

XENON

Corporate Overview

June 2019

Forward Looking Statement/Safe Harbor

This 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 our expectations regarding the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN1101, XEN901, XEN496, XEN007 and our other product candidates, the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101, XEN901, XEN496, XEN007 and our other product candidates, the anticipated timing of IND, or IND equivalent, submissions and the initiation of future clinical trials for XEN1101, XEN901, XEN496, XEN007 and our other product candidates, the efficacy of our clinical trial designs, our ability to successfully develop and achieve milestones in the XEN1101, XEN901, XEN496, XEN007 and other development programs, the design of our clinical trials and anticipated enrollment, and the progress and potential of our other ongoing development programs.

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 promising results in early clinical trials may not be replicated in subsequent clinical trials; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; any of our or our collaborators' product candidates 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; the impact of competition; 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.

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NOTE: Comparisons of XEN1101 and ezogabine are based on results in published literature, not based on data resulting from head-to-head trials, and are not direct comparisons of safety or efficacy. Different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that are not the same between the relevant trials may cause any comparisons of results from different trials to be unreliable.

Xenon Overview

- Small molecule, ion channel neurology-focused biopharma company
 - NASDAQ: XENE
- Multiple mid-to-late stage clinical trials underway in 2019
- Strong financial position
 - \$110.4M in cash, cash equivalents and marketable securities (as of Mar. 31/19)
 - ~25.8M common shares and 1M preferred shares (as of Mar. 31/19)

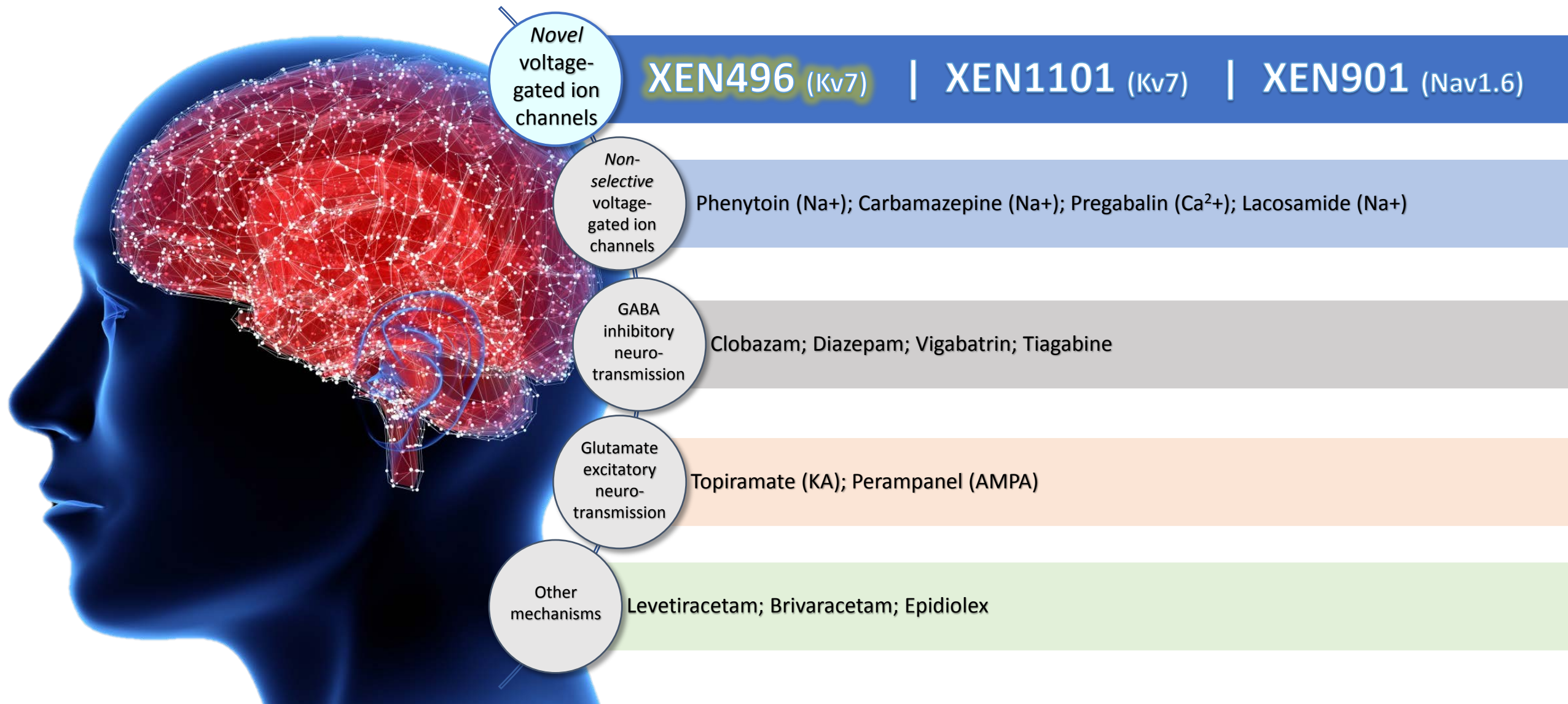


Ion Channel, Neurology-Focused Pipeline

Therapeutic Program <i>Indication</i>	Pre-clinical	Phase 1	Phase 2	Phase 3
XEN496 (Kv7 Potassium Channel Modulator) <i>Orphan Pediatric Epilepsy</i>				
XEN1101 (Kv7 Potassium Channel Modulator) <i>Adult Focal Epilepsy</i>				
XEN901 (Nav1.6 Sodium Channel Inhibitor) <i>Orphan Pediatric Epilepsy or Adult Focal Epilepsy</i>				
XEN007* (Cav2.1 and T-Type Calcium Channel Inhibitor) <i>Orphan Hemiplegic Migraine or Alternating Hemiplegia of Childhood</i>				
Ion Channel Modulators <i>Orphan Channelopathies</i>				
Nav1.7 Inhibitors <i>Pain (Partnered Program)</i>				
Genentech <i>A Member of the Roche Group</i>				

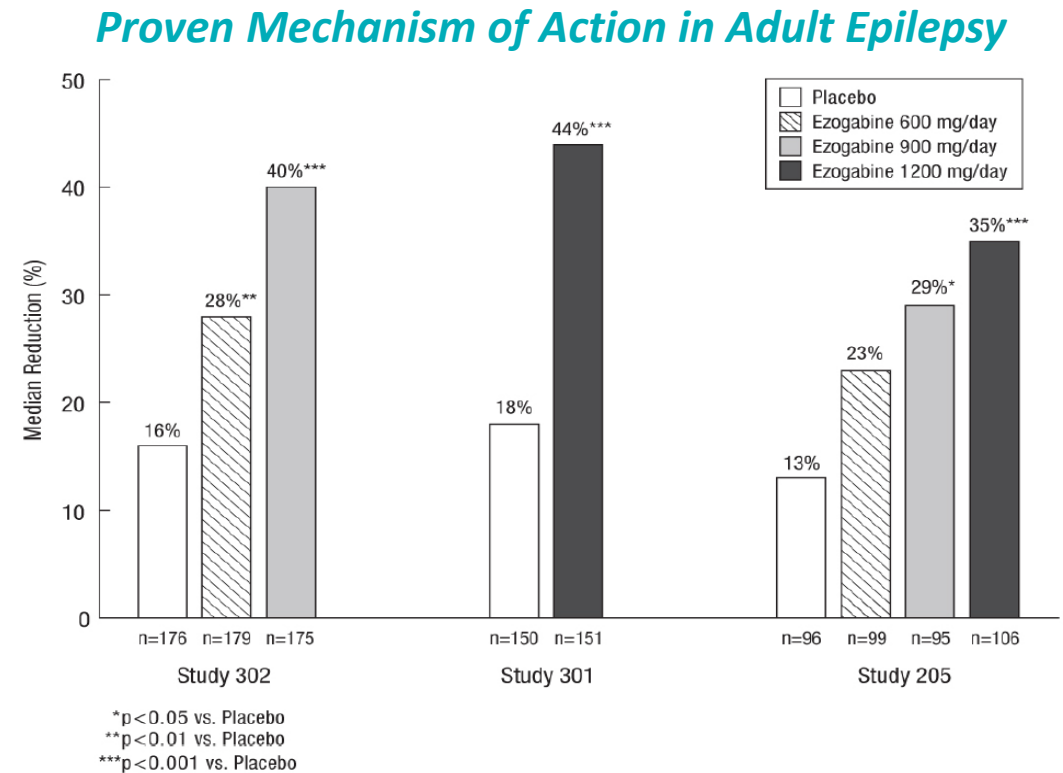
* Xenon has entered into key regulatory & manufacturing agreements related to XEN007; it is anticipated that a Phase 2 (or later stage) clinical trial could be initiated after receiving regulatory feedback.

Major Classes of Anti-Epileptic Drugs (AEDs)



XEN496: “Phase 3 Ready” Kv7 Potassium Channel Modulator

- XEN496, active ingredient ezogabine (retigabine)
- Only AED previously approved by FDA with MOA that potentiates Kv7-mediated potassium current
- Proven mechanism in adult focal seizures
- Potential for precision medicine approach to treat KCNQ2-EE pediatric epilepsy
- “Phase 3” ready
 - Regulatory support to conduct small, pivotal trial



XEN496 Precision Medicine Approach in Pediatric KCNQ2-EE Patients

About KCNQ2-EE

- Severe neurodevelopmental disorder caused by dominant negative missense mutations in the KCNQ2
- Presents during first week of life
 - Frequent daily refractory tonic seizures, status common
 - Most often associated with severe developmental delay
 - Present with language/social impairment, outbursts, repetitive and self injurious behaviours
 - Motor disabilities
 - Seizures wane by 4 years of age, can occur in clusters thereafter
- Incidence ~ 3/100,000 births
 - ~140 incident cases (50% of Dravet Syndrome)
 - ~1,000-2,000 prevalent U.S. cases

“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

Weckhuysen et al. “KCNQ2 encephalopathy: Emerging phenotype of a neonatal epileptic encephalopathy.” *Annals of Neurology*, January 2012.

Ezogabine Treatment of KCNQ2-EE Infants in Published Case Reports

Case Study of 11 KCNQ2-EE Patients <i>Millichap 2016</i>	Medical Record Review/Parent Interviews <i>Olson 2017 (8 Families)</i>
Ezogabine associated with improvements in seizures and/or development in: • 3 of the 4 infants treated before 6 month old were seizure free or occasional seizures <1/week • 2 of the 7 treated later • No serious adverse effects	Interviews/medical record review of KCNQ2-EE patients prescribed ezogabine: • Sustained improvement in seizure frequency in 5 of the 6 children with at least weekly seizures • Improvements in development or cognition in all 8 children • Urinary retention/hesitation in 3 patients, but overall well tolerated

Case Studies Suggest XEN496 is Efficacious in this Often Refractory Disease

XEN496: Steps Taken to Develop the First Precision Medicine AED

- ✓ Obtained regulatory right of reference authorization from GSK
- ✓ Pre-IND briefing meeting with FDA complete
 - Letters of support from KOLs, patients and key advocacy group to FDA
- ✓ Favorable FDA response accepting study of XEN496 in infants/young children
 - Single, small pivotal trial may be adequate to demonstrate efficacy
- ✓ Granted Orphan Drug Designation (ODD) from FDA
- ✓ Established steering committee of epilepsy experts and site selection underway
- ➔ Finalizing a pediatric-specific formulation with plans to test in healthy adult volunteer study in Q3:19
- ➔ Expect IND submission Q4:19 and initiate Phase 3 clinical trial in KCNQ2-EE thereafter

Regulatory Support for Single, Small Pivotal Trial in KCNQ2-EE Patients

Behind the Seizure™ Program



- Collaboration with Invitae and other industry partners
 - Launched Feb 2019 with comprehensive epilepsy gene panel
 - Invitae responsible for promotion of the program
- Offers no-cost testing to all children up to 60 months of age who has had an unprovoked seizure
- Hundreds of institutions have participated
- Physicians consent to contact from participating companies
- Timely reports on test results
- Supports patient ID for clinical studies
- Builds physician data base for commercialization
- Physician ZIP codes provided for prior 2-years of retrospective positives for genes of interest

Behind the Seizure™
Test early to expedite care
[PLACE AN ORDER](#)

No-cost epilepsy gene panel testing program

Invitae, BioMarin, Stoke Therapeutics, and Xenon Pharmaceuticals have partnered to offer Invitae's comprehensive epilepsy panel to any child up to 60 months old who has had an unprovoked seizure.

An epilepsy gene panel can bring you closer to understanding what's causing your patient's epilepsy, helping your patients and their caregivers benefit from deeper knowledge and timely care.

- **More than 50% of epilepsies have some genetic basis.** When a patient presents with seizures, genetic testing can help identify 100+ underlying genetic causes. Early genetic testing may be the most direct, cost-effective, and accurate diagnostic tool.¹
- **Many genes are actionable.** Gene panels increasingly help tailor your approach—more than 20 genes have been linked to specific treatment strategies. Identifying a seizure's underlying etiology can enable more precise treatment.
- **Delay can be devastating for patients with genetic epilepsy.** Some genetic epilepsies are neurodegenerative, and may initially present with subtle, non-specific symptoms like language development delay and/or motor disturbance. Genetic testing can help identify the cause of epilepsy before a patient experiences the hallmark signs of regression.
- **Genetic epilepsies may be hiding behind non-specific symptoms.** Language delay and motor disturbance may be the best predictors of finding genetic epilepsies.

Reference: 1. Pal DK, Pong AW, Chung WK. Genetic evaluation and counseling for epilepsy. *Nat Rev Neurol*. 2010;6:445–453.

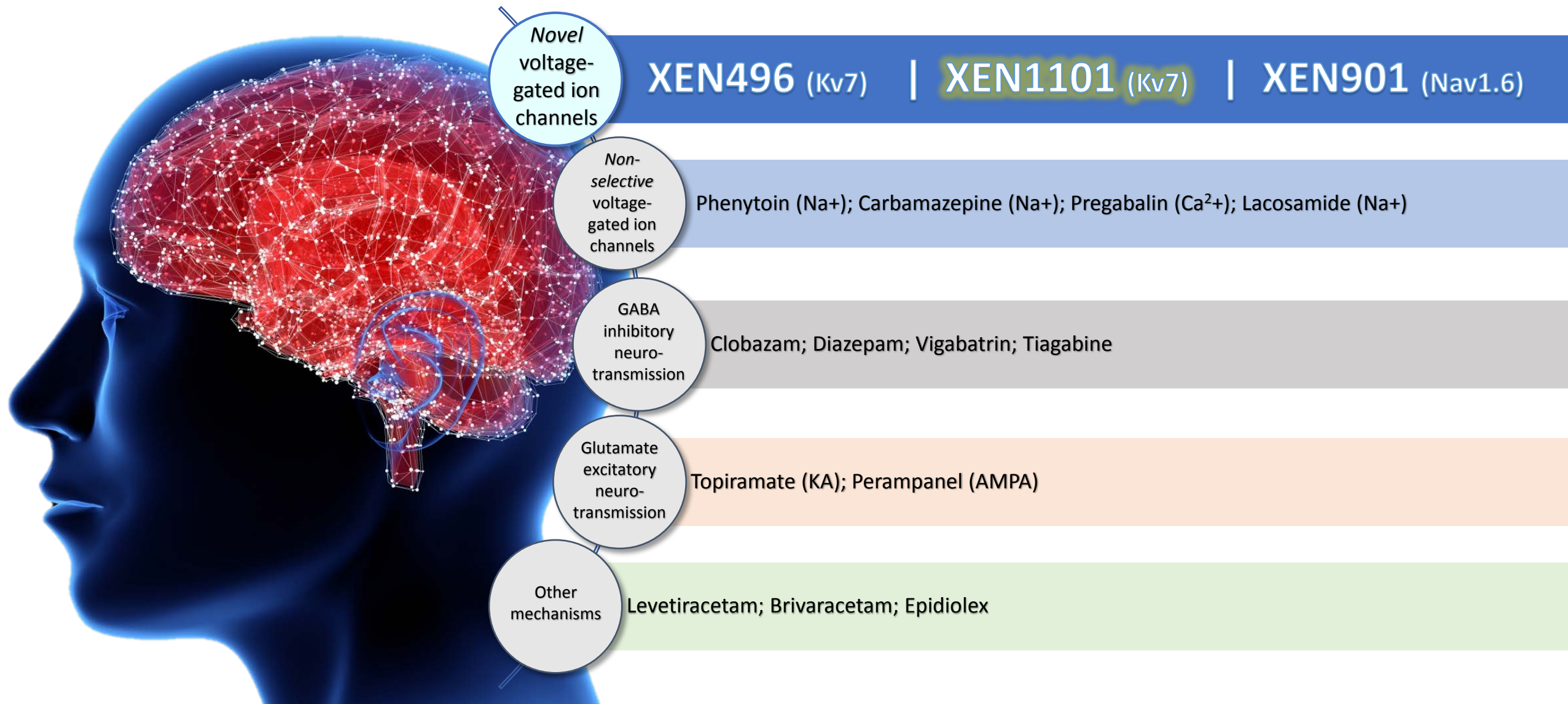
Eligibility
[Learn more](#)

Panel
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Ordering instructions
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<https://www.invitae.com/en/behindtheseizure/>

Major Classes of Anti-Epileptic Drugs (AEDs)



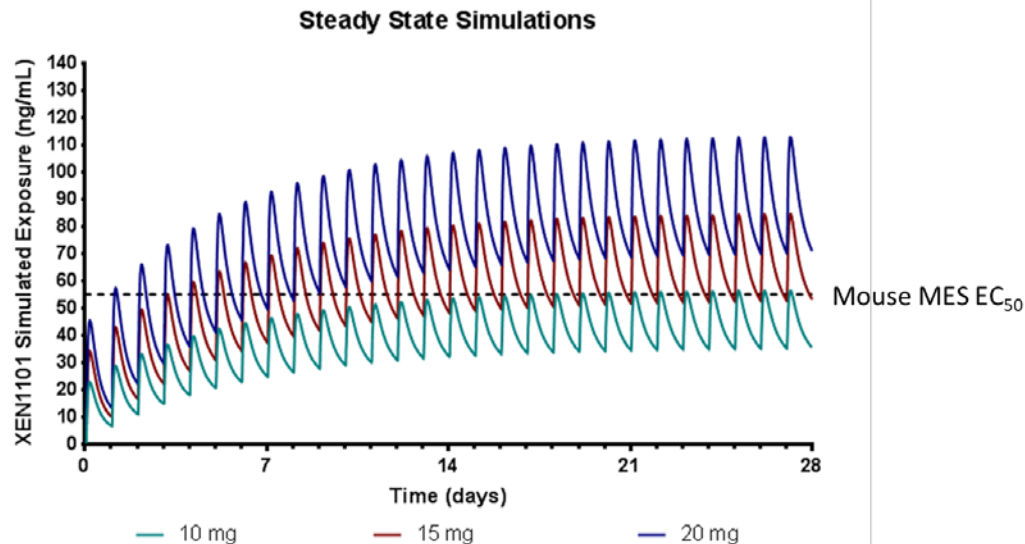
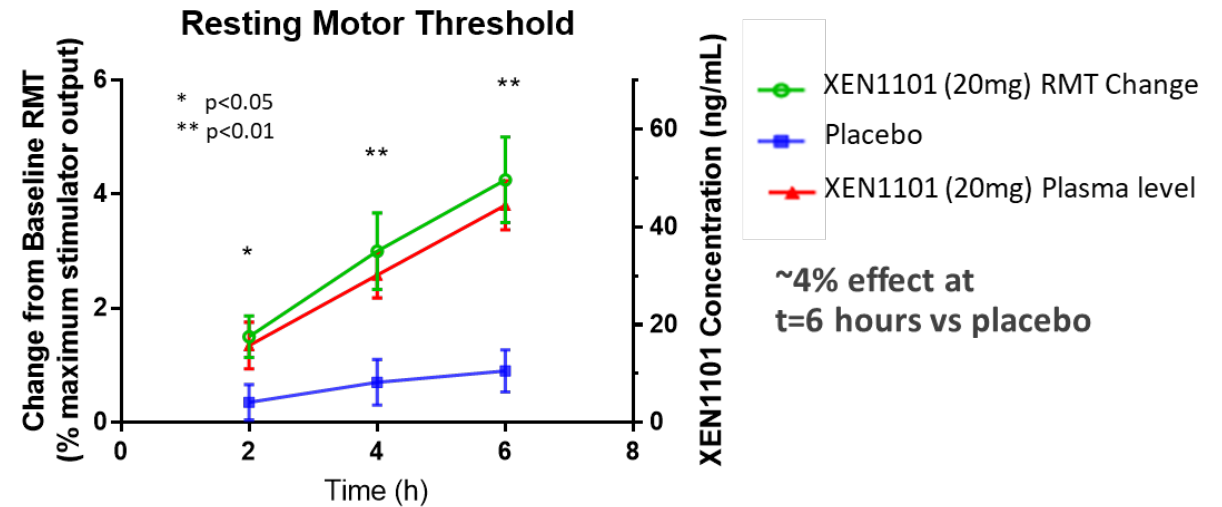
XEN1101: Potential “Next-Gen” Kv7 Potassium Channel Modulator

- Same proven MOA in adult focal seizures as ezogabine, but with improvements
 - More potent *in vitro* and *in vivo*
 - Improved PK
 - Once daily dosing plus modest selectivity predicts better tolerability
 - No pigmented dimers and no predicted discoloration liability
- Phase 1 studies completed
 - Robust TMS signal in Phase 1b study
 - PK supporting once-daily dosing
 - Mild, transient AE profile consistent with MOA (e.g. dizziness, sedation, blurred vision)
 - No safety signals in ECG or Safety Labs; no SAEs
- 300-patient Phase 2b clinical trial underway in Adult Focal Epilepsy

Summary of XEN1101 Phase 1b TMS Results

TMS was used to evaluate the corticospinal and cortical activity profile of XEN1101 compared to placebo in healthy male volunteers

- Significant plasma concentration dependent reduction of corticospinal (RMT) and cortical (TEP) excitability
- RMT effect of XEN1101 (20 mg) is ~2x ezogabine at 1/20th the dose (400 mg)

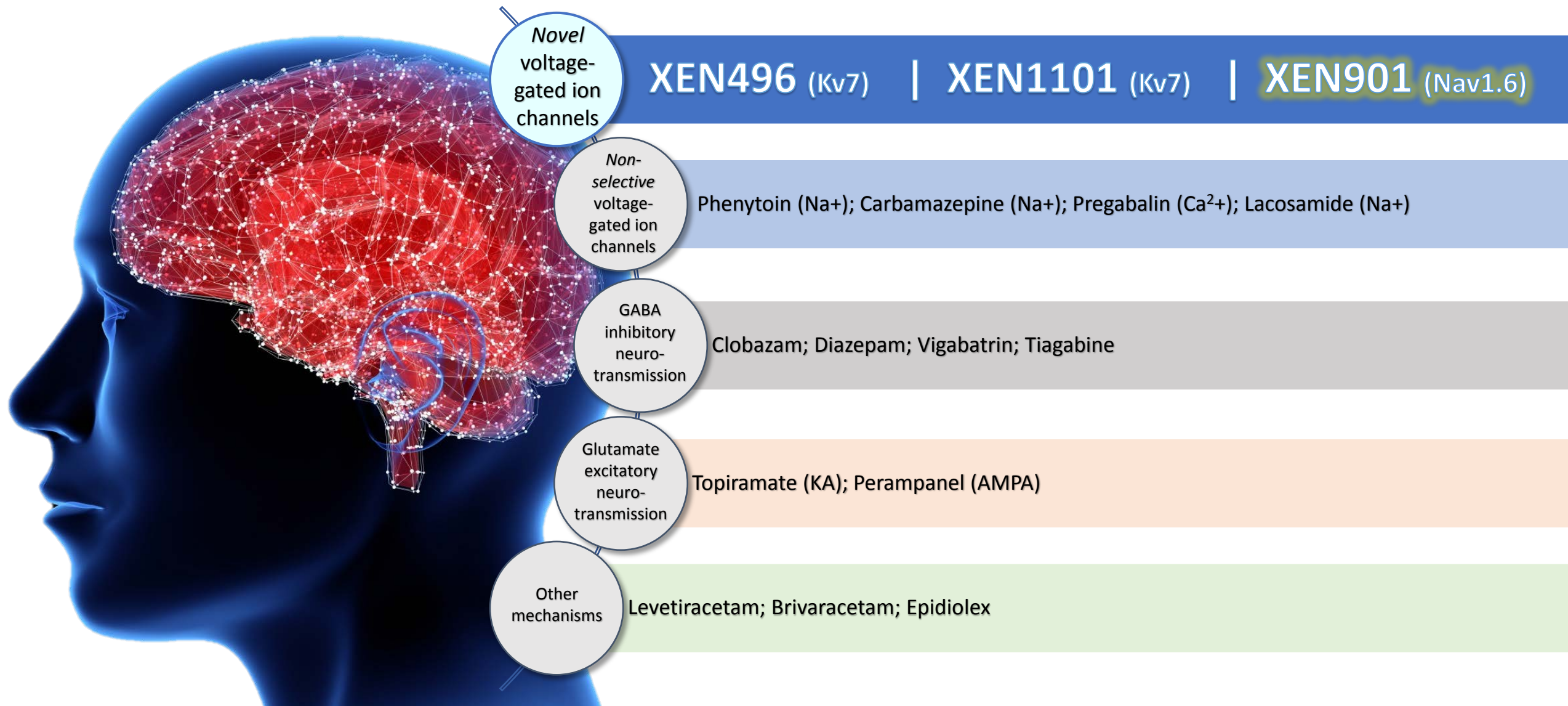


Chronic low daily dosing achieves exposures required for TMS and pre-clinical efficacy

XEN1101 Phase 2b Clinical Trial in Adult Focal Seizures Underway

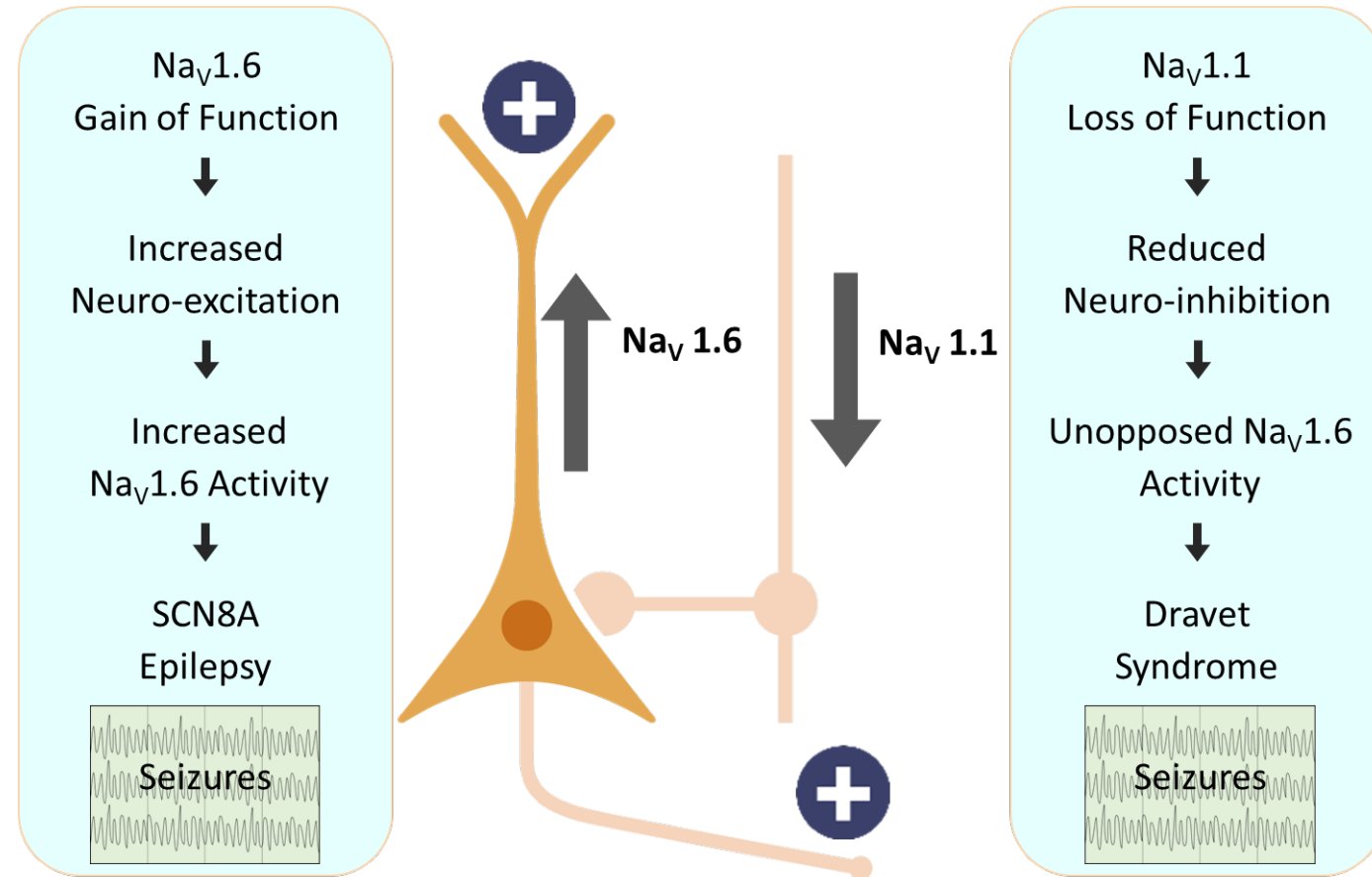
- Confidence to go from Phase 1 directly into a larger, randomized, placebo-controlled Phase 2b study based on:
 - Well-understood MOA
 - Ezogabine's known development path
 - Totality of XEN1101 data generated to date (preclinical, Phase 1, TMS studies)
- Site selection and patient enrollment now underway in U.S., Canada and Europe
- Randomized, double-blind, placebo-controlled, multicenter Phase 2b clinical trial will evaluate the clinical efficacy, safety and tolerability of XEN1101 as adjunctive treatment in adult patients with focal epilepsy
 - ~300 patients randomized (blinded) to 1 of 3 active treatment groups or placebo in a 2:1:1:2 fashion (XEN1101 25 mg : 20 mg : 10 mg : Placebo)
 - Primary endpoint is the median percent change in monthly focal seizure frequency from baseline compared to treatment period of active versus placebo

Major Classes of Anti-Epileptic Drugs (AEDs)



XEN901: A Novel, Unique Sodium Channel Inhibitor

- Precision medicine approach to address Early Infantile Epileptic Encephalopathy type 13 (EIEE13)
- Potential to achieve higher levels of seizure freedom with an improved side effect profile
- Favorable PK and safety profile in Phase 1
- Data from pilot TMS study supports cortical and corticospinal effect with XEN901

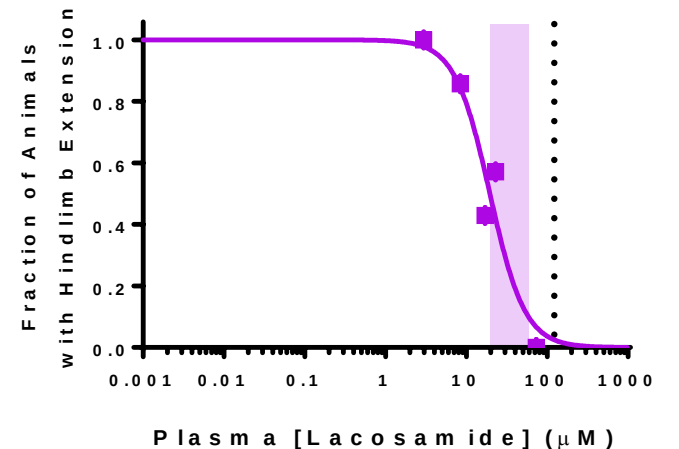
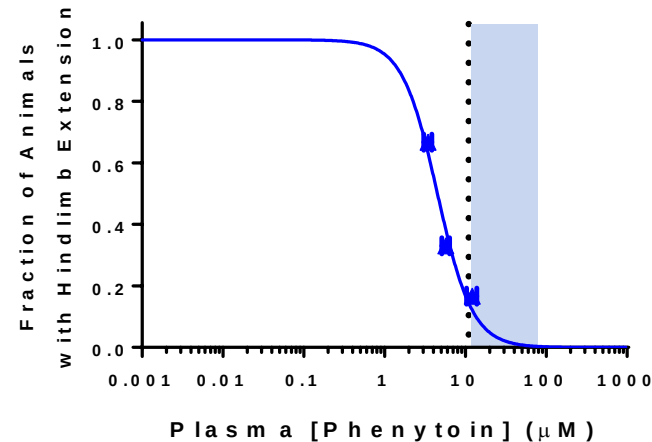
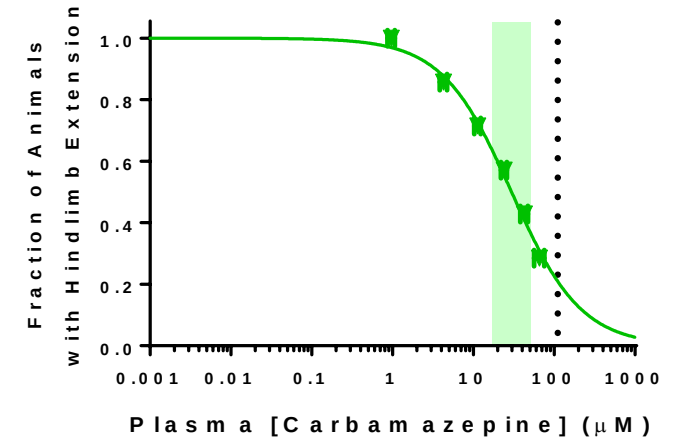
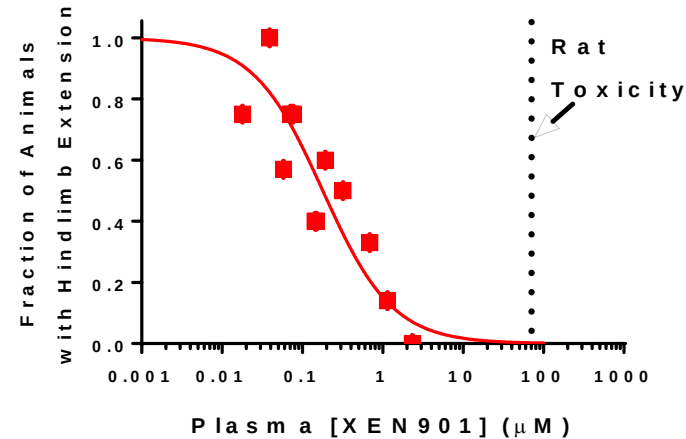


Potential “Best in Class” Sodium Channel Inhibitor

Striving for Seizure Freedom with XEN901

Rat MES Assay

- Current agents lack therapeutic index needed to achieve seizure freedom for many patients
- High therapeutic index of XEN901 could enable high level of efficacy with minimal adverse events



Shaded areas correspond to published clinical plasma concentrations

Summary of XEN901 Phase 1 Results

- Favorable pharmacokinetics (PK) data predicts BID or potentially QD dosing
- XEN901 overall generally safe and well tolerated at the doses examined
 - Majority of adverse events (AEs) were deemed unrelated to XEN901, and were mild or moderate, transient and resolved spontaneously
 - All AEs considered possibly related to XEN901 were mild; only nausea and dizziness were reported in more than 1 subject
 - No SAEs, deaths, or clinically significant ECG, vital signs or laboratory findings
- Pilot TMS study showed increases in RMT and AMT of ~2% suggesting activity in target CNS tissue

XEN901 Proposed Phase 2 Clinical Planning

NEXT STEPS:

- Continued planning for Phase 2 clinical development of XEN901 as a treatment of rare, pediatric forms of epilepsy, including SCN8A-EE, or for adult focal seizures
- Received FDA feedback on the clinical development of XEN901
 - Feedback supports advancing XEN901 directly into pediatric SCN8A gain-of-function epilepsy patients
 - Currently in the process of completing pediatric formulation development and juvenile toxicology studies
 - Intend to run Phase 1 PK study with pediatric formulation in late Q3/early Q4 and then initiate Phase 2, or later stage, clinical trial in SCN8A patients
 - Details on final trial design to be disclosed over the coming months

XEN007: Calcium Channel Inhibitor

- XEN007 contains flunarizine as the active ingredient
- Safe CNS calcium channel inhibitor
 - No effects on cardiovascular parameters, unlike other CaV inhibitors
 - ~30 years clinical use, including pediatrics
- Never developed in the U.S.
 - No other CNS-acting calcium channel inhibitor on U.S. market
- Xenon has obtained:
 - ODD for hemiplegic migraine (HM) and alternating hemiplegia of childhood (AHC)
 - Rare Pediatric Disease Designation for AHC
 - Exclusive access to regulatory files and reports for U.S. territories
 - Commercial drug product supply secured

Evaluating various development strategies for XEN007, including the support of at least one Phase 2 clinical trial in an orphan neurological indication

Multiple Catalysts & Value-Creating Milestones

XEN496

- Conduct PK study with new pediatric formulation in Q3:19
- Submit IND in Q4:19 to enable pivotal Phase 3 trial in pediatric KCNQ2-EE

XEN1101

- Phase 2b clinical trial in adult focal seizures underway in Canada, U.S. and Europe
- ~300 patients randomized in blinded manner to 1 of 3 treatment groups (or placebo)
- Top-line results anticipated in 2H:2020

XEN901

- Received regulatory feedback on pediatric strategy (Q2:19)
 - Pediatric formulation development and juvenile tox studies underway; conduct Phase 1 PK study with pediatric formulation in Q3/Q4
- Initiate Phase 2/3 clinical trial in pediatric epilepsy indication

XEN007

- Support initiation of at least one Phase 2 clinical trial in orphan neurological indication

For more information:

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