XENON®

Investor Webinar

“A Discussion with KOLs: XEN1101 and the Major Depressive Disorder (MDD) Landscape”

SEPTEMBER 19, 2023

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Please submit questions via chat anytime during the presentation.

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, addressable market, regulatory success and commercial potential of XEN1101; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in our XEN1101 development program; the timing and results of our interactions with regulators; our ability to successfully develop and obtain regulatory approval of XEN1101; and anticipated enrollment in our clinical trials and the timing thereof.

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.

Welcome and Introductions

Sanjay J. Mathew, MD

Marjorie Bintliff Johnson and Raleigh White Johnson, Jr. Vice Chair for Research Professor of Psychiatry & Behavioral Sciences Menninger Department of Psychiatry & Behavioral Sciences at Baylor College of Medicine

James W. Murrough, MD, PhD

Professor of Psychiatry and Neuroscience Director, Depression and Anxiety Center for Discovery and Treatment Icahn School of Medicine at Mount Sinai

Joined by Ian Mortimer, CEO, of Xenon Pharmaceuticals (moderator) with:

- Christopher Kenney, MD, Chief Medical Officer, Xenon
- Dr. Chris Von Seggern, Chief Commercial Officer, Xenon

Summary of Today's Discussion

Unmet Medical Need in MDD	*Dr. Sanjay Mathew*
K_V7 Mechanistic Background / Scientific Rationale / Clinical Experience with Ezogabine	*Dr. James Murrough*
XEN1101 Clinical Experience	*Dr. Christopher Kenney*
XEN1101 Potential Commercial Opportunity in MDD	*Dr. Chris Von Seggern*
Panel Discussion / Q&A	*Moderated by:* *Ian Mortimer*

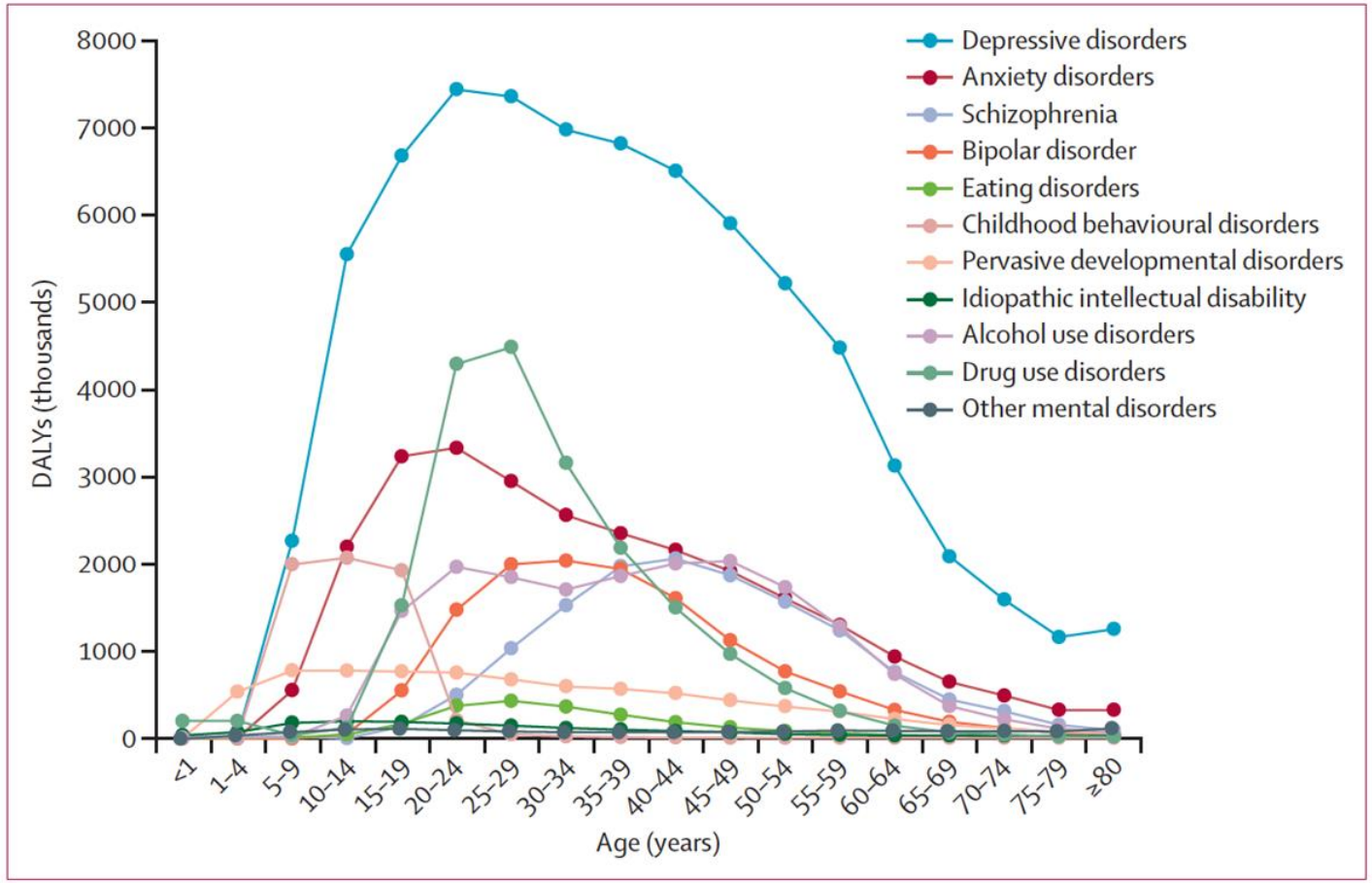
Overview of Unmet Medical Need in MDD

DR. SANJAY MATHEW

The Global Burden of Depression

- Among most common and disabling conditions worldwide
- 70 million years lost to disability
- Approximately 1 million suicides annually and rising
- Prevalence of MDD is significantly greater than other major psychiatric disorders

Depression Accounts for Greatest Disability Among all CNS Disorders



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

Source of figure: Whiteford et al. Lancet 2013

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.

Depression ≠ Simple "Chemical Imbalance" of Serotonin

Several Complex Factors Contribute to MDD

Definition

- Major depressive disorder is characterized by episodes of low mood or inability to experience pleasure that last for two weeks or more

Symptoms

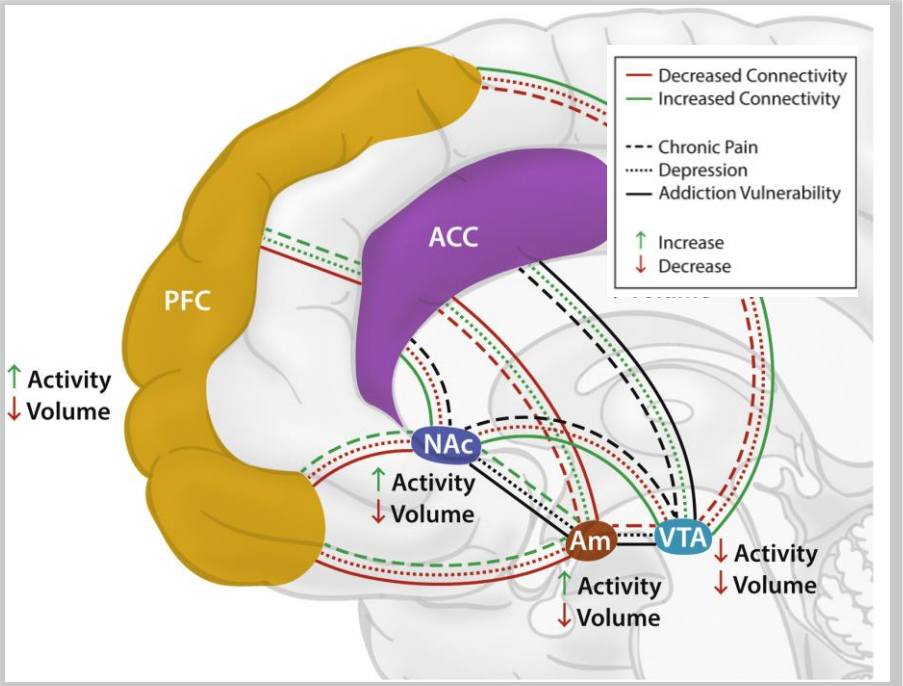
- In addition to low mood, patients may exhibit cognitive symptoms such as diminished ability to concentrate, fatigue, sleep disorders, guilt and suicidal thoughts
- Patients may also experience a reduction of physical movement and unexplained weight changes

Risk Factors

- History of other mental health disorders and chronic illness
- Family history of mental health disorders
- Traumatic or stressful events
- Substance use disorders
- Low self-esteem and pessimistic personality traits

Prognosis

- Patient response to treatment varies greatly amongst individuals with no prognostic biomarkers available to predict treatment response
- 1 in 3 patients do not respond to available treatments



- MDD is associated with hyperexcitability of the dopaminergic reward pathway
- Additional dysregulated connectivity and excitability are observed in broader neural networks including the prefrontal cortex and amygdala

Source of figure: Serafini et al. 2020

Sources: American Psychiatric Association, DSM-5. Nemeroff CB. Prevalence and management of treatment-resistant depression. *J Clin Psychiatry*. 2007; Fava, M. Definition and epidemiology of treatment-resistant depression. *Psychiatr Clin North Am*. 1996. Serafini et al. The Mesolimbic Dopamine System in Chronic Pain and Associated Affective Comorbidities. *Biol Psychiatry*. 2020. Xenon sponsored market research.

MDD is a Highly Prevalent Mental Health Disorder

- In 2021, 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

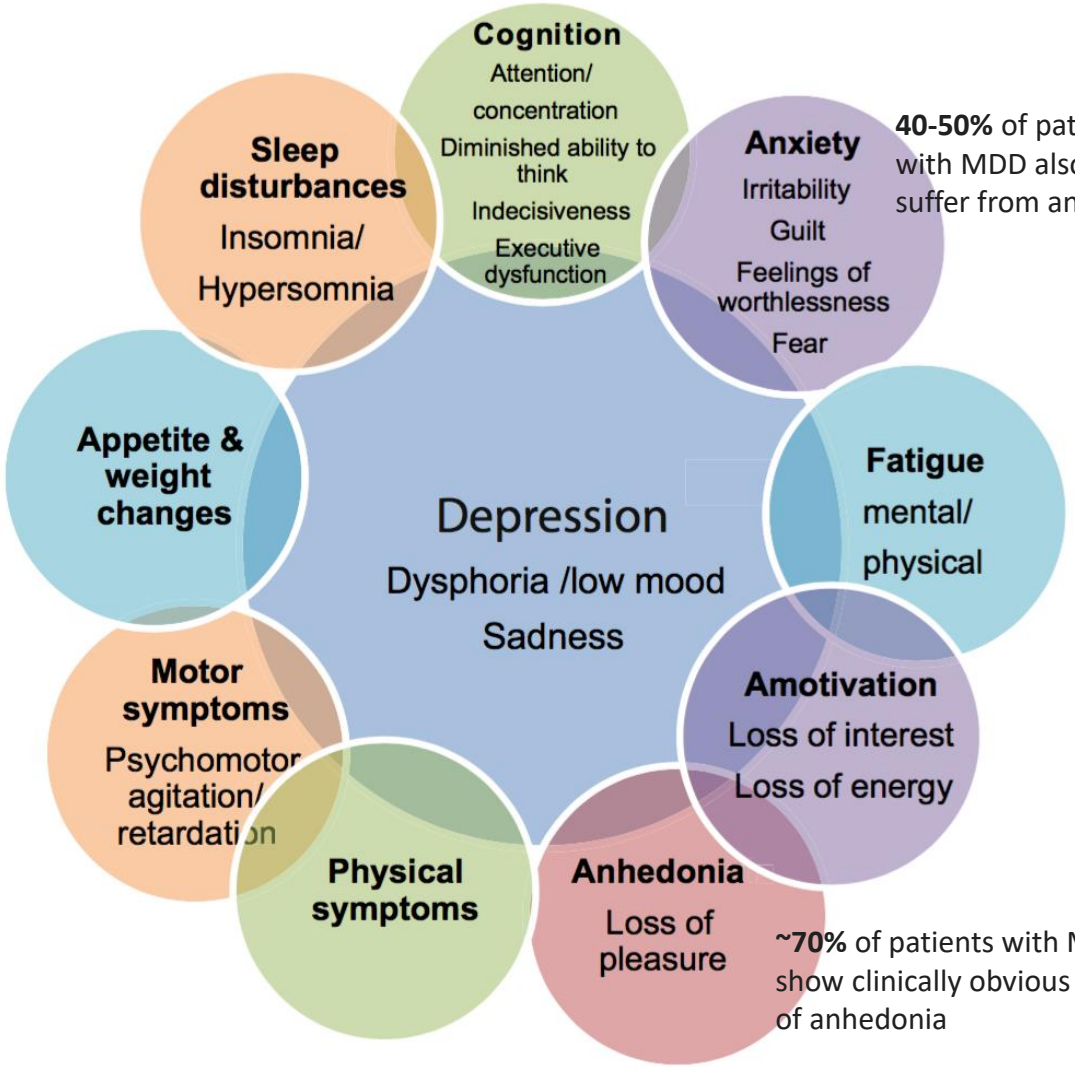
Diagnosis of Major Depressive Episode According to DSM-5

(Need 5 of 9 symptoms; either item 1 or 2 required)

1. Depressed mood nearly every day, most of the day
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
3. Significant unintentional weight loss or gain
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive guilt nearly every day
8. Diminished ability to think or concentrate nearly every day
9. Recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt or plan

Sources: Greenberg et al. The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018). *Pharmacoeconomics*. 2021; Nemeroff CB. Prevalence and management of treatment-resistant depression *Clin Psychiatry*. 2007; Results from the 2021 National Survey on Drug Use and Health: Detailed Tables SAMHSA 2022. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013.

Clinical Heterogeneity of Depression



40-50% of patients with MDD also suffer from anxiety

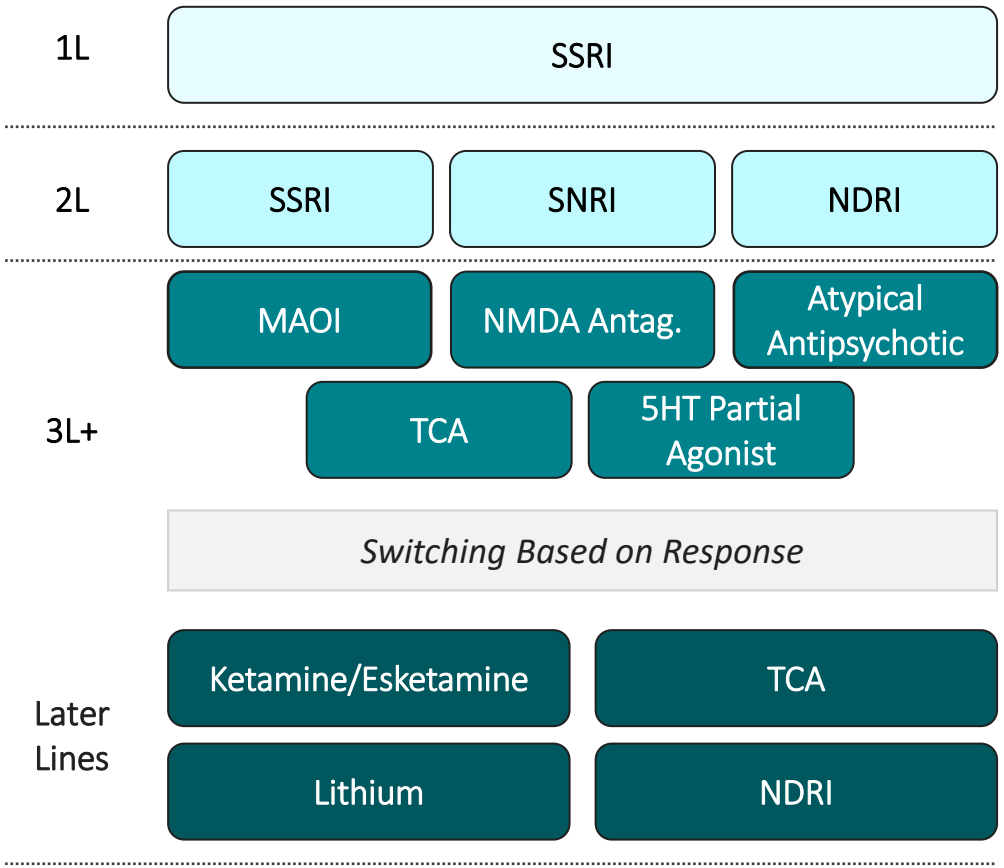
~70% of patients with MDD show clinically obvious features of anhedonia

Source of figure: Calabrese et al. J Affect Dis 2014

- The MDD patient population is varied in symptomatology, onset of symptoms, comorbidities and response to treatment
  - 70-80% of MDD patients experience recurring episodes of depression
- In patients with psychiatric disorders (e.g. borderline personality disorder, OCD, PTSD), risk for suicidal behavior is elevated when these conditions are comorbid with MDD
- Significant symptomatic overlap with Bipolar Disorder; depressive symptoms considered part of unipolar MDD in up to 40% of patients later diagnosed with BPD
- Of note, the prevalence of depression in association with epilepsy is ~15-50%

Sources: Shankman et al. The Different Facets of Anhedonia and Their Associations with Different Psychopathologies. *Anhedonia: A Comprehensive Handbook Volume I*. 2014; Kessler et al. Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys. *Epidemiol Psychiatr Sci*. 2015; Jackson and Turkington. Depression and anxiety in epilepsy. *J Neurol Neurosurg Psychiatry*. 2005; Su and Si. Progress and challenges in research of the mechanisms of anhedonia in major depressive disorder. *Gen Psychiatr*. 2022; Kanner AM. Depression in epilepsy: prevalence, clinical semiology, pathogenic mechanisms, and treatment. *Biol Psychiatry*. 2003. Elger et al. . Diagnosing and treating depression in epilepsy. *Seizure*. 2017. Xenon sponsored market research.

Treatment Paradigm in Major Depressive Disorder



- SSRIs are the first-line therapy of choice for MDD patients due to **reasonable efficacy and tolerability**
- Patients with no response to first-line therapy may be switched onto a **second SSRI or SNRI,** while those with partial response may receive adjunctive therapy

- Patients failing second-line therapy are generally considered more difficult to treat, with **40 – 50% of 3L+ patients receiving adjunctive treatment**
  - **Treatment selection varies** with HCP preference and patient characteristics (e.g., insurance, comorbidities, symptoms, previous utilized therapies)
  - **Branded agents** are typically reserved after generic SSRI/SNRIs due to payer management

- **Ketamine** is reserved for highly refractory patients and limited to later lines due to administration challenges and payer access
- **Somatic therapies** (e.g., ECT, TMS) occasionally used as an alternative to later-line agents

ECT: Electroconvulsive Therapy; LoT: Lines of Therapy; MDD: Major Depressive Disorder; NDRI: Norepinephrine Dopamine Reuptake Inhibitor; SNRI: Serotonin-Norepinephrine Reuptake Inhibitor; SSRI: Selective Serotonin Reuptake Inhibitor; TCA: Tricyclic Antidepressant; TMS: Transcranial Magnetic Stimulation

Sources: Kern et al. Treatment patterns and sequences of pharmacotherapy for patients diagnosed with depression in the United States: 2014 through 2019. *BMC Psychiatry*. 2020; Xenon sponsored market research.

Primary Drivers of Treatment Selection

Treatment Selection is Driven by Personal Preference, Efficacy, and Safety

Efficacy

- Personal preference relies upon **experience** with a class of medication and **familiarity with a drug's side effect profile**
- Choice of treatment is often influenced by the ability to address pertinent symptoms (e.g. insomnia, appetite)

Comorbidities

- **Anxiety and insomnia** warrants the use of additional treatment with hypnotics (e.g. zolpidem) and atypical antipsychotics (e.g. quetiapine, aripiprazole)
- History of **substance abuse** discourages use of ketamine, esketamine and benzodiazepines
- Treatments for additional medical conditions warrant considerations of **kidney or liver toxicity**, as well as implications for drug-drug interactions

Safety / Tolerability

- Individual factors such as **personality issues and history of suicide attempt** are considered as part of overdose risk
- Common adverse events such as **sexual dysfunction** and **weight gain** influence treatment decisions particularly in patients 3L+

Source: Xenon sponsored market research.

Current Unmet Needs in MDD Therapies

A Need for Novel MOAs with Robust Efficacy, Faster Kinetics and Improved Safety

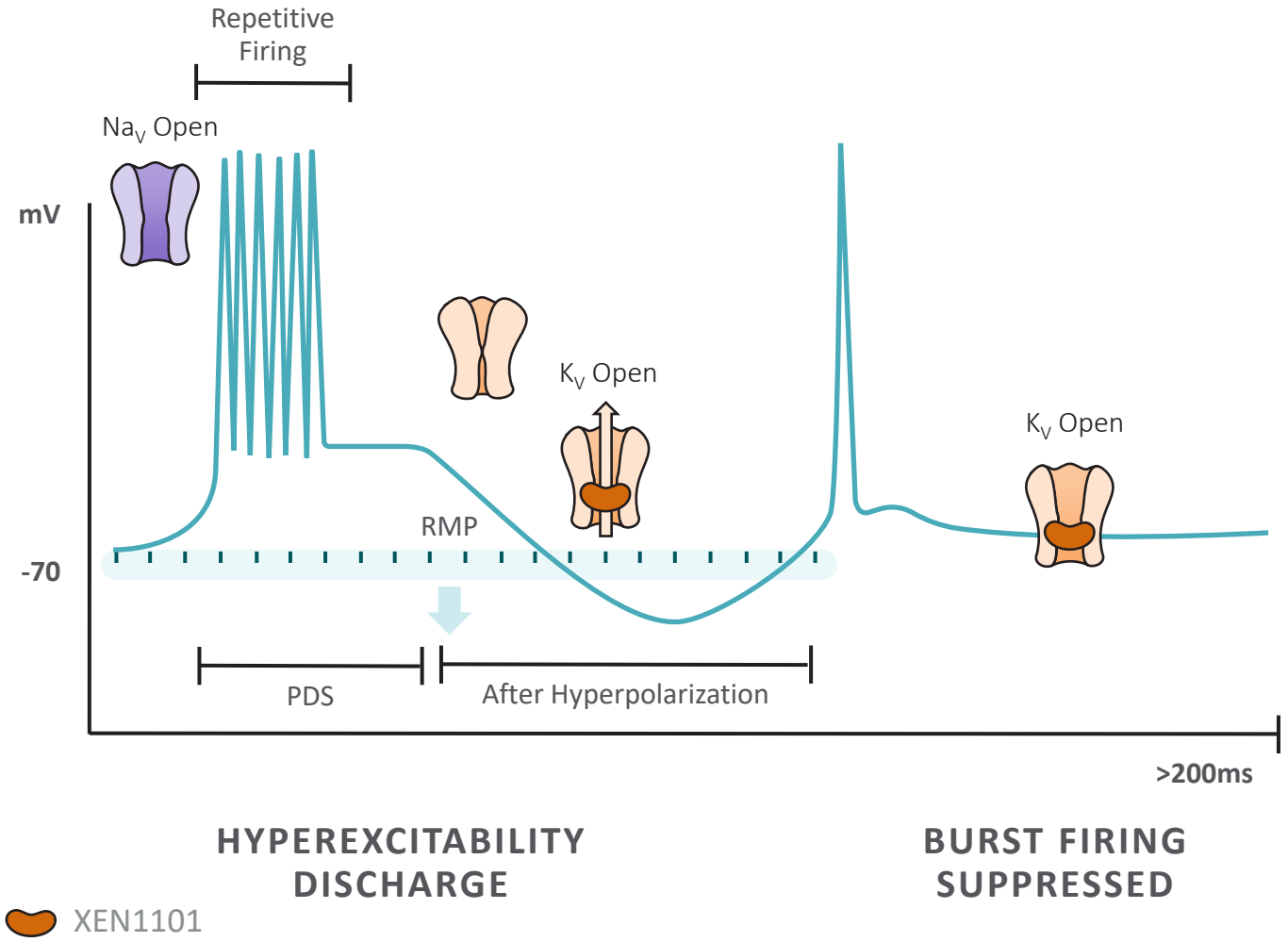
Key Unmet Needs	Key Insights
Novel Mechanisms of Action	• Excitement over non-SSRI/SNRI mechanisms of action is widespread • A need for novel mechanisms of action to guide treatment selection for patient subgroups
Efficacy	• Current treatments offer low response rates and few patients reach remission with currently available treatments • Subtypes of MDD remain difficult to treat (e.g. melancholic depression, etc)
Safety/ Tolerability	• Weight gain and sexual dysfunction continue to be common complaints
Kinetics of Onset	• Rapid relief of symptoms is one of the major challenges of standard of care (SOC) • A need for agents with more rapid onset of efficacy as current SOC have a delayed therapeutic response

Source: Xenon sponsored market research.

Overview of K_V7 Mechanism / Scientific Rationale for Use of K_V7 Modulators in MDD

DR. JAMES MURROUGH

K_V7 Channels Have a Critical Role in Neuronal Firing

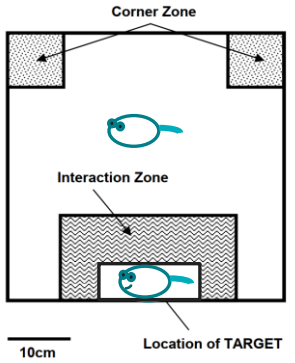


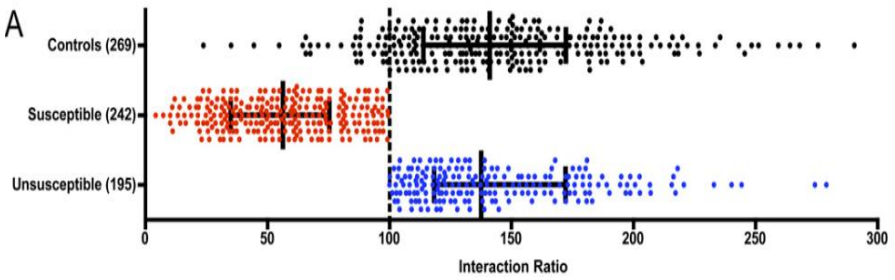
Adapted from Badawy et al. 2009

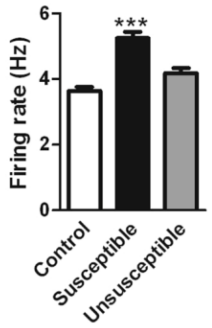
- K^+ channels repolarize membranes to end the action potential
- K_V7 channels are translated from the KCNQ gene family (Q1–Q5)
- Exert important inhibitory control over neuronal firing
- Control unwanted burst and spontaneous firing that can lead to seizures

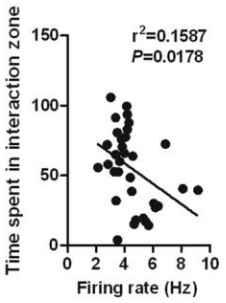
K_V7 Channels and Resilience to Chronic Social Defeat Stress

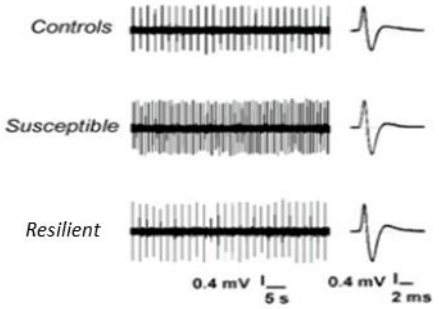
- Model of stress related depression
- Discordant behavioral outcomes to CSDS resulting in susceptible and resilient animals
- Studied to understand the molecular basis of resilience in stress induced depression
- Tonic firing rather than hyperexcitability of the VTA in the reward system leads to resilient mice
- Gene expression studies showed upregulation of potassium channel including $K_V7.3$ (KCNQ3) correlate with resilient phenotype
- Suggests resilience to CSDS is an active molecular process of stress-coping











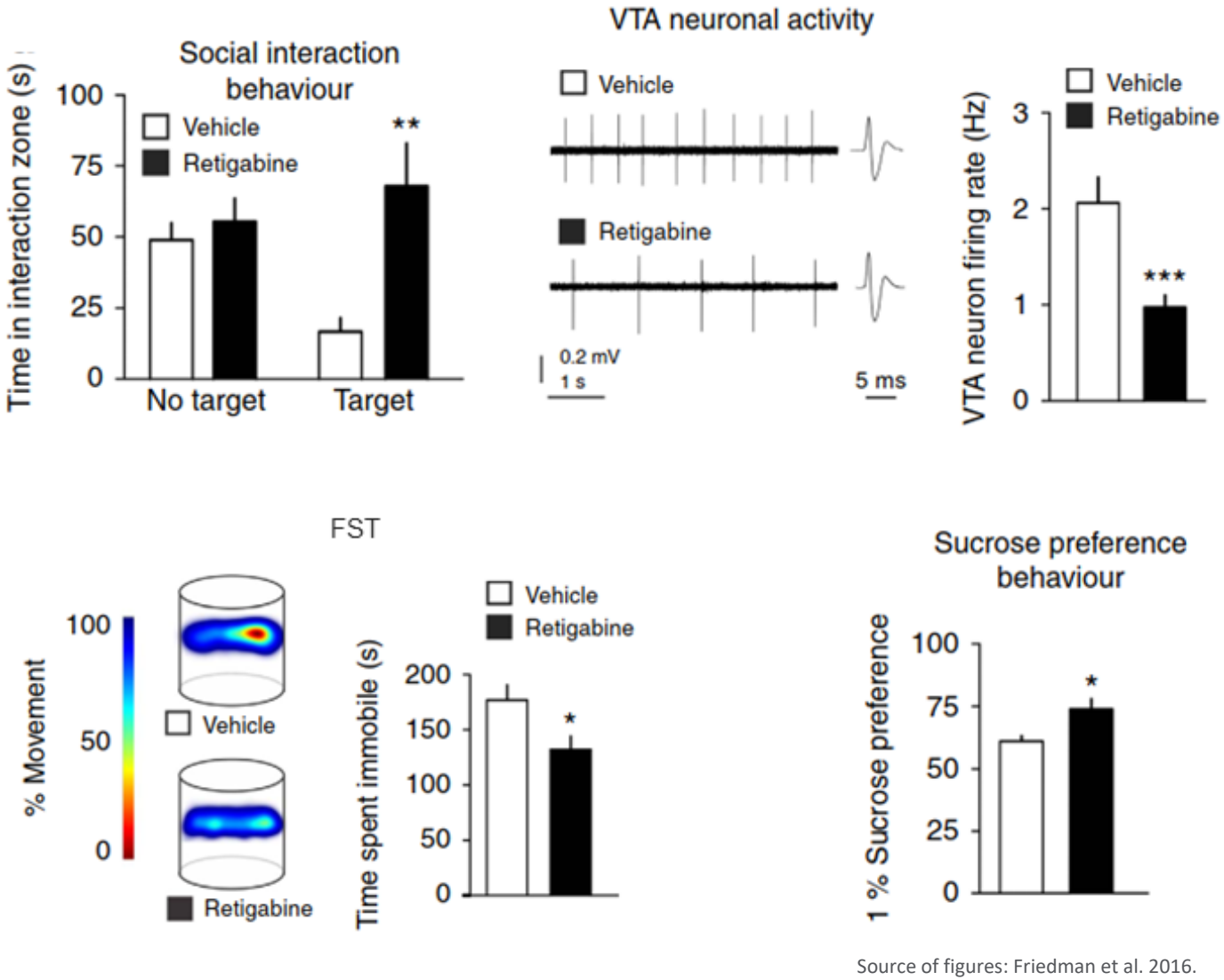
Ventral Tegmental Area

***Gene* (Definition)**	Susceptible	Unsusceptible
Gal (Galanin)	⇑	⇔
Gdnf (Glia derived neurotrophic factor)	⇔	⇑
Kcnf1 (Voltage gated K^+ channel F1)	⇔	⇑
Kcnh3 (Voltage gated K^+ channel H3)	⇔	⇑
Kcnk4 (K^+ channel K4 [TRAAK])	⇔	⇑
Kcnq3 (Voltage gated K^+ channel Q3)	⇔	⇑
Kif1b (Kinesin family member 1B)	⇔	⇓
Lcn2 (Lipocalin-2)	⇑	⇑

Source of figures: Krishman, Cell 2007; Cao, J Neuroscience 2010

Role of K_V7 Channels in Active Resilience

- $K_V7.3$ forms heterotetramers with $K_V7.2$ to effect the M-current and blunt VTA hyperexcitability
- K_V7 opener (ezogabine/retigabine) dosed 8-days (1 mg/kg ip) reversed the susceptibility phenotype mimicking the resilient phenotype
  - Blunted VTA hyperexcitability and normalized social interaction
  - Improved sucrose preference a measure of anhedonia



Source of figures: Friedman et al. 2016.

The KCNQ Channel "Hypothesis" of Depression

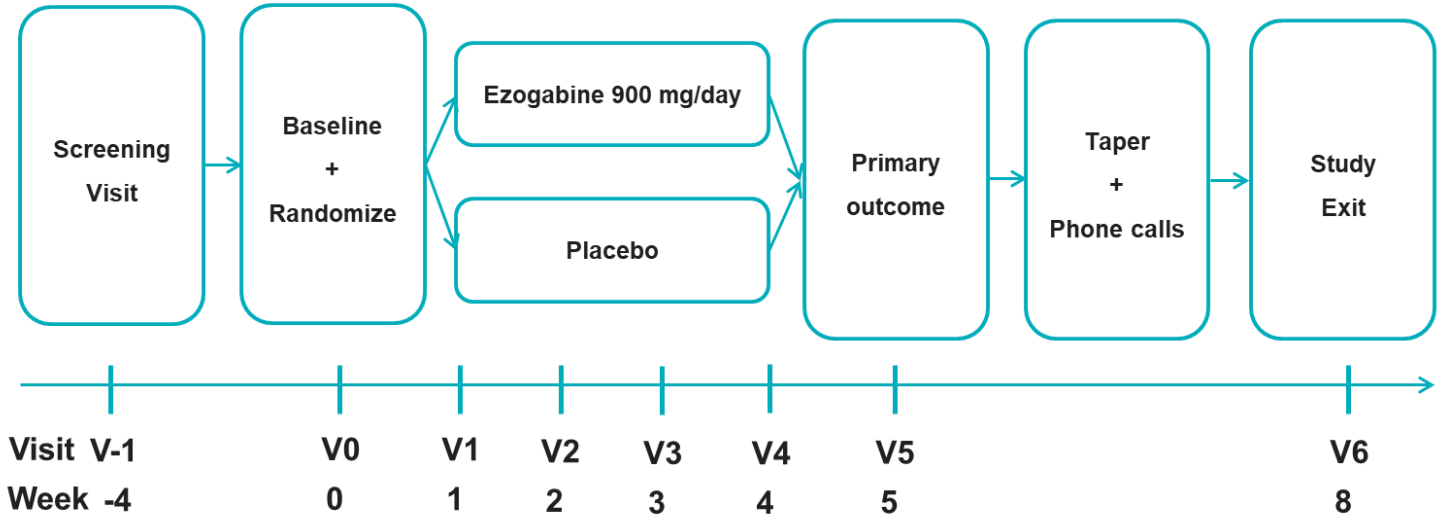
- Patients with depression may have deficient signaling at KCNQ2/3 channels (within the reward system)
- Enhancing signaling at KCNQ2/3 channels may improve symptoms of depression and symptoms of anhedonia

Goal: Design and conduct clinical studies to test this hypothesis

Developing KCNQ Channel Modulators for Mood Disorders

"R61 Trial"

- Design: Phase IIa, randomized, parallel arm, placebo-controlled clinical trial
- Primary Objective: To establish target engagement of a KCNQ channel opener (ezogabine) in patients with depressive disorder and anhedonia
- Secondary Objectives: To determine if treatment with ezogabine is associated with a reduction in clinical symptoms of depression and anhedonia, and modulation of behavioral responses to reward
- Target Enrollment: N=48 adults with depressive disorder
- Intervention: Ezogabine up to 900 mg daily or matching placebo
- Duration: 5-week treatment period (includes 4-week titration)



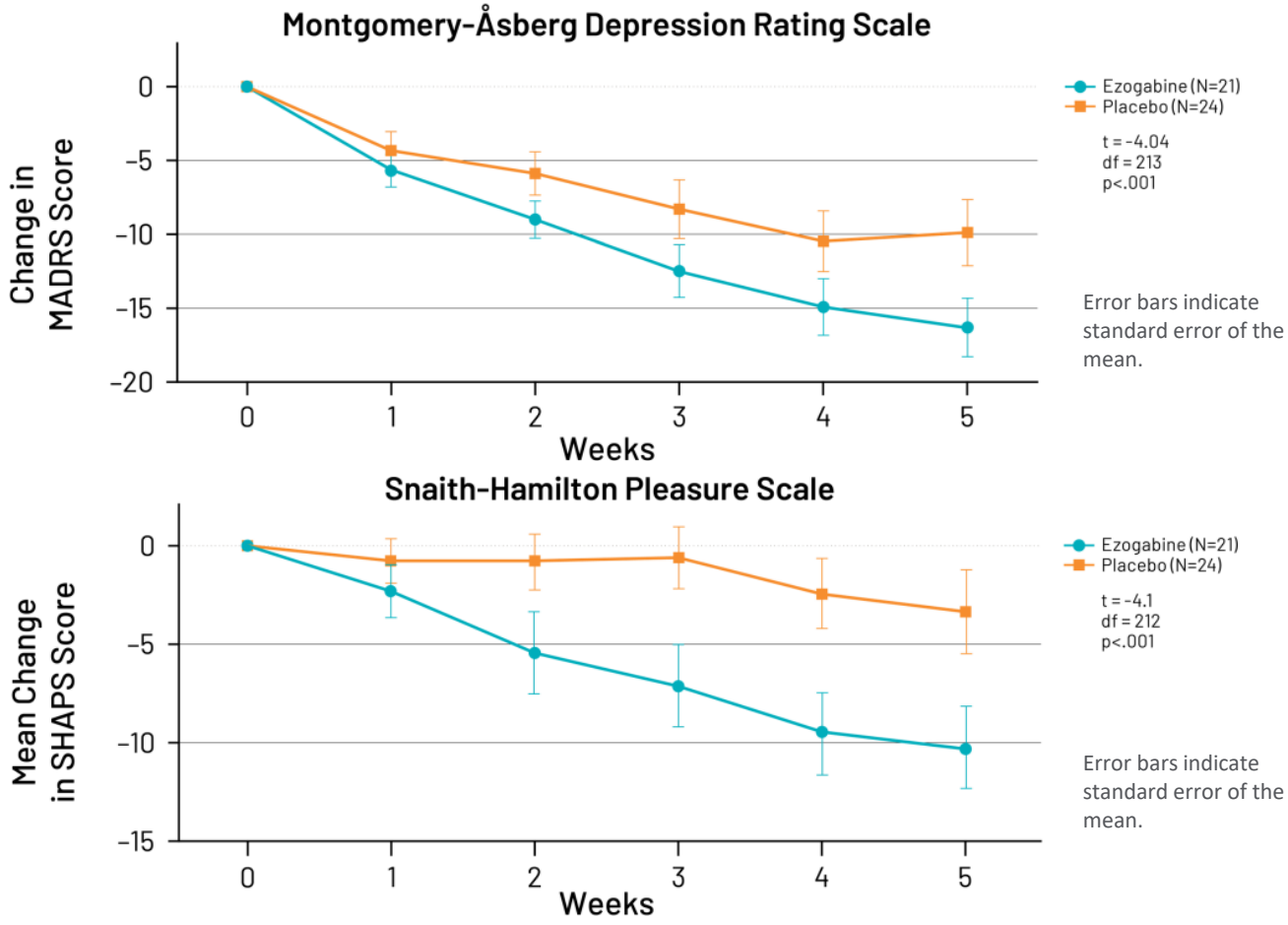
MRI outcome	Change in activation within the bilateral VS from baseline (V0) to week 5 (V5) as measured by fMRI during the IFT.
Clinical outcome	Depression (MADRS, QIDS-SR) Anhedonia (SHAPS, TEPS) Other Measures (CGI)

The study was supported by NIMH grant R61MH111932. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Supportive Clinical Data to Explore K_V7 Modulators in MDD

- 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)
- Ezogabine was generally safe and well tolerated
  - 95% of patients randomized to ezogabine reached the primary outcome

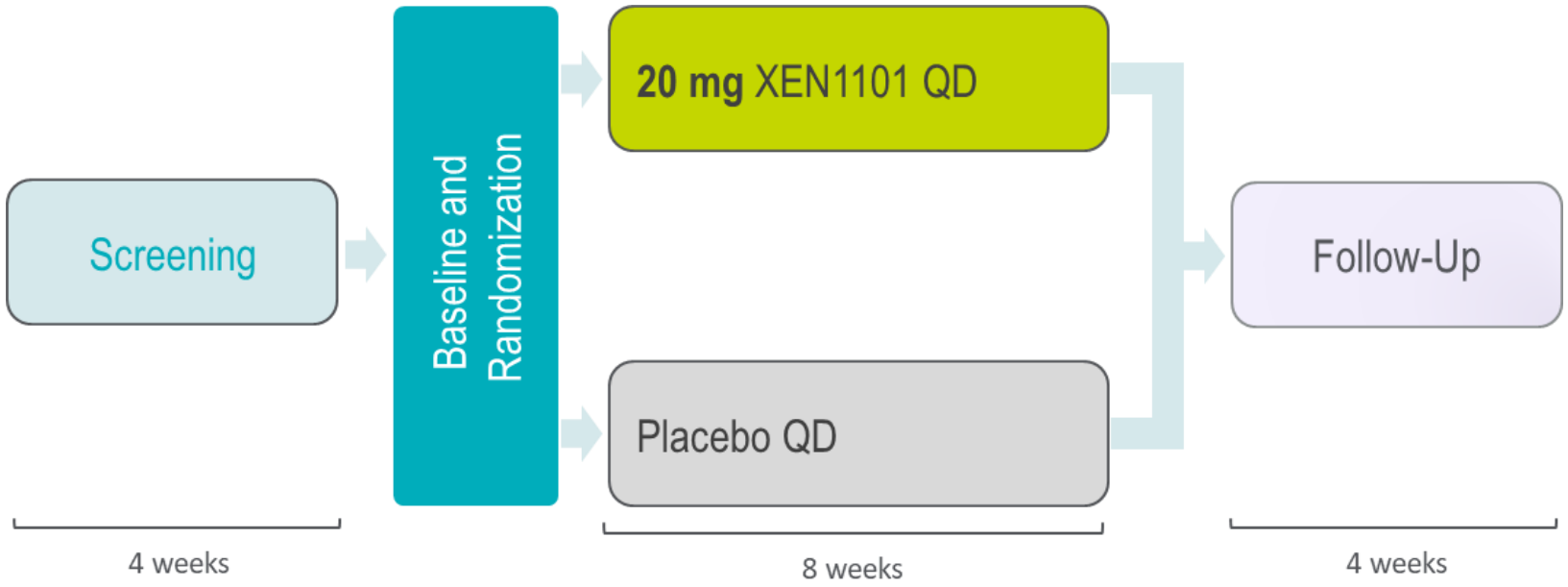
Figures reproduced from Costi et al. Depression symptoms assessed by the Montgomery-Åsberg Depression Rating Scale. Anhedonia symptoms assessed by the Snaith-Hamilton Pleasure Scale.



Source: Costi et al. Impact of the KCNQ2/3 Channel Opener Ezogabine on Reward Circuit Activity and Clinical Symptoms in Depression: Results From a Randomized Controlled Trial. *Am J Psychiatry*. 2021.

The study was supported by NIMH grant R61MH111932. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

NIMH-Funded Trial of XEN1101 for MDD



- Patient enrollment in ongoing investigator-sponsored Phase 2 proof-of-concept, multi-site, randomized, parallel-arm, placebo-controlled clinical trial of XEN1101 for the treatment of MDD
  - ~60 patients randomized in a 1:1 fashion to XEN1101 (N=30) or matching placebo (N=30), taking 20 mg once a day of either XEN1101 or placebo for 8 weeks
  - Primary objective is to investigate the effect of XEN1101 on brain measures of reward using functional Magnetic Resonance Imaging (fMRI); secondary endpoints include clinical measures of depression and anhedonia

Conclusions from Work to Date

- Mechanistically novel treatments for depression are urgently needed
- Basic research indicates that enhancing signaling at KCNQ channels within the reward circuit may be pro-resilient, and anti-depressant
- Experimental medicine studies hold potential to translate insights from basic research into clinical development programs
- Ezogabine, a first-in-human KCNQ channel opener, provides first proof-of-concept test of the KCNQ channel hypothesis of depression
- Future research on the potential of the KCNQ channel as a treatment target for depression and anhedonia is warranted

Clinical Experience with XEN1101

DR. CHRIS KENNEY

XEN1101 Pre-Clinical and Clinical Experience Summary

Promising Pre-Clinical Results

- XEN1101 demonstrated pre-clinical efficacy across various seizure models
- XEN1101 was assessed in acute rodent models of depression and anhedonia (FST and PRT) indicating an anti-depressant effect of XEN1101, with beneficial impacts on mood at doses and plasma concentrations that are efficacious for seizure reduction

Phase 1 Studies Show Promising Drug Profile and Tolerability

- Phase 1 SAD and MAD studies demonstrated favorable PK supporting QD dosing
- XEN1101 was well tolerated at up to 30mg, with majority of AEs mild and CNS related

TMS Demonstrates strong PK-PD Relationship

- Phase 1b TMS study showed that XEN1101 reduced corticospinal excitability, suggesting strong PK-PD relationship; additionally, the effect was greater than that of ezogabine
- SAD/MAD and TMS studies informed Phase 2b dose selection

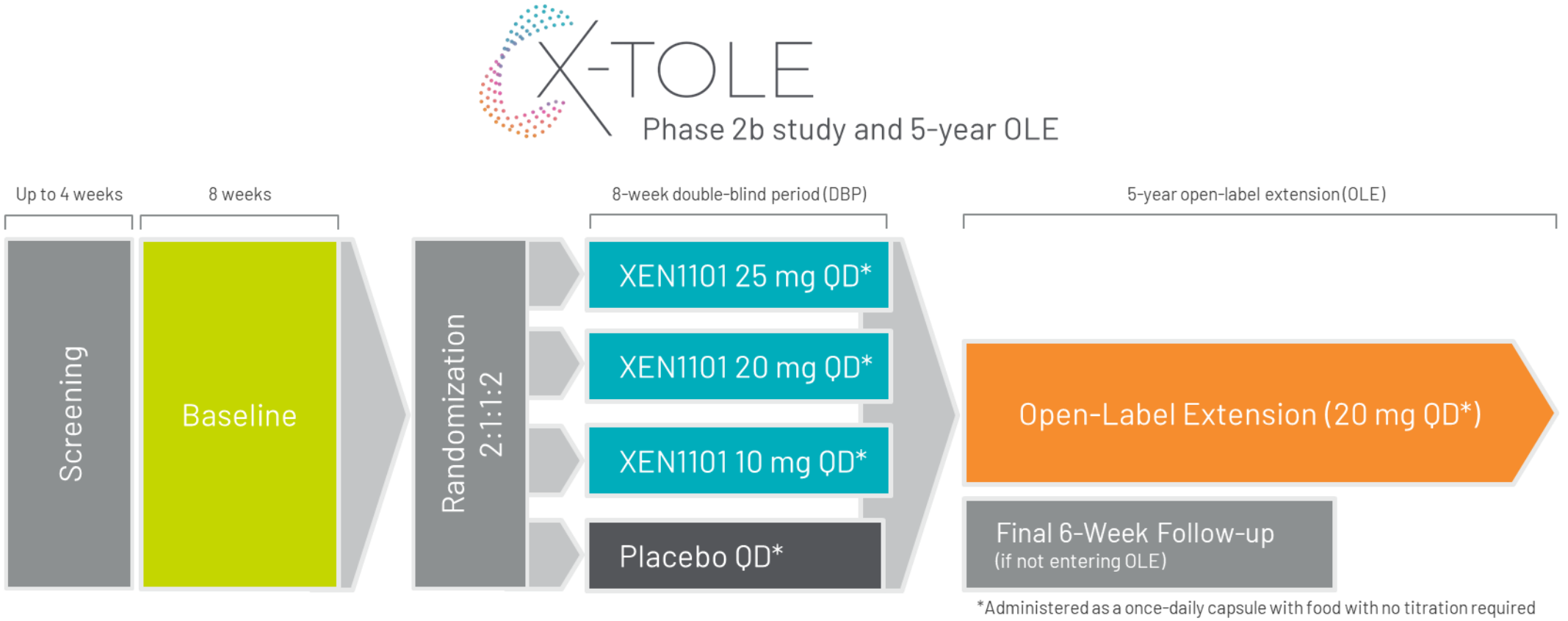
X-TOLE Phase 2b Results

- XEN1101 showed a dose-dependent and highly statistically significant reduction in FOS across endpoints, and was generally well tolerated
- Interim analysis from ongoing open-label extension indicates long-term efficacy of XEN1101, which continues to be generally well-tolerated with AEs consistent with prior results and other ASMs

Ongoing Clinical Development of XEN1101

- Ongoing Phase 3 clinical trials in focal onset seizures (X-TOLE2, X-TOLE3) and primary generalized tonic-clonic seizures (X-ACKT)
- Last patient enrolled in Phase 2 X-NOVA study in MDD, with topline expected in late November to mid-December

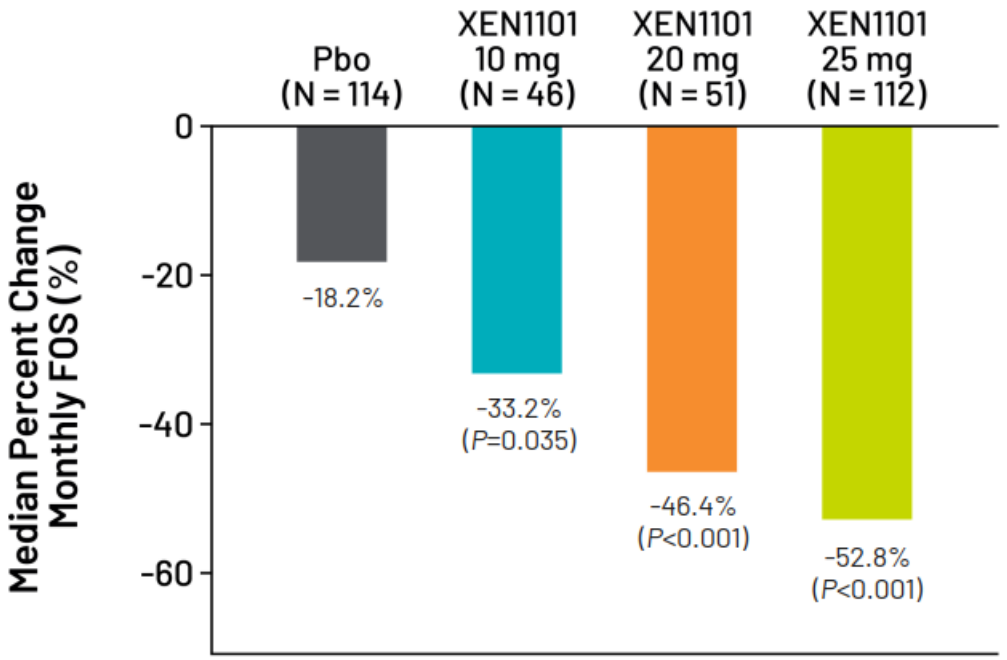
XEN1101 X-TOLE Phase 2b Trial in Focal Onset Seizures



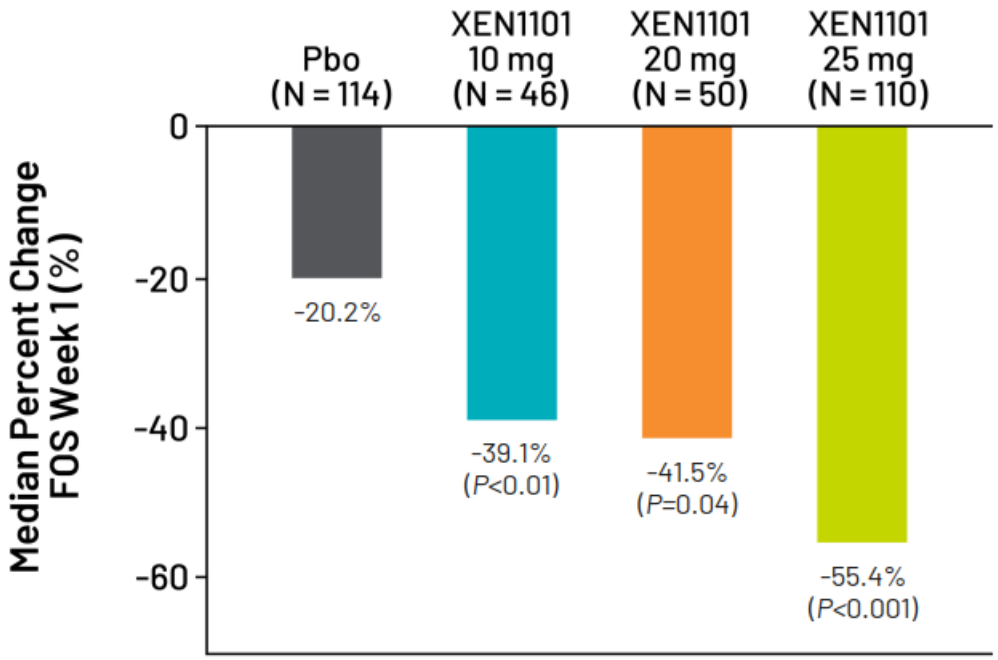
Topline results reported in October 2021 with additional OLE data presented at AES 2022 and AAN 2023

Compelling X-TOLE Results Informed Dose Selection for X-NOVA

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



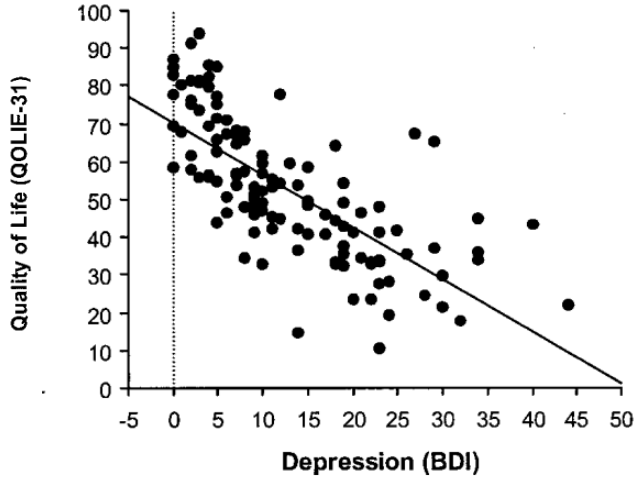
Median Percent Change from Baseline in Weekly Focal Onset Seizure (FOS) Frequency During Week 1 of the Double-Blind Period



XEN1101 demonstrated compelling efficacy in double-blind period, with rapid onset of efficacy at Week 1

Depression is a Common Comorbidity in Persons with Epilepsy

- The prevalence of depression in people with epilepsy reported in the literature ~15-50%
- Greater severity of depression associated with higher seizure frequency
- Depression is an independent and strong predictor of reduced QOL
- Lifetime history of depression may predict resistance to treatment
- Depression is a significant cause of non-adherence to anti-seizure medications (ASMs)



Source of figure Boylan et al. 2004.

Sources: Elger et al. Diagnosing and treating depression in epilepsy. *Seizure*. 2017. D'Alessio et al. Reduced expression of the glucocorticoid receptor in the hippocampus of patients with drug-resistant temporal lobe epilepsy and comorbid depression. *Epilepsia*. 2020. Kanner et al. Depression and epilepsy: epidemiologic and neurobiologic perspectives that may explain their high comorbid occurrence. *Epilepsy Behav*. 2014. Boylan et al. Depression but not seizure frequency predicts quality of life in treatment-resistant epilepsy. *Neurology*. 2004.

XEN1101 X-NOVA Phase 2 Clinical Trial

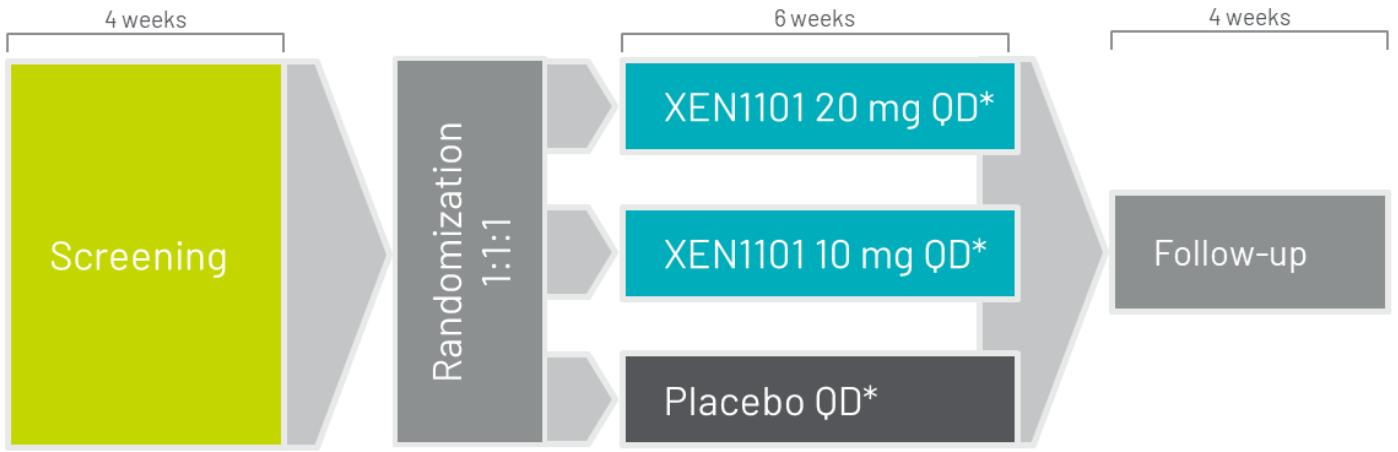
- **X-NOVA Study Design:**

  Randomized, placebo-controlled Phase 2 clinical trial in ~150 subjects with MDD

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

- **Secondary Objective:**
  - Assess the efficacy of 10 mg and 20 mg doses of XEN1101 compared to placebo on improvement of anhedonia symptoms using SHAPS score change through week 6

X-NOVA



*Administered as a once-daily capsule with food with no titration required

Patient enrollment complete in X-NOVA Phase 2 clinical trial in MDD with topline data anticipated in late November to mid-December 2023

XEN1101 Commercial Opportunity in MDD

DR. CHRIS VON SEGGERN

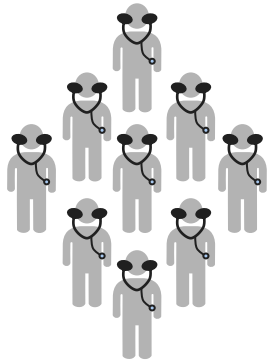
Summary of MDD Market Research

1 MDD Treatment Landscape

MDD Landscape Overview and Patient Demographics

Treatment Paradigm and Unmet Medical Need

2 Market Research to Understand Potential XEN1101 Opportunity in the Future Treatment Paradigm



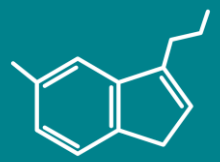
Research including Key Opinion Leaders and high-volume prescribing psychiatrists

Market Research Goals

- Pinpoint Drivers of Clinical Decision Making
- Understand Remaining Unmet Needs in MDD
- Identify Key Attributes Desired in Future Treatments

Focus of Commercial Overview

Opportunity for Novel Therapies Remains Significant

Driver	Description	Implication
 **Novel MOA**	• Both **physicians and payers** expressed **interest in** MDD products in development with **novel MOAs** • Viewed as a **potential means for targeted treatment of unaddressed MDD subpopulations**	*Products with novel MOAs will likely be utilized in those who do not respond initially to generic therapies*
 **Improvements Over SOC**	• **Improved and/or differentiated safety and tolerability** is considered **by physicians as a key unmet need** particularly limiting sexual dysfunction and weight gain • **Kinetics of efficacy onset** has generated **excitement among physicians** for novel therapies	*Branded use is largely limited to 3L+, with novel treatments highlighting differentiation to target first-branded use*
 **Clinical Opportunity**	• **Novel entrants are seeking key MDD sub-populations** (e.g. non-responders and targeted symptom domains) in addition to general MDD • **Anhedonia** is one of the **most common and challenging co-morbidities** of depression to treat, thus creating a large opportunity for a novel treatment	*XEN1101 has the potential to demonstrate improvement in anhedonia, which physicians suggest would be a key differentiator*

Source: Xenon sponsored market research.

Sum of Potential Attributes (Based on Physician Feedback)

- Preference for novel MOA
- MDD and anhedonia benefit
- Lack of sexual dysfunction
- Efficacy in-line with other approved therapeutics
- Potential for adjunctive use with SSRI / SNRI1 due to novel MOA differentiates from select competitors[1]

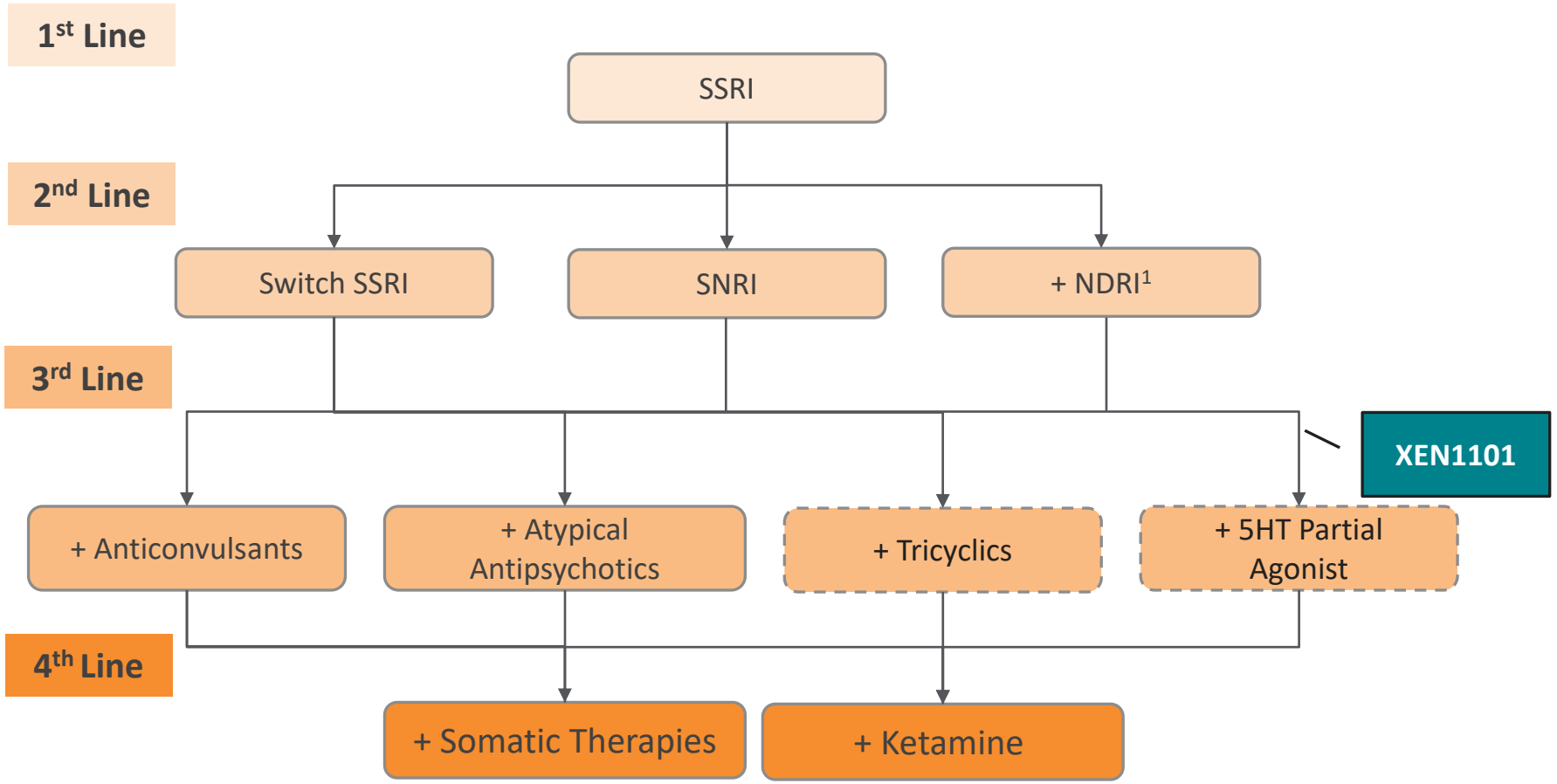
XEN1101 has the potential to offer a compelling clinical profile for MDD patients with residual unmet medical need

[1] Assuming no DDIs with SSRI / SNRI are observed.

Source: Xenon sponsored market research.

Physician Research Suggests Potential 3rd Line Use for XEN1101

MDD Lines of Therapy



"I could see Product X moving earlier in the algorithm – in front of current augmentation strategies because I have problems with current S/E profiles" – KOL

"I would prescribe this as a 2nd line medication after SSRIs, particularly in patients struggling with motivation and anhedonia" – Community Physician

Key Takeaways

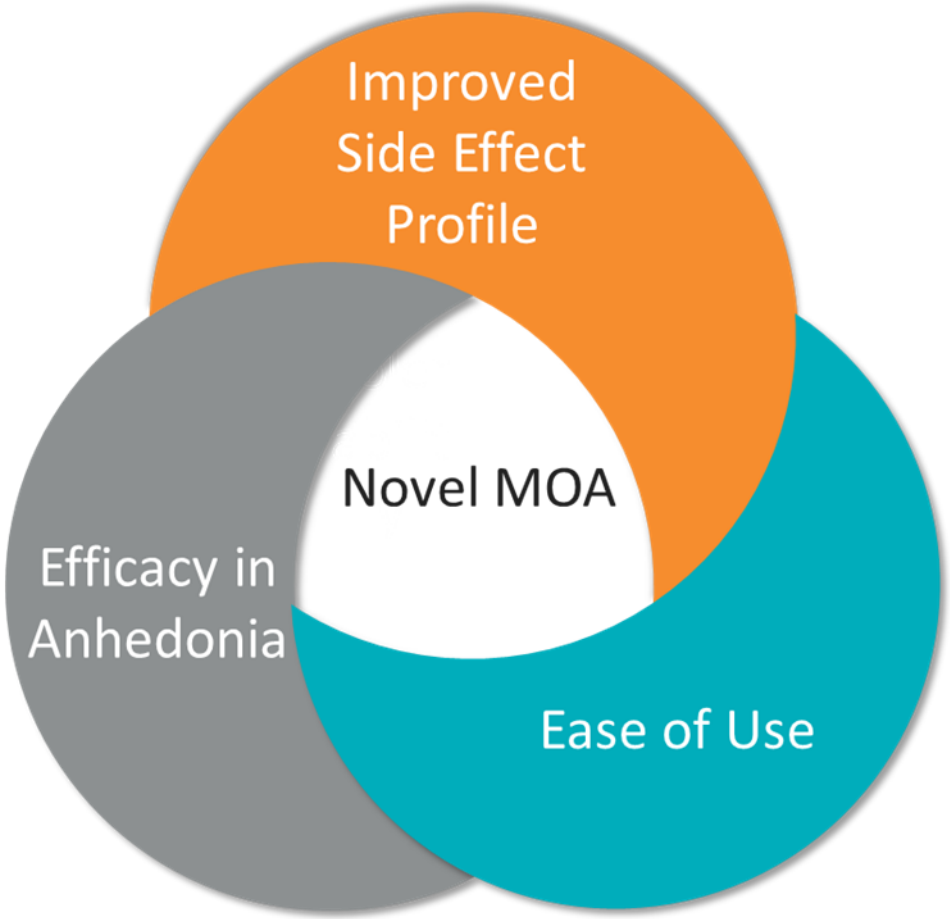
- Physicians expressed interest in the novel MOA of XEN1101 and willingness to try it in difficult to treat patients to assess efficacy and tolerability
- Payers will likely require first- and second-line use of SSRIs/SNRIs, with branded products typically reserved for 3L+
- Opportunity exists for novel mechanisms that offer efficacy in anhedonia with a differentiated safety profile

[1] NDRI – Norepinephrine and Dopamine Reuptake Inhibitor

Used less frequently in clinical practice

Source: American Academy of Clinical Psychiatrists, Xenon sponsored market research.

Summary of Potential Value Proposition of XEN1101



- Novel MOAs enable clinicians to **attempt a new treatment modality if initial therapies are unsuccessful**

- **Anhedonia** represents a common comorbidity that **frequently persists among MDD patients**

- **No evidence to date of sexual dysfunction**

- **Physicians view QD dosing at night positively** for ease of use
- **Lack of titration and low DDI risk** provides convenience for patients

Source: Xenon sponsored market research.

Conclusions

IAN MORTIMER

Summary of Today's Discussion

Unmet Medical Need in MDD

- MDD represents large patient population with a significant disease burden, despite the availability of numerous treatment options
- Novel MOAs are needed as the most commonly used antidepressants largely share the same mechanism of action

K_V7 Mechanistic Background / Scientific Rationale

- XEN1101 is a differentiated "next generation" K_V7 potassium channel modulator being developed for the treatment of epilepsy and other neurological disorders
- Preclinical and clinical studies suggest K_V7 channel potentiators, including ezogabine, may be beneficial for patients with depression and anhedonia

XEN1101 Clinical Experience

- Patient enrollment complete in X-NOVA Phase 2 clinical trial in MDD with topline data anticipated in late November to mid-December 2023
- A phase 2 NIMH-funded, investigator-led study with XEN1101 in MDD patients is ongoing

XEN1101 Commercial Opportunity in MDD

- In market research, physicians reacted positively to the potential profile of XEN1101:
  - Efficacy in anhedonia
  - Novel MOA (not SSRI/SNRI)
  - Lack of sexual dysfunction
  - Ease of use (low DDI risk, lack of titration, etc.)

Source: Xenon sponsored market research.

Q&A with Speakers

SUBMIT YOUR QUESTIONS VIA CHAT FORM

Thank you for joining us today!

FOR MORE INFO, PLEASE EMAIL: INVESTORS@XENON-PHARMA.COM