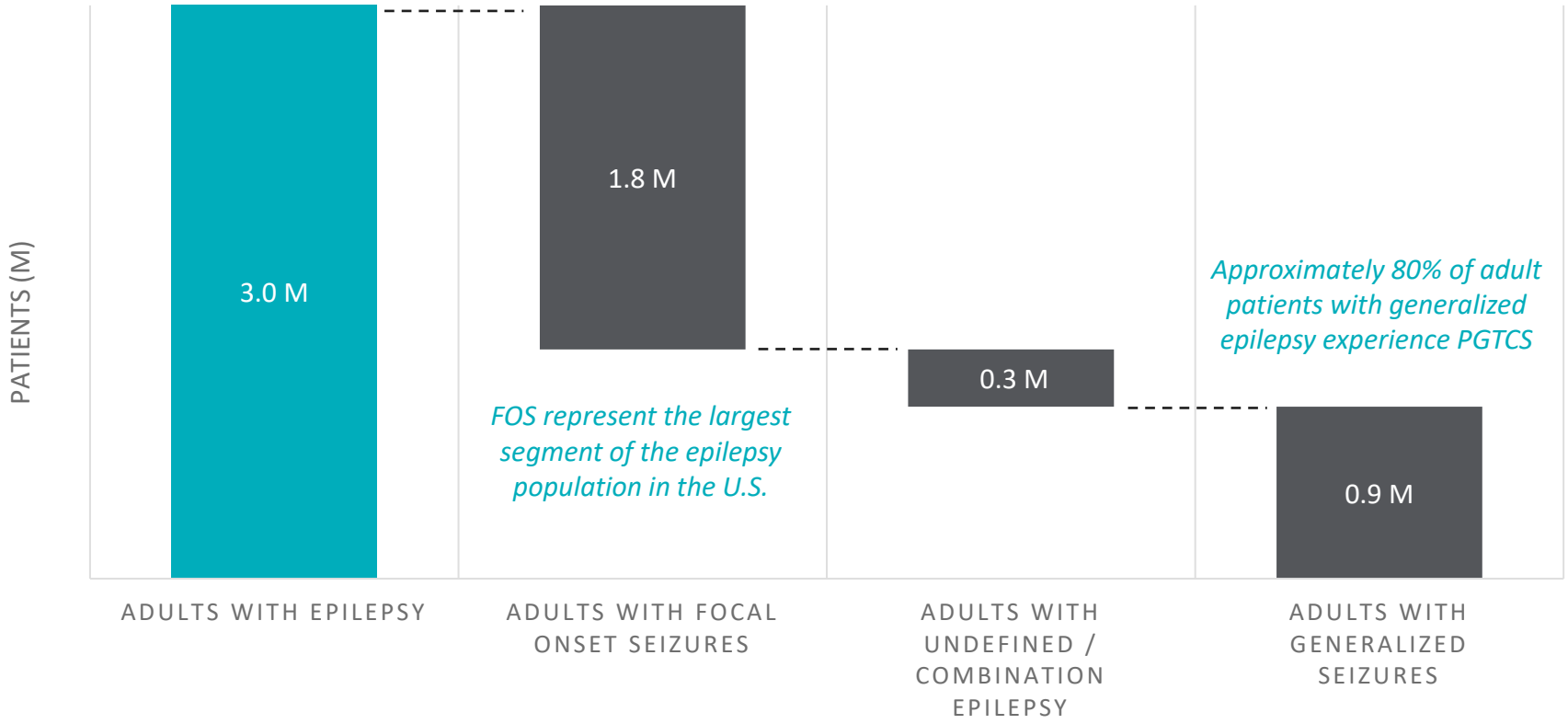
Overview of XEN1101 in Epilepsy

X-TOLE, X-TOLE2, X-TOLE3, AND X-ACKT CLINICAL TRIALS

A Significant Unmet Medical Need in Epilepsy

- Epilepsy is the fourth most **common neurological condition**
  - Hallmark symptoms include **focal seizures** - seizures that start in one brain hemisphere (either aware or unaware) and **generalized seizures** - (the most common of which are tonic clonic / convulsive seizures)
- Despite the availability of multiple anti-seizure medications (ASMs), a **substantial unmet medical need exists**

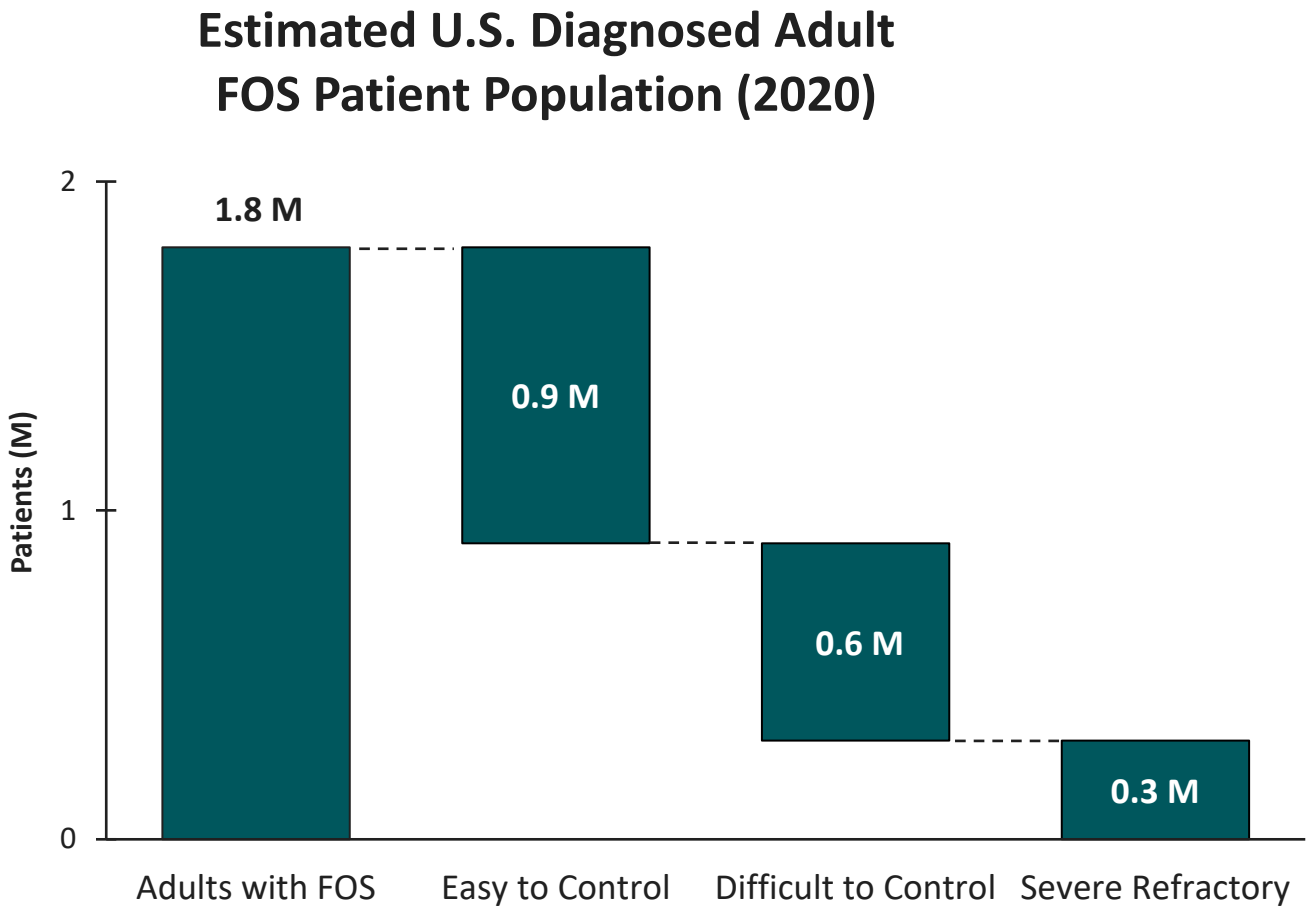
Estimated U.S. Diagnosed Adult Epilepsy Patient Population (2020)



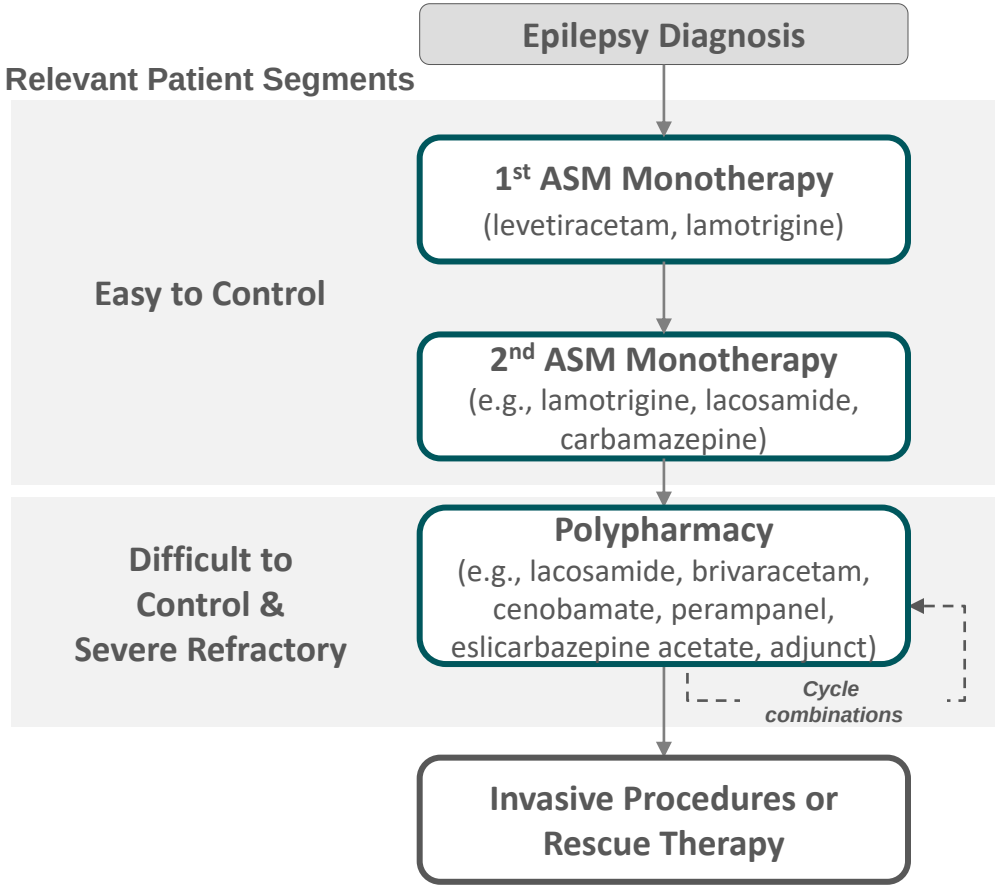
Approximately 470,000 children under the age of 18 have epilepsy in the U.S.

Source: Xenon-sponsored market research

Adult Focal Onset Seizure Landscape



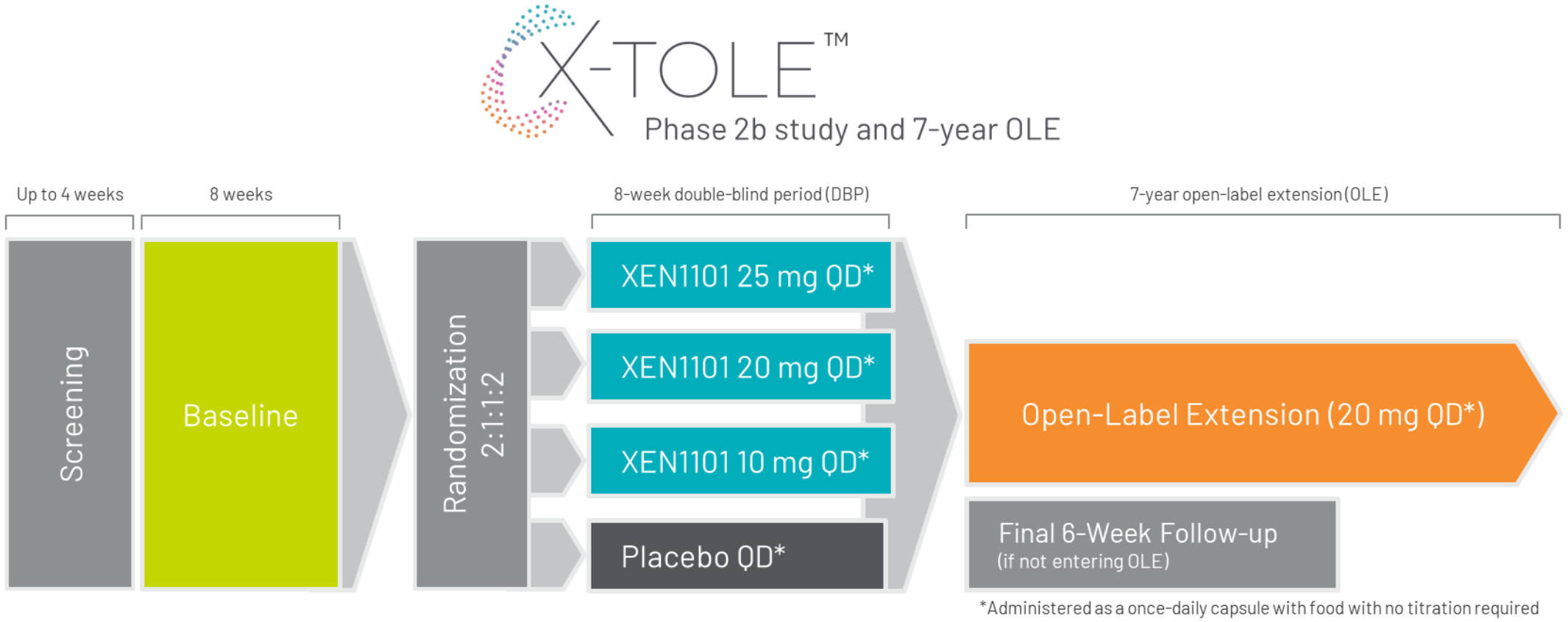
Treatment goal is to optimize efficacy while managing comorbidities and maximizing quality of life



PGTCS treatment paradigm is consistent with FOS with the exception that carbamazepine and derivatives are not commonly used in PGTCS. In addition, brivaracetam and cenobamate are not currently indicated for PGTCS.

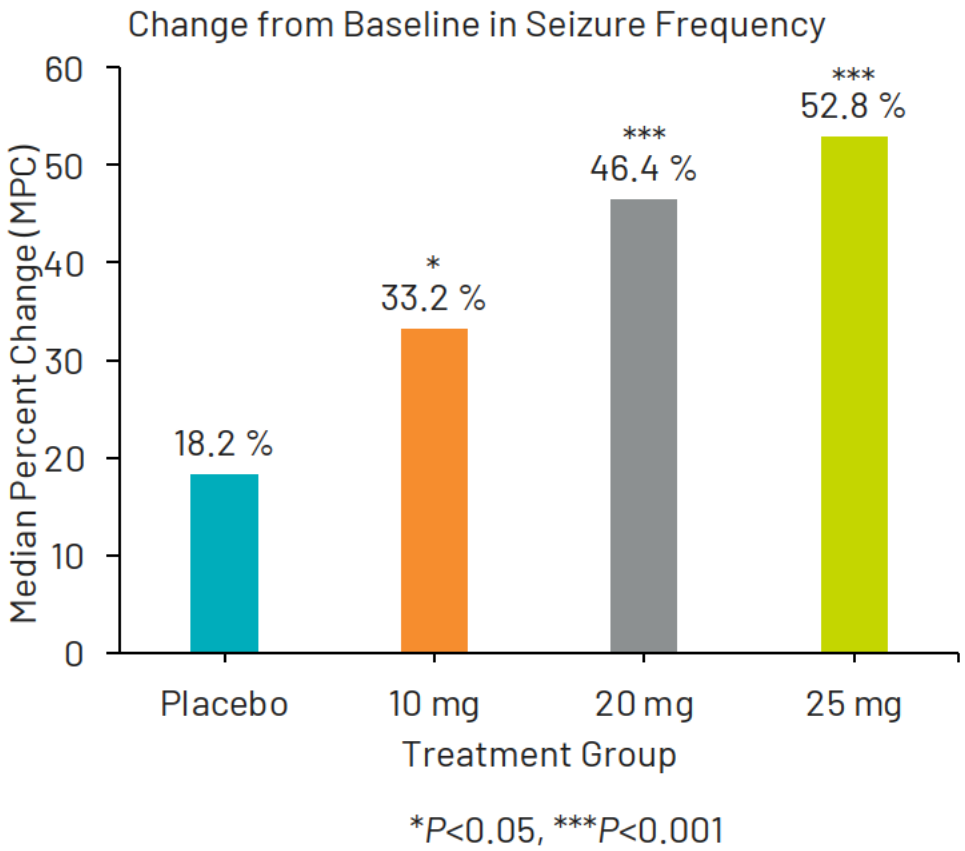
Source: Xenon-sponsored market research

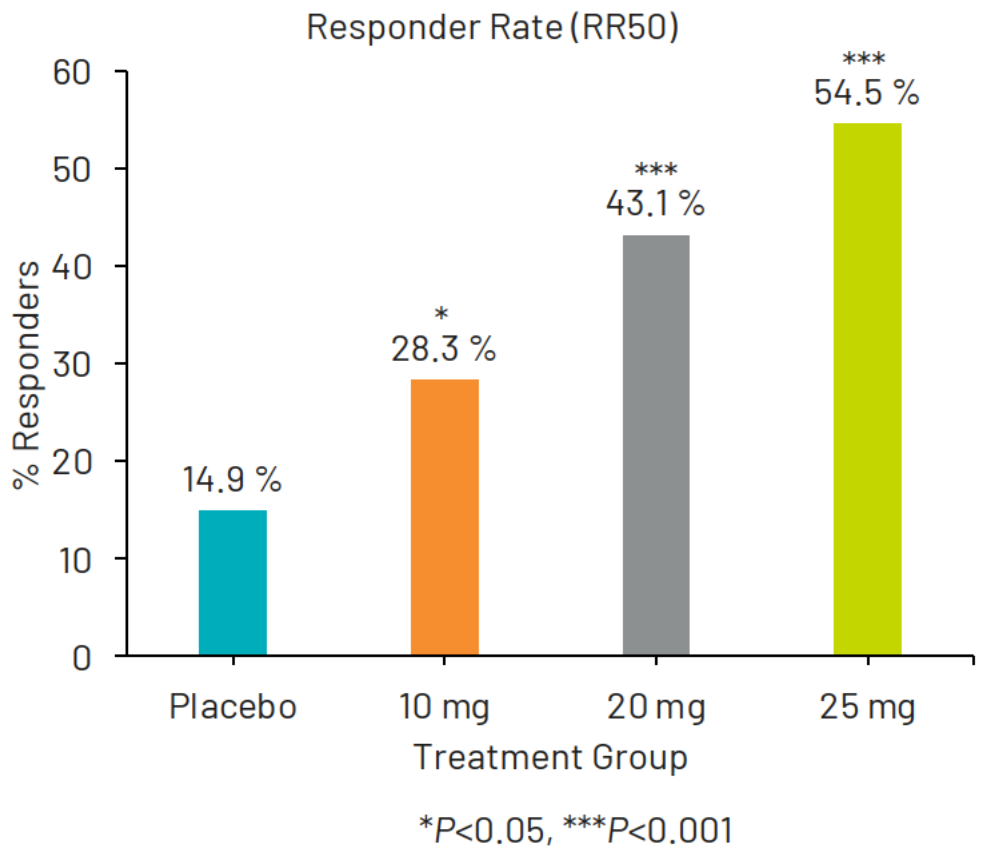
XEN1101 X-TOLE Phase 2b Trial



Topline results reported in October 2021 and subsequent *ad hoc* analyses and OLE data presented at AES meetings

Compelling Phase 2b Efficacy Results





XEN1101 was administered as a once-daily capsule with food.

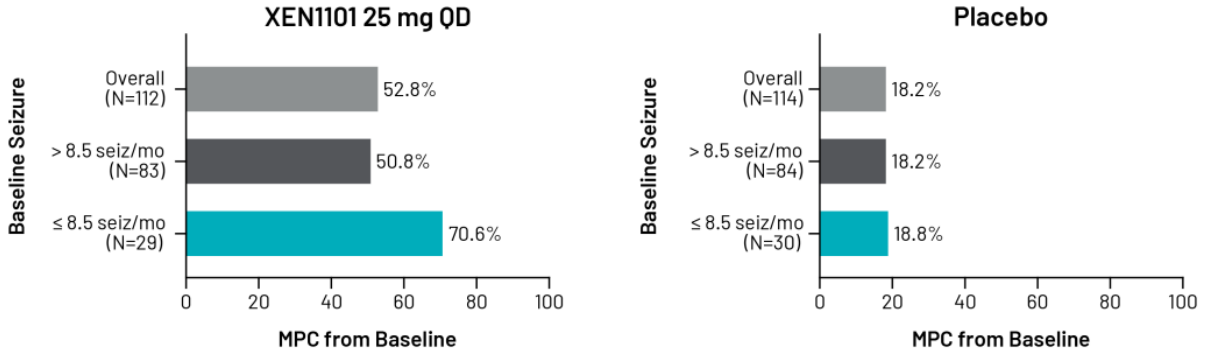
Highly significant and dose dependent reduction in seizures

Source: "Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, in Adults with Focal Epilepsy (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

X-TOLE Sub-Group Analyses (Double-Blind Period)

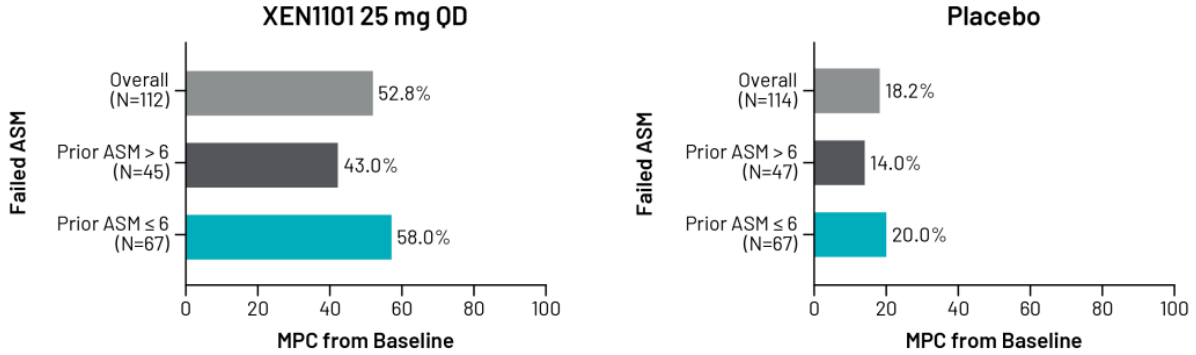
Baseline Seizure Sub-Group Analysis

- 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



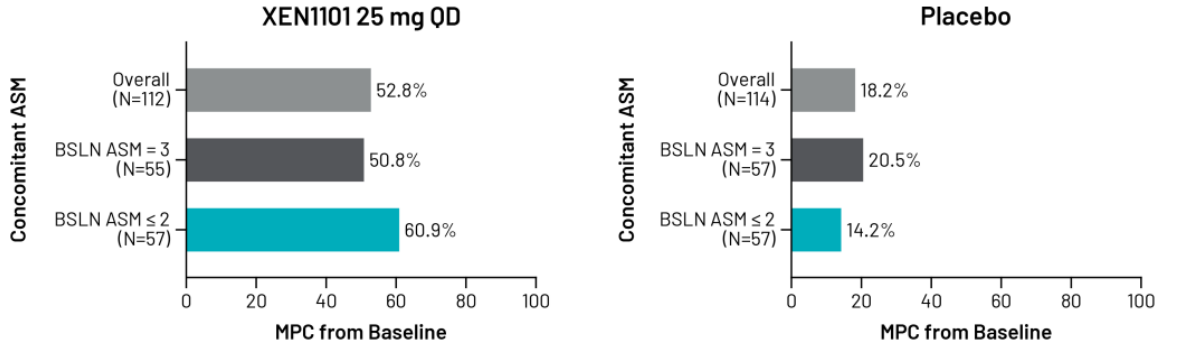
Prior Failed ASMs Sub-Group Analysis

- 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

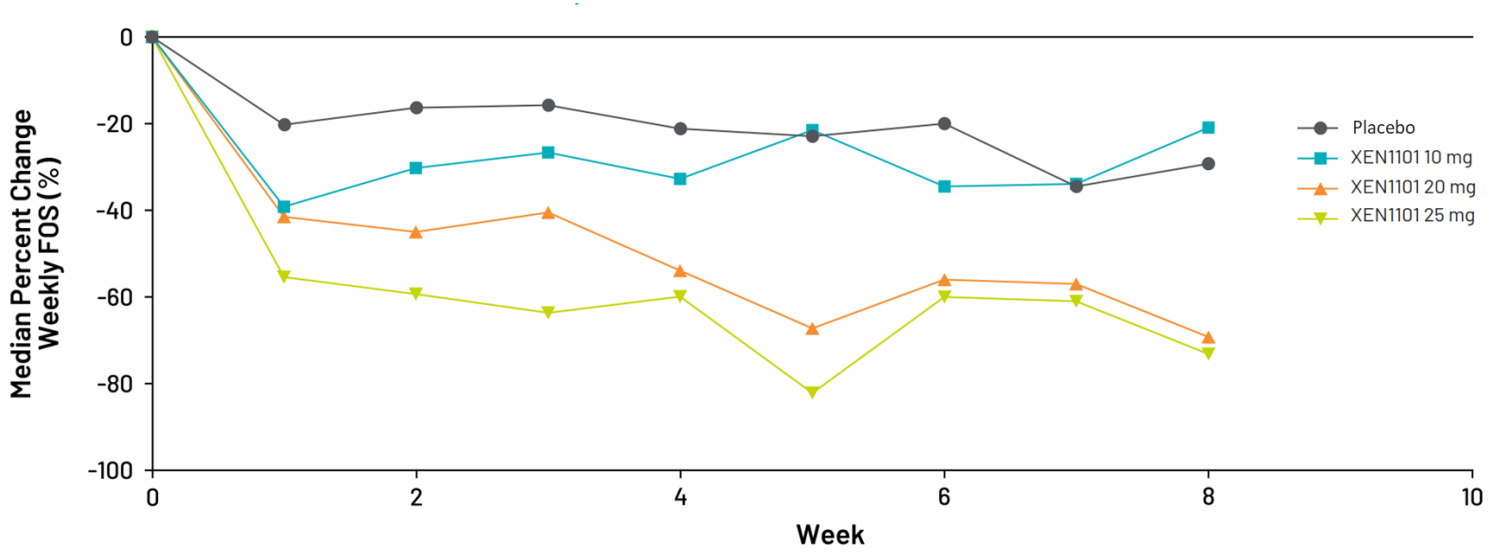
- Median monthly FOS reduction was 60.9% for subjects with 1-2 concomitant ASMs and 50.8% for subjects with 3 concomitant ASMs



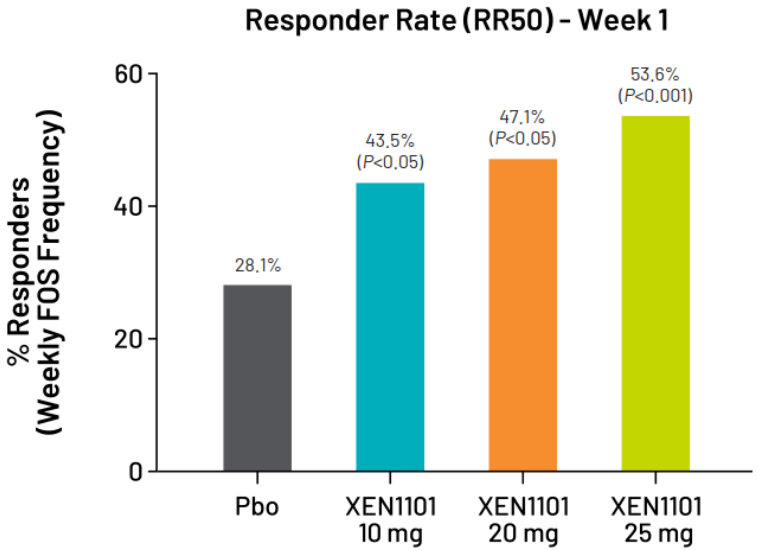
Notes: XEN1101 was administered as a once-daily capsule with food. The post hoc analysis was categorized by ≤ 8.5 and > 8.5* seizures per month for baseline seizure burden, ≤ 6 and > 6 prior failed ASMs (median), and = 3 or ≤ 2 concomitant ASMs (pre-specified).

XEN1101 Rapid Onset of Efficacy (Double-Blind Period)

Median Percent Change from Baseline in Weekly Focal Onset Seizure (FOS) Frequency in DBP



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



XEN1101 was administered as a once-daily capsule with food.

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

Source: "Rapid Onset of Efficacy of XEN1101, a Novel Potassium Channel Opener, in Adults with Focal Epilepsy: Results from a Phase 2b Study (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

X-TOLE: Safety and Tolerability Data

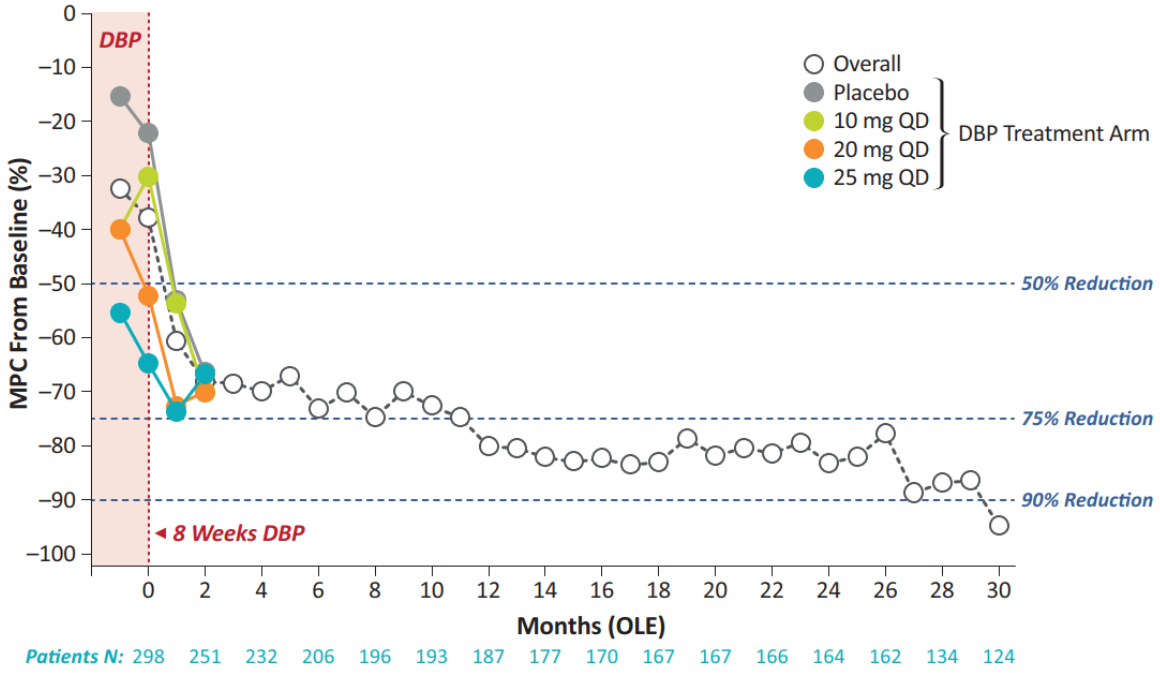
- X-TOLE Double-Blind Period
  - XEN1101 was generally well-tolerated in this study with adverse events consistent with other commonly prescribed ASMs
    - The most common reported treatment emergent adverse events (TEAEs) across all XEN1101 dose groups were dizziness (24.6%), somnolence (15.6%) and fatigue (10.9%), as compared to the placebo group which reported dizziness (7.0%), somnolence (7.0%) and fatigue (5.3%)
    - The most common TEAEs leading to discontinuation across all XEN1101 dose groups were dizziness (4.7%), balance disorder (2.4%), dysarthria (1.9%) and gait disturbance (1.9%)
    - Serious adverse events (SAE) incidence was low and balanced across groups (3.3% across all XEN1101 dose groups as compared to 2.6% in the placebo group)
- X-TOLE Open-Label Extension*
  - XEN1101 20 mg QD was generally well tolerated in OLE, and the safety profile observed was similar to that of the DBP; no new safety signals were identified

* Results are from interim data from the open-label extension of X-TOLE (cutoff date September 5, 2023).

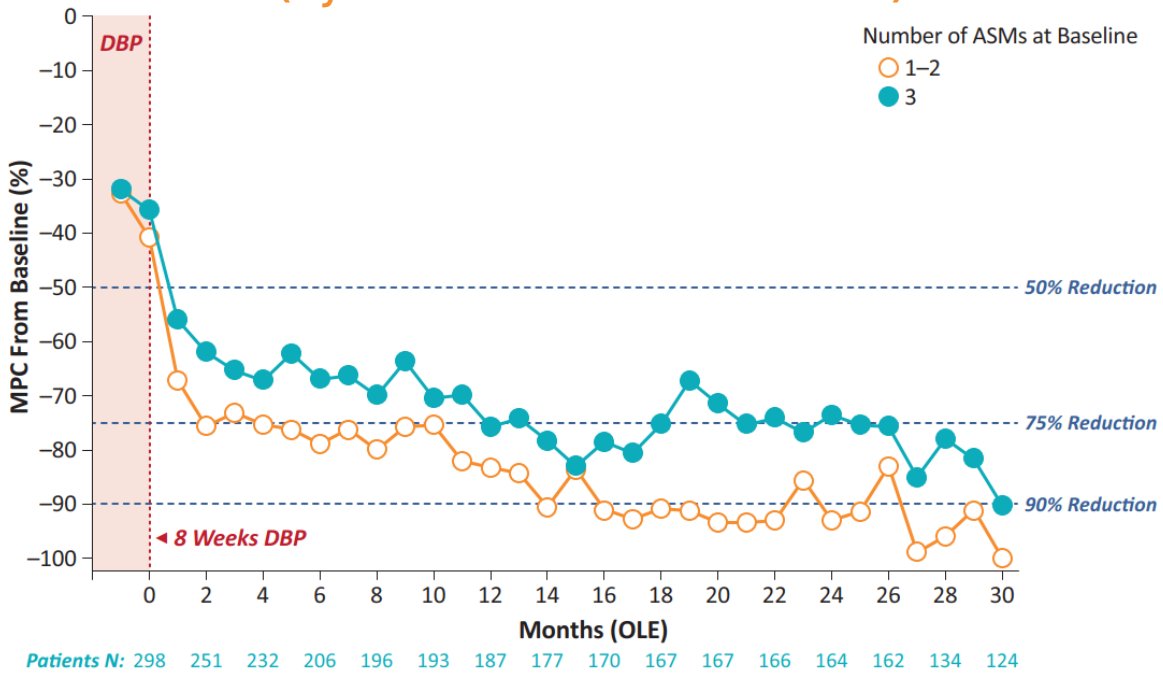
Sources: "Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, in Adults with Focal Epilepsy (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).
"Interim Long-Term Safety and Efficacy of XEN1101, a Potent, Selective Potassium Channel Opener: Update From an Ongoing, Open-Label Extension of a Phase 2b Study (X-TOLE) in Adults With Focal Epilepsy." 2023 Annual Meeting of the American Epilepsy Society (AES).

Compelling Long-Term Efficacy Results in OLE

MPC in Monthly FOS Frequency During DBP and OLE



MPC in Monthly FOS Frequency During DBP and OLE (by Baseline Number of ASMs)

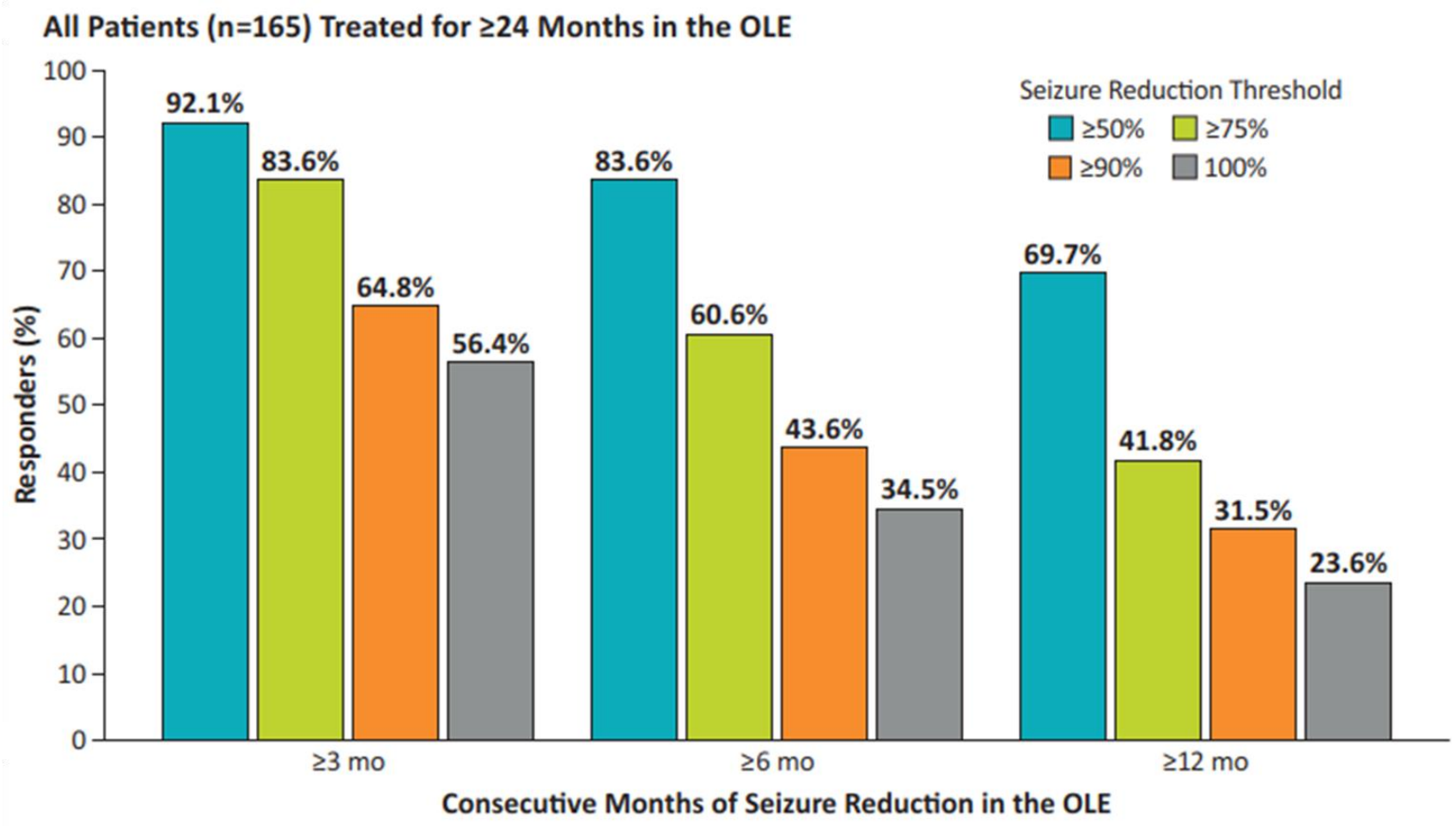


Notes: XEN1101 was administered as a once-daily capsule with food. Monthly seizure rate was calculated for 28 days per month. Following DBP, all patients received 20 mg QD with food at start of OLE. 1 patient was not included in seizure frequency data because of non-compliance with seizure diary. ASM, antiseizure medication; DBP, double-blind period; FOS, focal onset seizures; MPC, median percentage change; OLE, open-label extension. The results presented here are interim data from the open-label extension of X-TOLE (cutoff date September 5, 2023).

Sustained monthly reduction in seizure frequency in OLE from DBP baseline with even greater improvements in patients on fewer baseline ASMs

Source: "Interim Long-Term Safety and Efficacy of XEN1101, a Potent, Selective Potassium Channel Opener: Update From an Ongoing, Open-Label Extension of a Phase 2b Study (X-TOLE) in Adults With Focal Epilepsy." 2023 Annual Meeting of the American Epilepsy Society (AES).

Compelling Seizure Reduction and Seizure Freedom



*These interim data (cutoff date September 5, 2023) are from the X-TOLE open-label extension in which patients received open-label XEN1101 at a dose of 20 mg once daily (QD) with food.

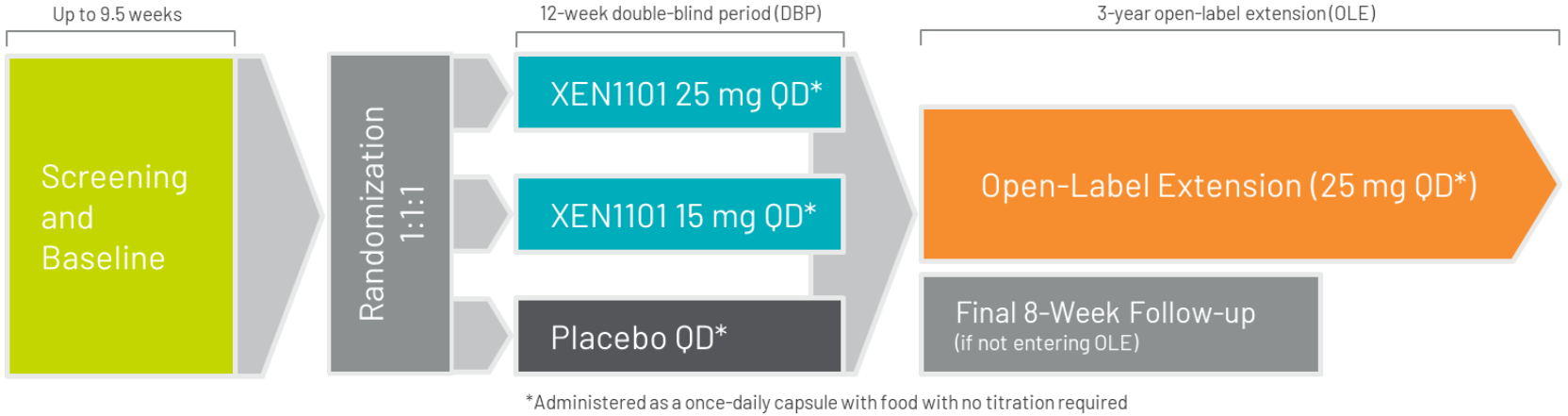
Seizure freedom for ≥12-month consecutive durations was achieved in almost 1 in 4 patients

Source: "Interim Long-Term Safety and Efficacy of XEN1101, a Potent, Selective Potassium Channel Opener: Update From an Ongoing, Open-Label Extension of a Phase 2b Study (X-TOLE) in Adults With Focal Epilepsy." 2023 Annual Meeting of the American Epilepsy Society (AES).

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

- XEN1101 Phase 3 epilepsy program in focal onset seizures and primary generalized tonic-clonic seizures underway
- 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)

X-TOLE 2 3™



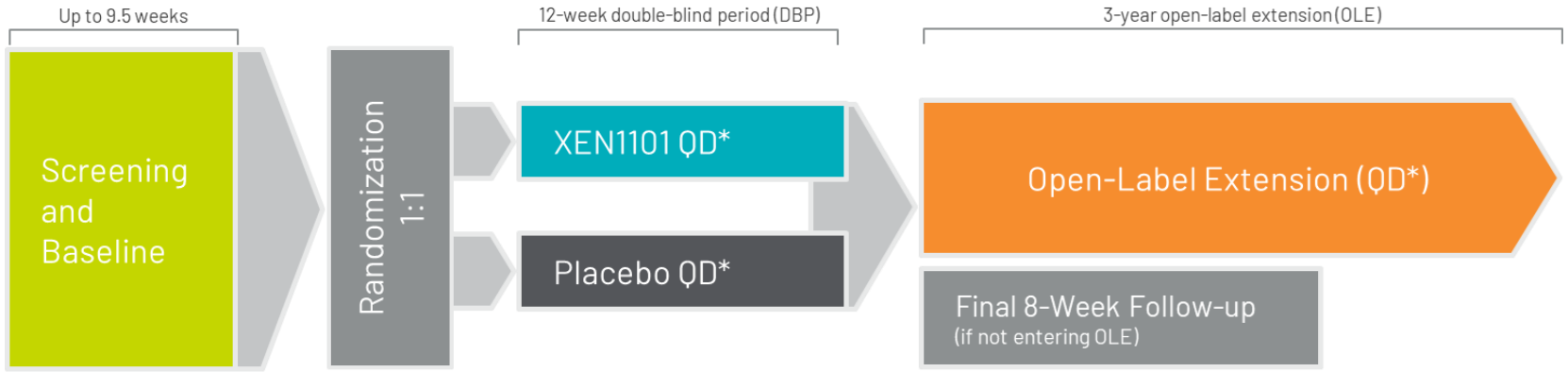
- **Primary Objective:**
  - Assess effect of XEN1101 vs placebo on reducing focal onset seizure frequency
- **Secondary Objectives** include assessing the effect on XEN1101 vs placebo on RR50, early treatment effect as measured at Week 1, and PGI-C

Patient enrollment in X-TOLE2 anticipated to be complete in late 2024 to early 2025

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)

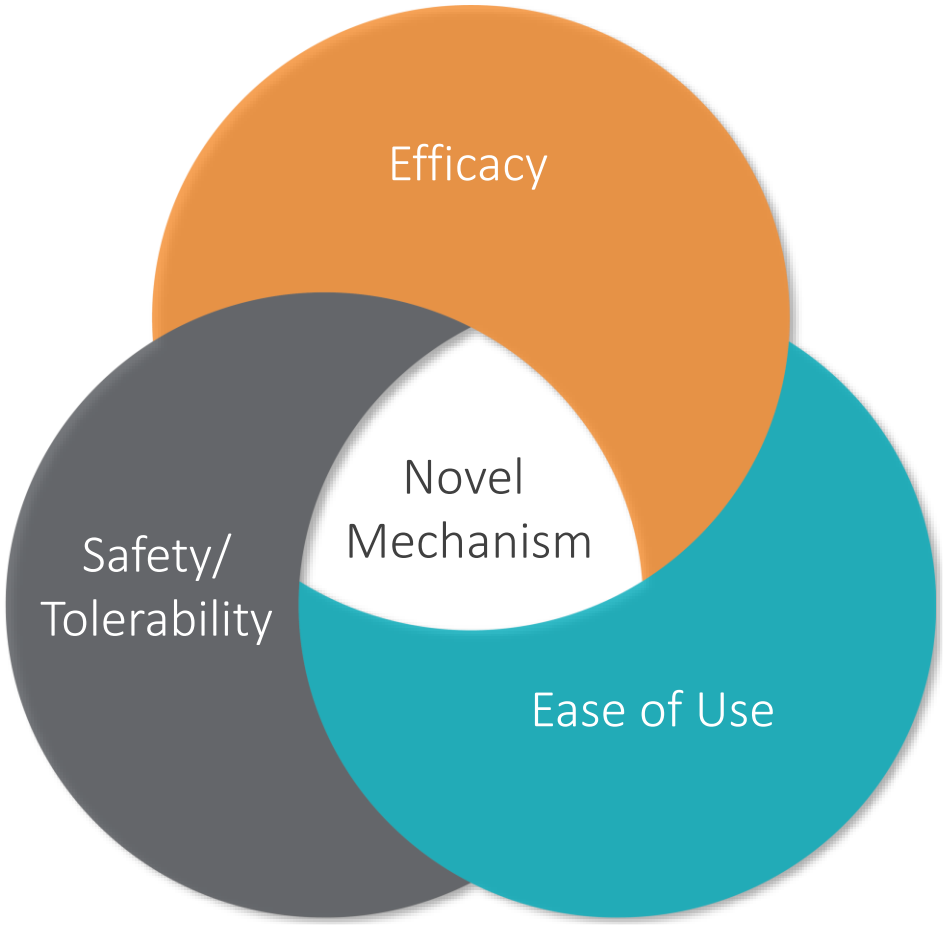
X-ACKT™



*Administered as a once-daily capsule with food with no titration required. Subjects aged ≥12 years and <18 years will receive either XEN1101 15 mg, XEN110125 mg, or placebo; subjects aged ≥18 years will receive either XEN110125 mg or placebo.

- **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

Value Potential of XEN1101 in Epilepsy



- Unique and novel Kv7 mechanism can be leveraged in rational polypharmacy

- Compelling and durable efficacy in difficult to treat adult focal onset seizure patient population
- Rapid efficacy as demonstrated by statistical significance at Week 1

- Generally well-tolerated with adverse event profile in line with other anti-seizure medications
- Long-term safety data with more than 600 hundred patient years

- One pill, once daily with food
- No titration required

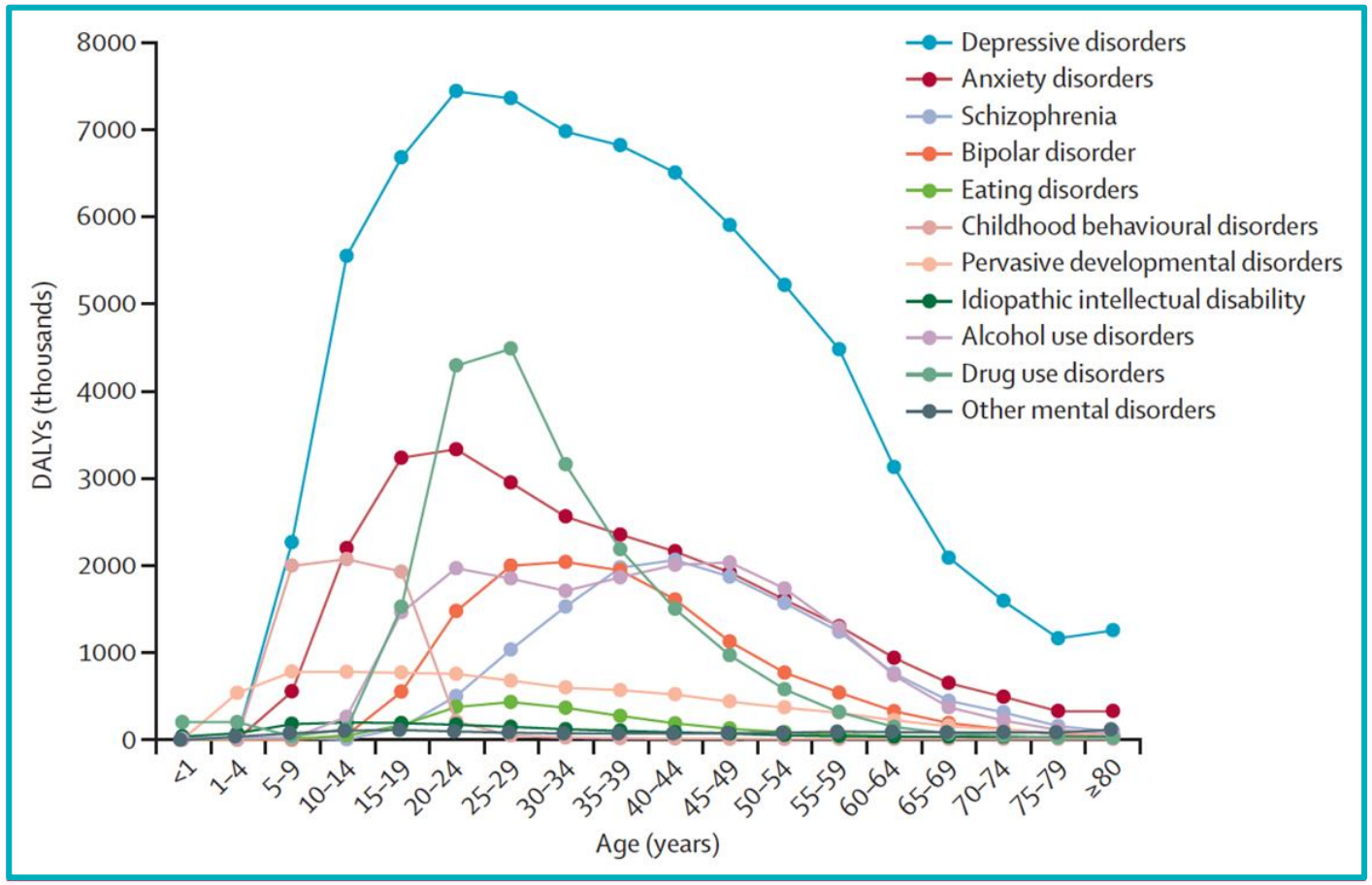
Overview of XEN1101 in Major Depressive Disorder (MDD)

X-NOVA CLINICAL TRIAL AND PHASE 3 PROGRAM INITIATION

MDD is a Highly Prevalent Mental Health Disorder

- In 2022, the MDD diagnosed prevalent population in the U.S. was approximately 21 million adults
  - ~55% treated with pharmacotherapy
  - 1 in 3 patients are inadequately managed on pharmacotherapy
- Anhedonia is a common comorbidity of MDD
  - Associated with poorer treatment outcomes

Depression Accounts for Greatest Disability Among All Central Nervous System Disorders

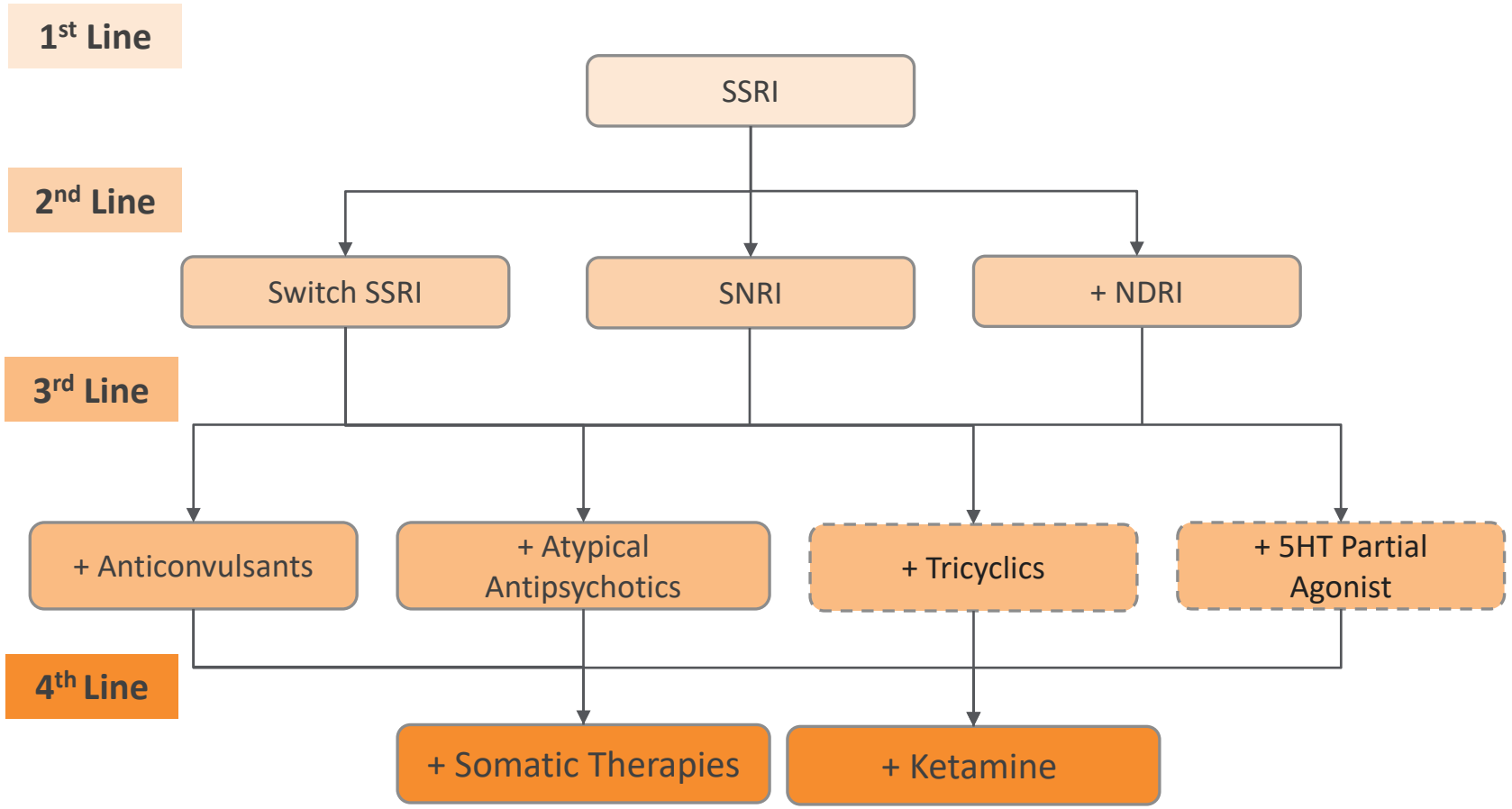


Disability-adjusted life years (DALYs) for each mental and substance use disorder in 2010, by age

Sources: Whiteford et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet*. 2013; Kern et al. Treatment patterns and sequences of pharmacotherapy for patients diagnosed with depression in the United States: 2014 through 2019. *BMC Psychiatry*. 2020; Fava, M. Definition and epidemiology of treatment-resistant depression. *Psychiatr Clin North Am*. 1996.

MDD Treatment Paradigm

MDD Lines of Therapy



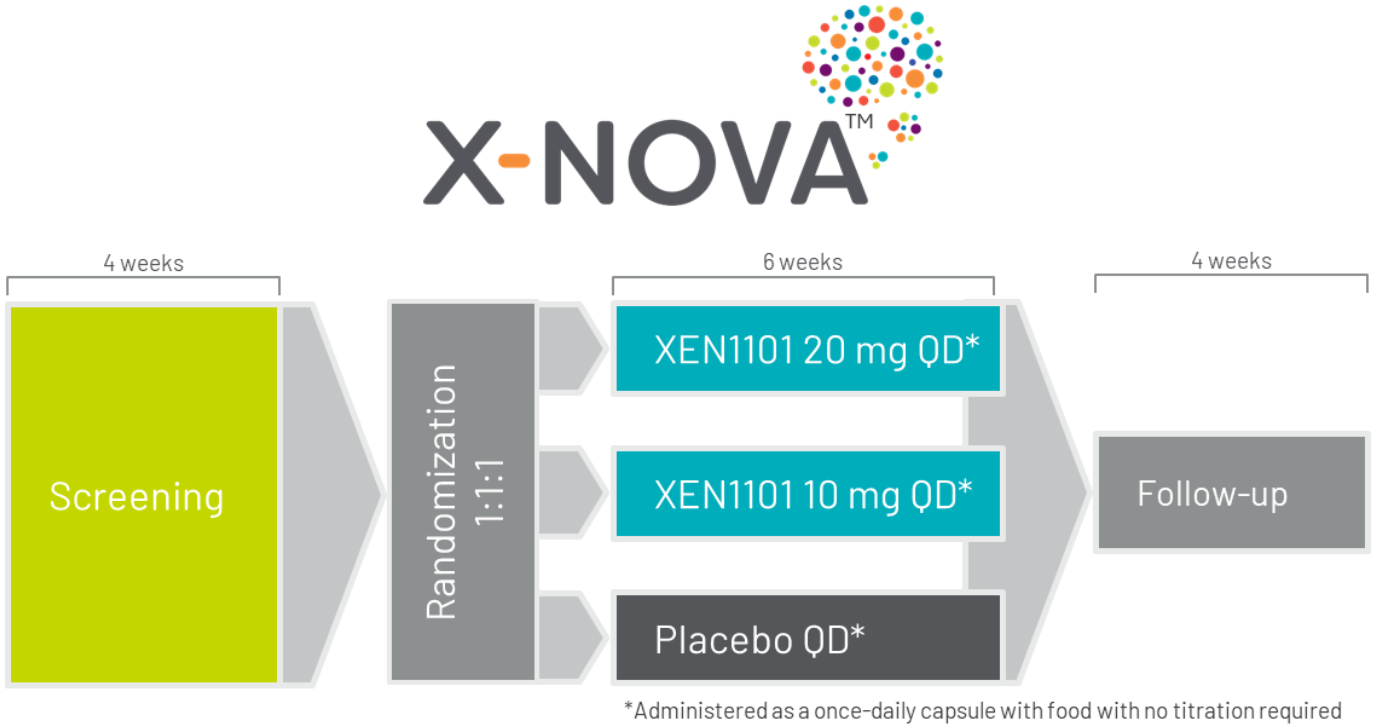
Treatment Considerations

- Physicians typically use multiple SSRIs/SNRIs, prior to progressing to branded therapy
- Poorly managed patients may seek alternative MOAs in 3L+
- Opportunity exists for novel mechanisms that offer efficacy in anhedonia with a differentiated safety profile

Source: Xenon-sponsored market research

XEN1101 X-NOVA Phase 2 Clinical Trial in MDD

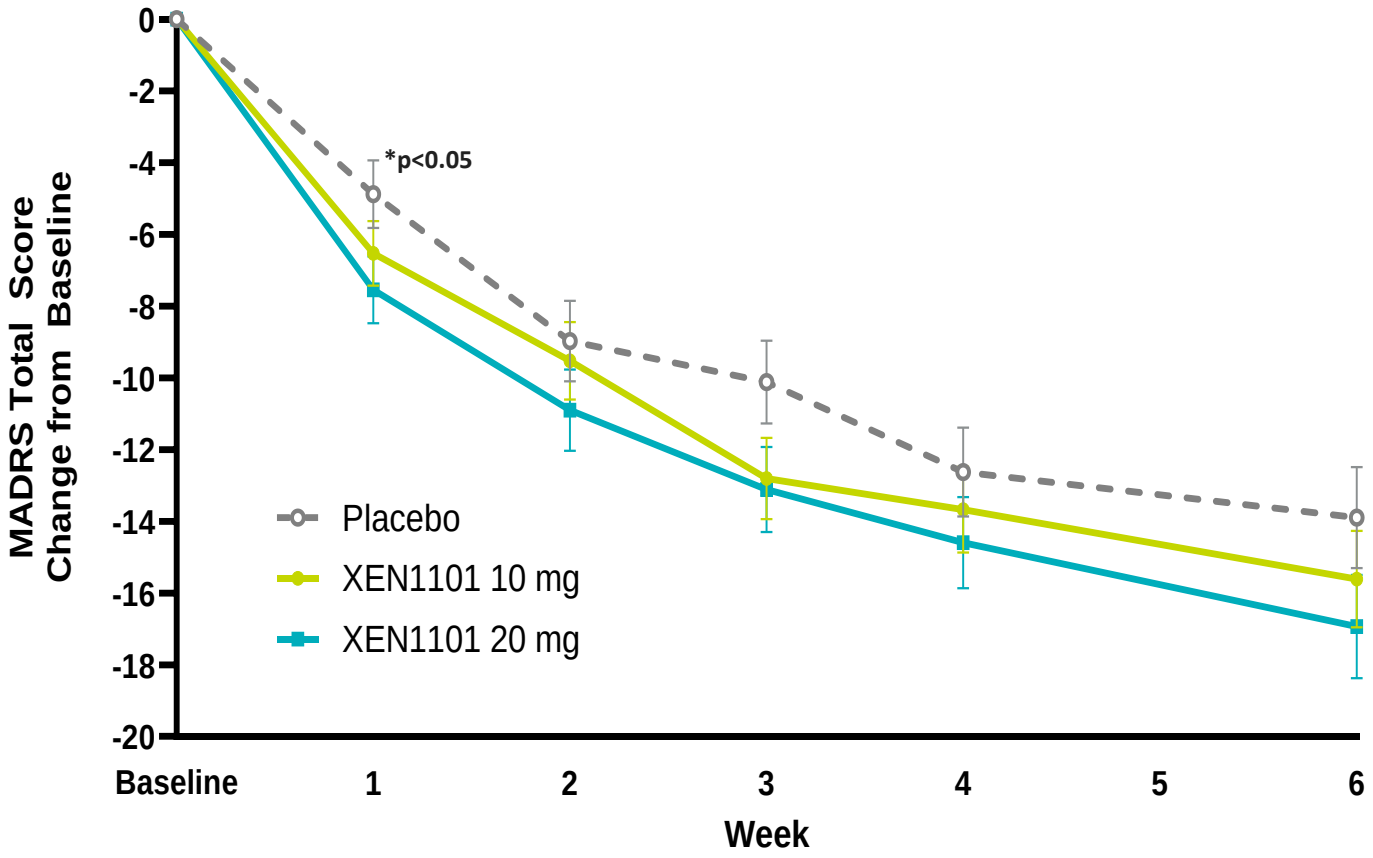
- Conducted a proof-of-concept, randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety, tolerability, and efficacy of XEN1101 in major depressive disorder



- **Primary Objective:**
  - Montgomery-Åsberg Depression Rating Scale (MADRS) score change through Week 6
- **Key Secondary Objective:**
  - Snaith-Hamilton Pleasure Scale (SHAPS) score change through Week 6

Topline data from Phase X-NOVA study announced in November 2023

Primary Efficacy Endpoint:
Change in MADRS Total Scores at Week 6 (mITT)



	Placebo (N=54)	XEN1101 20 mg (N=53)
MADRS total score change from baseline at Week 6 (LSMean)	-13.90	**-16.94**
Difference vs. placebo		**-3.04**
p-value		0.135

MADRS = Montgomery Åsberg Depression Rating Scale; LSMean (SEM) shown
mITT Population: All randomized subjects who receive at least 1 dose of study treatment and at least 1 postrandomization MADRS

A clear dose response and a clinically meaningful 3.04 difference in MADRS at Week 6 in the XEN1101 20 mg group

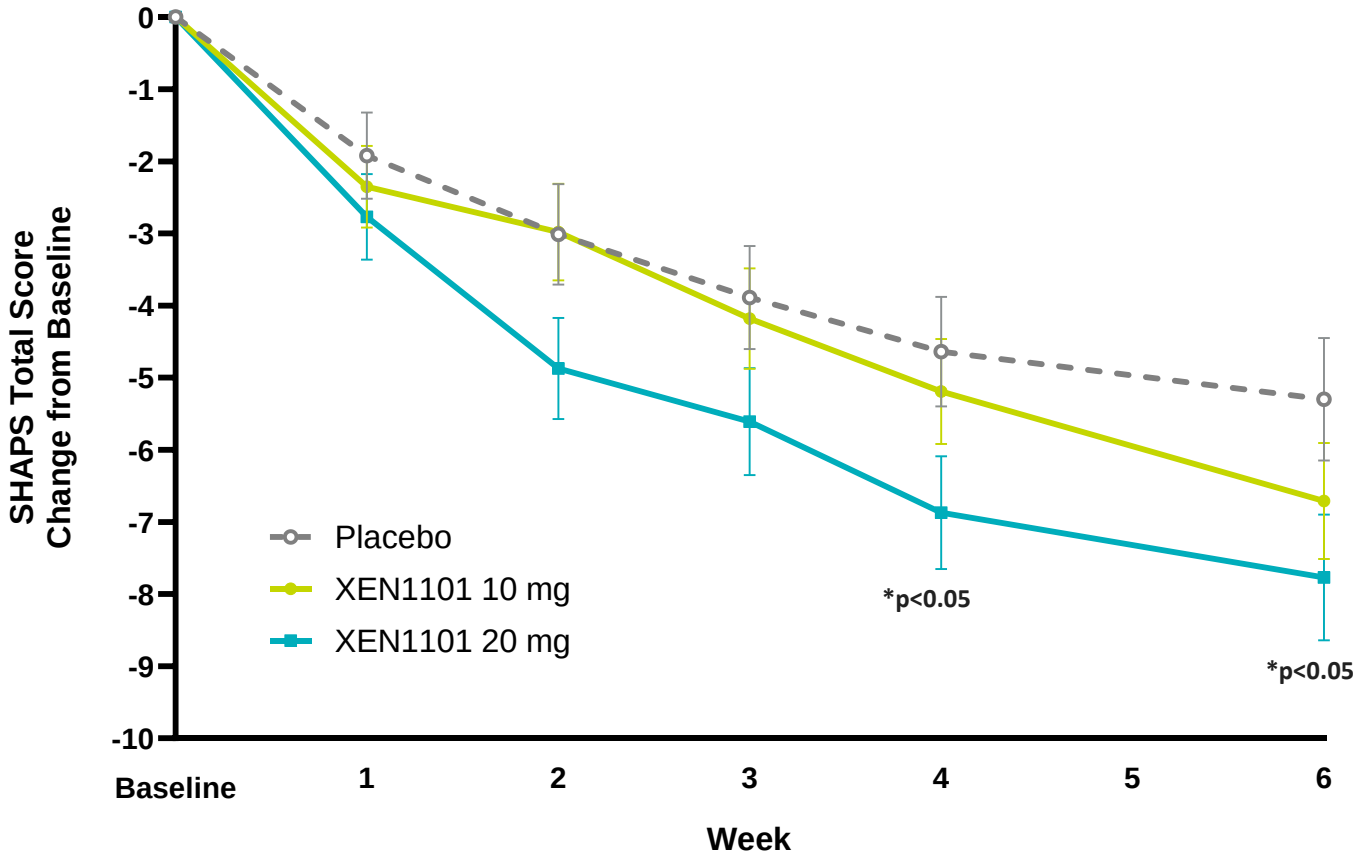
Pre-Specified Endpoint
Improvement in Depressive Symptoms:
Change in HAM-D17 Total Score (mITT)

	Placebo (N=54)	XEN1101 20 mg (N=53)
HAM-D17 total score change from baseline at Week 6 (LSMean)	-10.18	-13.26
Difference vs. placebo		-3.08
p-value		**0.042***

HAM-D17: Hamilton Depression Rating Scale was assessed at screening, baseline, and Week 6

Improvement in depressive symptoms assessed by HAM-D17 total scores was statistically significant at Week 6

Secondary Efficacy Endpoint:
Change in SHAPS Total Score at Week 6 (mITT)



	Placebo (N=54)	XEN1101 20 mg (N=53)
SHAPS total score change from baseline at Week 6 (LSMean)	-5.30	-7.77
Difference vs. placebo		-2.46
p-value		**0.046***

SHAPS = Snaith-Hamilton Pleasure Scale; LSMean (SEM) shown

Anhedonia symptom improvement: Statistically significant change in SHAPS at Week 6 with XEN1101 20 mg

X-NOVA: Summary of Safety and Tolerability Data

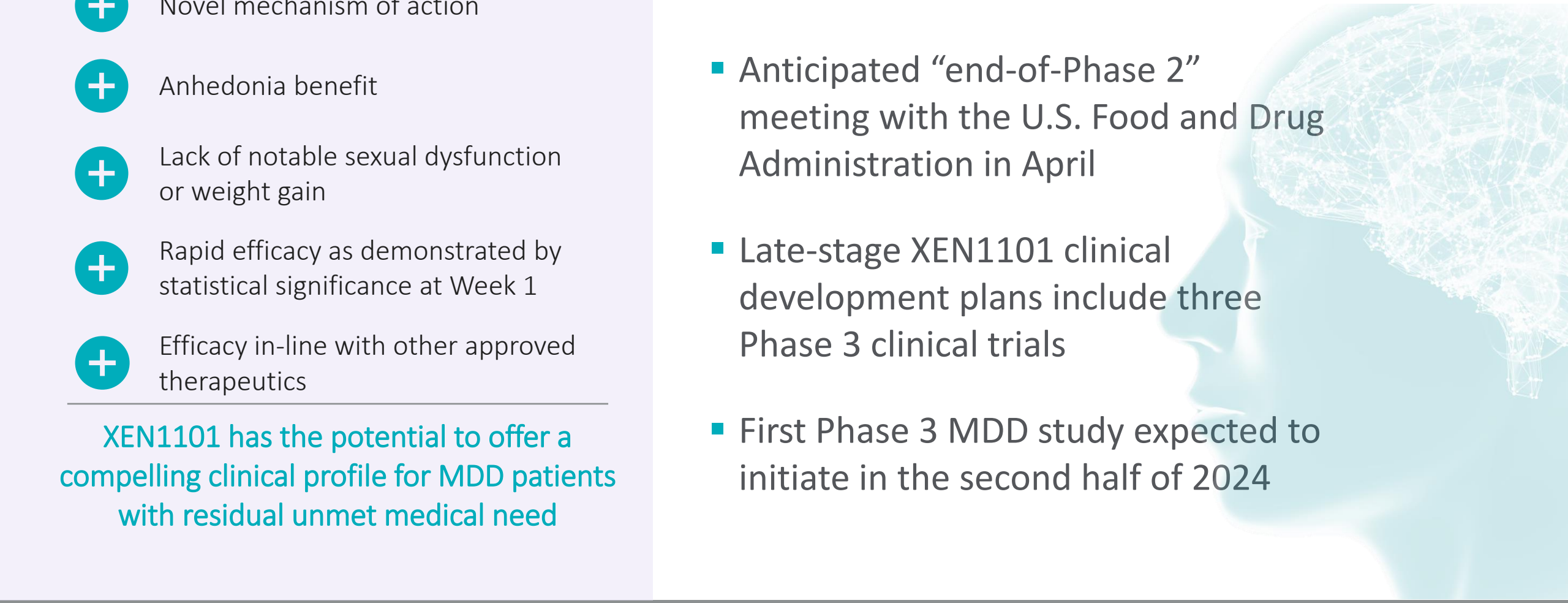
- XEN1101 was generally well-tolerated with similar rates of overall adverse events reported across all treatment arms
  - The most commonly reported TEAEs in the XEN1101 20 mg group included dizziness (17.9%), somnolence (10.7%), headache (8.9%) and disturbance in attention (8.9%), as compared to the placebo group which reported dizziness (7.3%), somnolence (1.8%), headache (12.7%) and disturbance in attention (0%)
  - Rates of discontinuation were similar across all treatment arms and rates of discontinuation due to TEAEs were low with three patients in the XEN1101 20 mg group (5.4%), as compared to two patients in the placebo group (3.6%)
  - No SAEs were reported in the two XEN1101 treatment groups, and there were two patients (3.6%) in the placebo group who experienced a treatment-emergent SAE
  - XEN1101 was not associated with notable weight gain; patients did not report notable sexual dysfunction

XEN1101 Potential Attributes in MDD

- Novel mechanism of action
- Anhedonia benefit
- Lack of notable sexual dysfunction or weight gain
- Rapid efficacy as demonstrated by statistical significance at Week 1
- Efficacy in-line with other approved therapeutics

XEN1101 has the potential to offer a compelling clinical profile for MDD patients with residual unmet medical need

Next Steps in XEN1101 Phase 3 MDD Program:



- Anticipated “end-of-Phase 2” meeting with the U.S. Food and Drug Administration in April
- Late-stage XEN1101 clinical development plans include three Phase 3 clinical trials
- First Phase 3 MDD study expected to initiate in the second half of 2024

Source: Xenon-sponsored market research

Xenon's Ongoing Pre-Clinical and Product Life Cycle Work

- Leveraging Xenon's deep ion channel expertise to develop promising drug candidates that target sodium and potassium channels
- Goal to advance multiple candidates into IND-enabling studies in 2024 and 2025

Potassium Channel Program

- Strong conviction in broad applicability of **Kv7** mechanism and strength of Xenon's discovery platform
- Next generation molecules to be explored in epilepsy and MDD
- Further potential pipeline expansion into other psychiatric indications beyond MDD, as well as pain and potentially other disorders

Sodium Channel Program

- Leveraging Xenon's extensive knowledge and prior work to advance **Nav1.7** program in pain
  - Xenon scientists contributed to early work linking loss of function in SCN9A gene (Nav1.7) to pain, based on strong human genetic validation
- Ongoing work in **Nav1.1** channel in epilepsy, based on genetic evidence of underlying pathophysiology of Dravet Syndrome

Potential Value-Creating Milestone Opportunities

XEN1101 Phase 3 Program (Epilepsy)

- Phase 3 clinical trials (X-TOLE2/X-TOLE3) in FOS underway; patient enrollment in X-TOLE2 expected to be complete in late 2024/early 2025
- Phase 3 clinical trial (X-ACKT) in PGTCS underway to support registration in additional epilepsy indication
- NDA submission planned based on efficacy data from Phase 2b X-TOLE and first Phase 3 trial (X-TOLE2)

XEN1101 (MDD/Other)

- Topline data from Phase 2 X-NOVA POC clinical trial reported in November 2023
- End-of-Phase 2 meeting with FDA anticipated in April, with first XEN1101 Phase 3 study in MDD expected to initiate in 2H:2024
- Mount Sinai investigator-sponsored Phase 2 POC in MDD underway
- Evaluating potential development in additional neurological indications

Pre-clinical Programs

- Leveraging Xenon's extensive ion channel expertise to identify validated drug targets and develop new product candidates
- Development candidates targeting Kv7, Nav1.1, and Nav1.7 expected to enter IND-enabling studies in 2024 and 2025

Partnered Programs

NBI-921352 (XEN901) / Neurocrine Biosciences

- Phase 2 clinical trial underway with NBI-921352 in pediatric SCN8A-DEE

For more information

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