XENON

XENON

EILAT XV Conference:
New Anti-Epileptic Drugs and Devices

July 27-30, 2020

Presented by: Dr. Simon Pimstone, CEO
Xenon Pharmaceuticals Inc.

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 the anticipated impact and timing of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations; the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN496, XEN1101, XEN007, and other proprietary products, and those related to NBI-921352, FX-301, and other partnered product candidates; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN496, XEN1101, XEN007 and other proprietary and partnered product candidates; the anticipated timing of IND, or IND equivalent, submissions and the initiation of future clinical trials for XEN496, XEN1101, XEN007, and other proprietary products, and those related to NBI-921352, FX-301, and other partnered candidates; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in the XEN496, XEN1101, XEN007 and other proprietary development programs; the timing and results of our interactions with regulators; the potential to advance certain of our product candidates directly into Phase 2 or later stage clinical trials; anticipated enrollment in our clinical trials and the timing thereof; the progress and potential of our other ongoing development programs; the potential receipt of milestone payments and royalties from our collaborators; our expectation of having sufficient cash to fund operations into 2022; and the timing of potential publication or presentation of future clinical data.

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 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; 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 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 not permit certain of our product candidates to advance directly into a Phase 2 or later clinical trials, 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; 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.

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

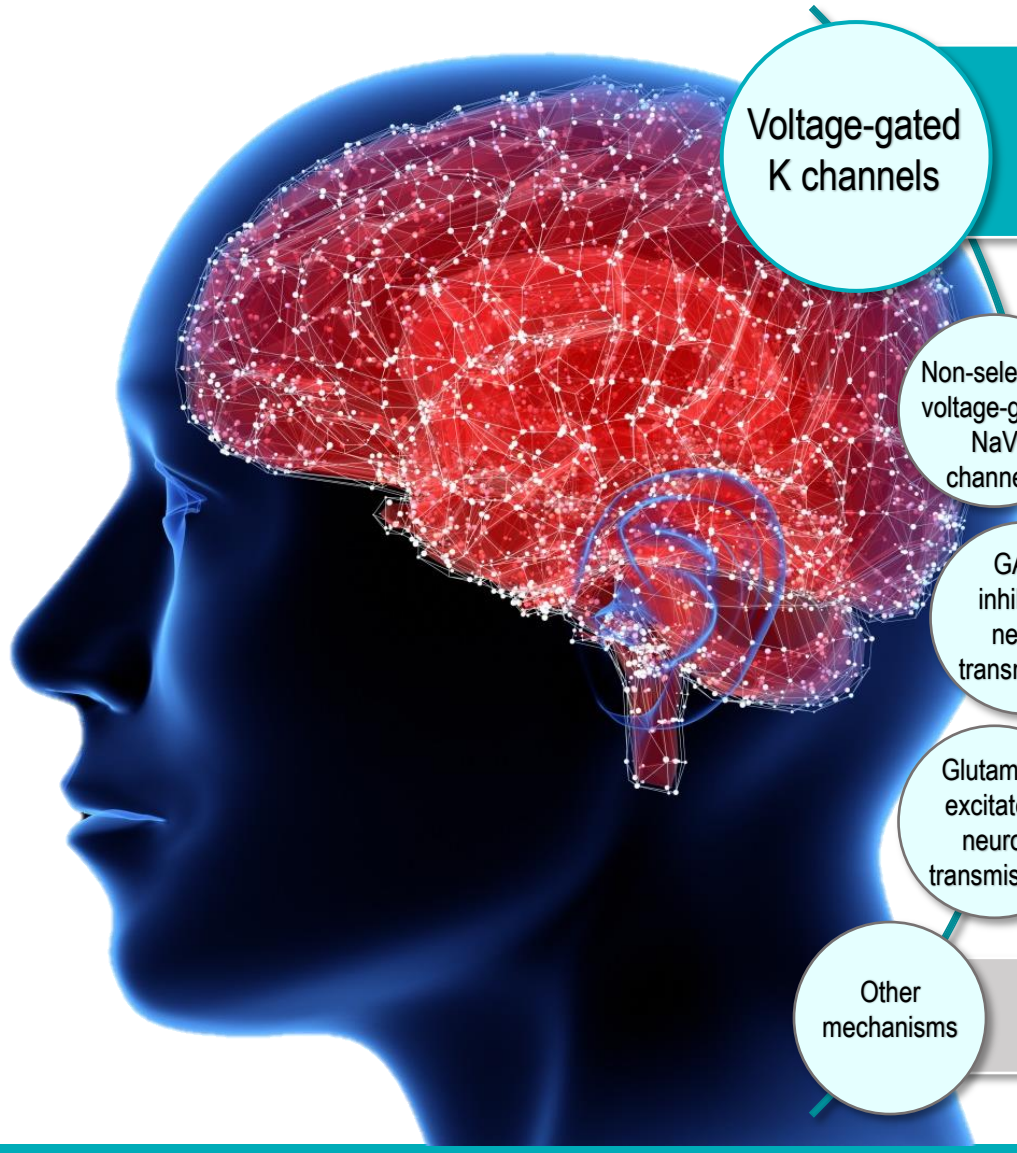
- Small molecule, ion channel neurology-focused biopharma company (NASDAQ: XENE)
- Mid-to-late stage clinical trials and important clinical data anticipated over next 12-18 months
- Solid financial position and strong partnerships with collaborators
  - Up to $1.7B in potential milestone payments related to Neurocrine collaboration, including $25M milestone expected in 2020

Ion Channel, Neurology-Focused Pipeline

Therapeutic Program *Indication*	Pre-clinical	Phase 1	Phase 2	Phase 3
XEN496 (Potassium Channel Modulator) *Orphan Pediatric Epilepsy*				
XEN1101 (Potassium Channel Modulator) *Adult Focal Epilepsy*				
XEN007* (Calcium Channel Inhibitor) *Childhood Absence Epilepsy*				
Ion Channel Modulators *Orphan Channelopathies*				
NBI-921352 (XEN901) and $Na_V1.6/1.2$ Sodium Channel Inhibitors *Epilepsy (Orphan Pediatric and Adult Focal)* — Neurocrine Biosciences				
FX301 *Post-operative Pain* — flexion				
$Na_V1.7$ Inhibitors *Pain* — Genentech, A Member of the Roche Group				

*A physician-led, Phase 2 proof-of-concept study is ongoing to examine XEN007 as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant childhood absence epilepsy (CAE).

Xenon's K_V7 Channel Modulators for Adult and Pediatric Epilepsies



Voltage-gated K channels

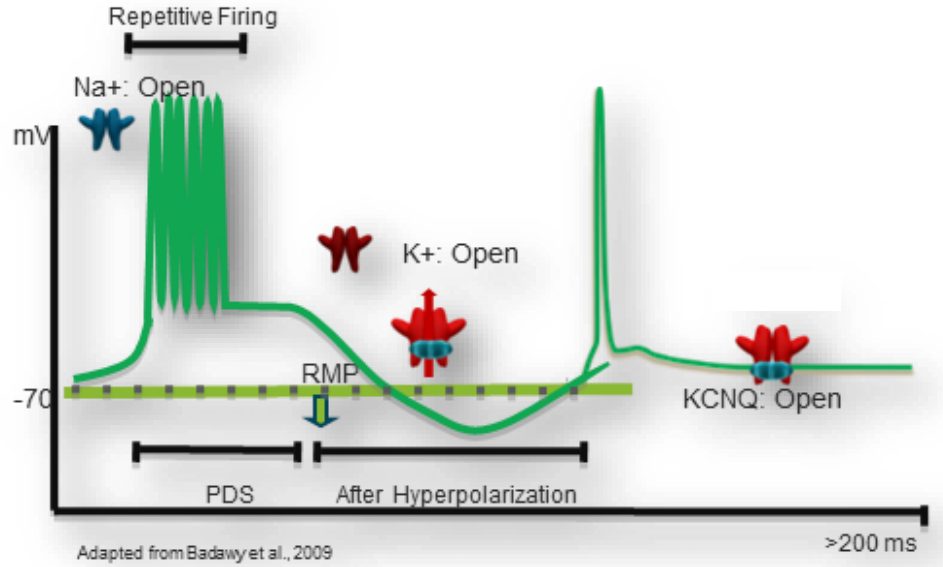
XEN1101 (K_V7) | XEN496 (K_V7)

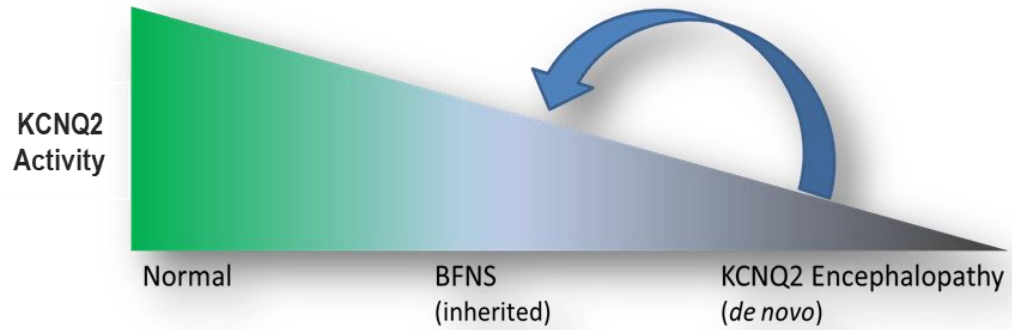
Major Classes Of Approved Anti-Seizure Medications (ASMs)

Non-selective voltage-gated NaV channels	Phenytoin (Na+); Carbamazepine (Na+); Pregabalin (Ca^{2}+); Lacosamide (Na+)
GABA inhibitory neuro-transmission	Clobazam; Diazepam; Vigabatrin; Tiagabine
Glutamate excitatory neuro-transmission	Topiramate (KA); Perampanel (AMPA)
Other mechanisms	Levetiracetam; Brivaracetam; Cannabidiol (CBD); Cenobamate

The KCNQ2 Potassium Channel

- KCNQ2 dampens neuronal hyper-excitability
- K+ channels have important inhibitory control over neuronal firing in the CNS
- Repolarize membranes to end the action potential
- K+ channel opener (enhancer) would decrease hyper-excitability in the brain





Medical Need Exists in KCNQ2-DEE

- Severe seizure and neurodevelopmental disorder caused by dominant negative missense mutations in the KCNQ2 gene
- Presents during first week of life
  - Frequent daily refractory tonic seizures, status common
  - Most often associated with developmental delay
- Scottish national cohort study (Symonds et al.) birth rate of pathogenic KCNQ2 variants 1/17,000
  - Compared to Dravet Syndrome 1/12,200 births
- 9,413 Invitae epilepsy panel tests (Truty et al.), 219 subjects with KCNQ2 genotype
  - 116 VUS
  - 103 LP/P
- Further characterization of VUS likely to identify many more variants as LP/P
  - Collaborating with RIKEE registry of >800 subjects to identify pathogenic VUS
  - 40% of BFNS families reported with delayed psychomotor development (Steinlein et al.)
- GeneDx identified 159/8,565 tests as KCNQ2 pathogenic variants (Lindy et al.)
  - Compared to Dravet Syndrome 322/8,565 tests

Symonds, JD et al. "Incidence and phenotypes of childhood-onset genetic epilepsies: a prospective population-based national cohort." Brain : a journal of neurology vol. 142,8 (2019): 2303-2318.

Truty, R et al. "Possible precision medicine implications from genetic testing using combined detection of sequence and intragenic copy number variants in a large cohort with childhood epilepsy". *Epilepsia Open*. 2019; 4: 397– 408.

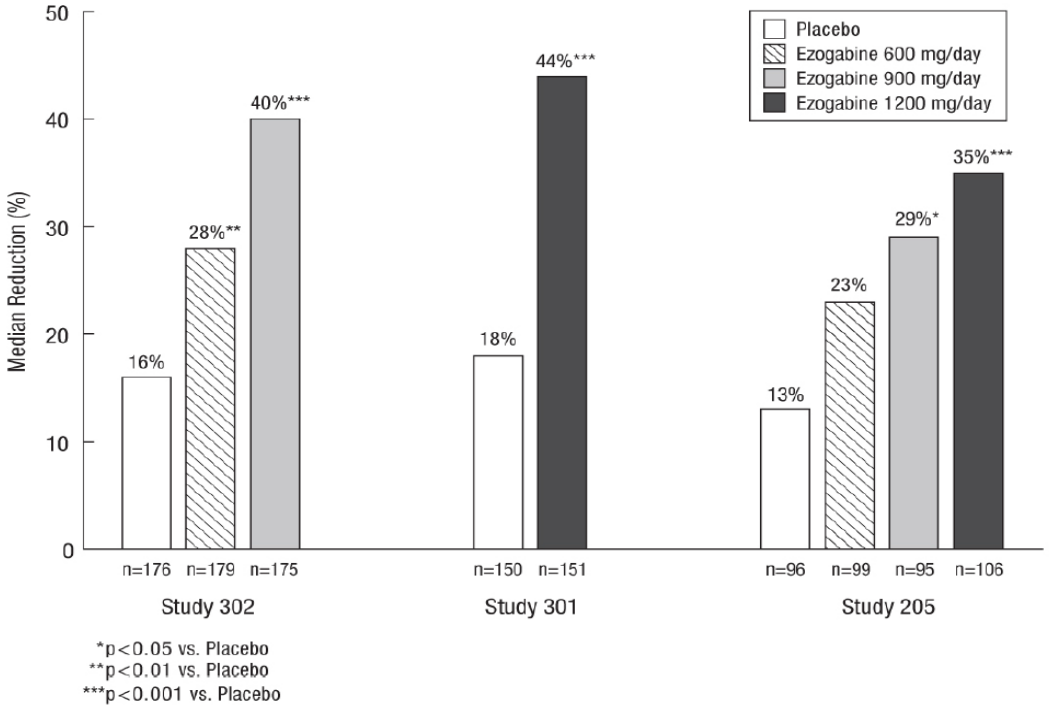
Steinlein, O.K. et al. "Benign familial neonatal convulsions: Always benign?". *Epilepsy research*. 2007. 73. 245-9.

Lindy, AS et al. "Diagnostic outcomes for genetic testing of 70 genes in 8565 patients with epilepsy and neurodevelopmental disorders." *Epilepsia*. 2018; 59: 1062– 1071.

XEN496: Proven Kv7 Mechanism in Adult Focal Epilepsy

- XEN496, active ingredient ezogabine (retigabine)
- Only anti-seizure medication previously approved by FDA with MOA that potentiates K_V7-mediated potassium current
- Removed from market in 2017 for commercial reasons
- Anectodal evidence suggesting activity in KCNQ-DEE
  - Off label use
  - In vivo KO data
- Strong rationale for precision medicine approach to treat KCNQ2-DEE pediatric epilepsy

Proven Mechanism of Action in Adult Epilepsy



Precision Medicine Approach in Pediatric KCNQ2-DEE Patients

Ezogabine and KCNQ2-DEE Proof-of-Concept

Case Studies Suggest Ezogabine is Active in this Often Refractory Disease

Case Study of 11 KCNQ2-DEE Patients *Millichap 2016*	**Medical Record Review/Parent Interviews** *Olson 2017* (8 Families)
Ezogabine use (assessed by the treating physicians and parents) was associated with : • improvement in seizures and/or development in 3 of the 4 patients treated before 6 months of age, and 2 of the 7 patients treated later • 3 of the 4 infants treated before 6 months old were seizure free or occasional seizures <1/week • No serious side effects were observed	Interviews/medical record review of KCNQ2-DEE 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

Millichap, John J et al. "KCNQ2 encephalopathy: Features, mutational hot spots, and ezogabine treatment of 11 patients." Neurology. Genetics vol. 2,5 e96. 22 Aug. 2016.

Olson et al. 2017 AES Annual Meeting, Abstract 3.176.

XEN496: Precision Medicine in KCNQ-DEE

- Key Hurdles Overcome
  - ✓ GSK provided right of reference to FDA
  - ✓ *Orphan Drug Designation* and *Fast Track* designation granted
  - ✓ Steering committee
  - ✓ Support from patient advocacy groups
  - ✓ Developed a pediatric friendly formulation
  - ✓ Completed adult PK study with data supporting Phase 3 trial design
  - ✓ Improving access to diagnosis through the Behind the Seizure™ program and other partnerships
  - ✓ Patient/caregiver surveys to inform trial design and endpoints completed

New, Proprietary, Pediatric-Friendly Formulation of XEN496

- Granule formulation, packaged as single-dose sprinkle capsules
  - Sprinkle capsules containing different weights of XEN496 based on patient's weight/targeted drug level
  - Parents/caregivers open the capsules and disperse the granules into the chosen semi-solid or liquid food "carrier"
- PK study in 24 adult healthy volunteers is complete
  - 400 mg dose in fed or fasted states
  - XEN496's absorption and elimination curves comparable to historical PK data for IR ezogabine tablets
  - Results support planned XEN496 Phase 3 trial in KCNQ2-DEE

XEN496 Granules

Typical sprinkle capsule

Patient/Caregiver Surveys to Inform Trial Design and Endpoints

- Caregiver survey to obtain additional phenotypic information regarding the seizure history of KCNQ2-DEE as well as Anti-Seizure Medication (ASM) use, with a focus on ezogabine
- Conducted in collaboration with The KCNQ2 Cure Alliance

Results: Demographics and Seizure Burden of Survey Patients

Demographics	
Data available	67 complete responses for analysis; Exclusions as follows: • 8 non-English speaking origin • 6 known GOF • 3 atypical phenotype
Locations (n)	USA (31); Canada (5); UK (7); Australia (7)
Patient Age, n (%)	18 (36%) younger than 4 years 32 (64%) older than 4 years
Age of seizure onset after birth	Day 0=26%. Day 1=40%, Day 2=24% Days 3-5=10%
Initial seizure frequency (n=49)	63% had more than 10 seizures per day 35% had between 2-10 seizures per day 2% had 1 seizure per day
Current seizure frequency (n=50)	28% had seizures over past 30 days 38% had seizures over past 90 days 46% had seizures over past 180 days

* Patients used ezogabine and Potiga® interchangeably in their responses

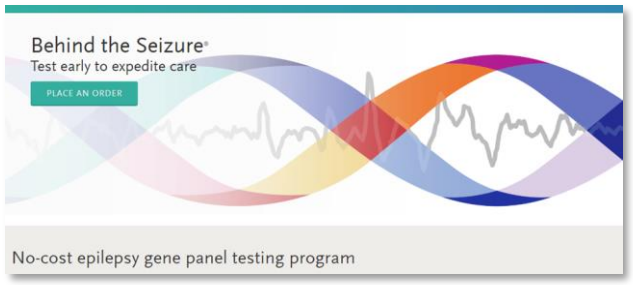
Results: Patients with Previous Experience with Ezogabine

- 7 Patients had access to ezogabine, one early in disease course
- No discontinuations due to adverse effects

Did you see any improvements in your child's seizures, behaviour or development while they were taking ezogabine? ALL SEVEN RESPONDENTS ANSWERED "YES"
"Cognitive improvements documented [by] therapists who did not know the child was on Potiga and [by] parent observation."
"Started at 3 months old, achieved seizure freedom around 5 months old for approximately 6 months when infantile spasms started."
"Child was not having seizures, but starting Potiga coincided with improvements in EEG and attention/awareness."
"Seizure control and developmental gains - smiling, eating by mouth."
"We had full seizure control lasting months and only saw seizures with fevers and illness. He was showing gains of function moving his limbs more and was more aware of his surroundings."
"Alertness, better development, EEG improved."
"His seizures immediately decreased in frequency and he stopped having longer seizures about 2 months after he started."

Xenon's Strategic Alliances

Behind the Seizure®
Invitae, BioMarin, Xenon, Stoke, Biogen, Encoded, Praxis, Neurogene, PTC



- Offers no-cost testing to any child < 8 years with an unprovoked seizure
- Launched Feb 2019, 190+ gene panel
- >320 institutions have participated
- Support patient ID for clinical studies
- ~150 positive tests to date:
- ~3-4% of 0-2 year old children tested

KCNQ2 Cure (unity, love, strength, hope)

- Working closely on Study design and feasibility
- Joining KOL meetings
- Supported patient surveys
- Involved in regulatory filings
- Funding a multicenter natural history study

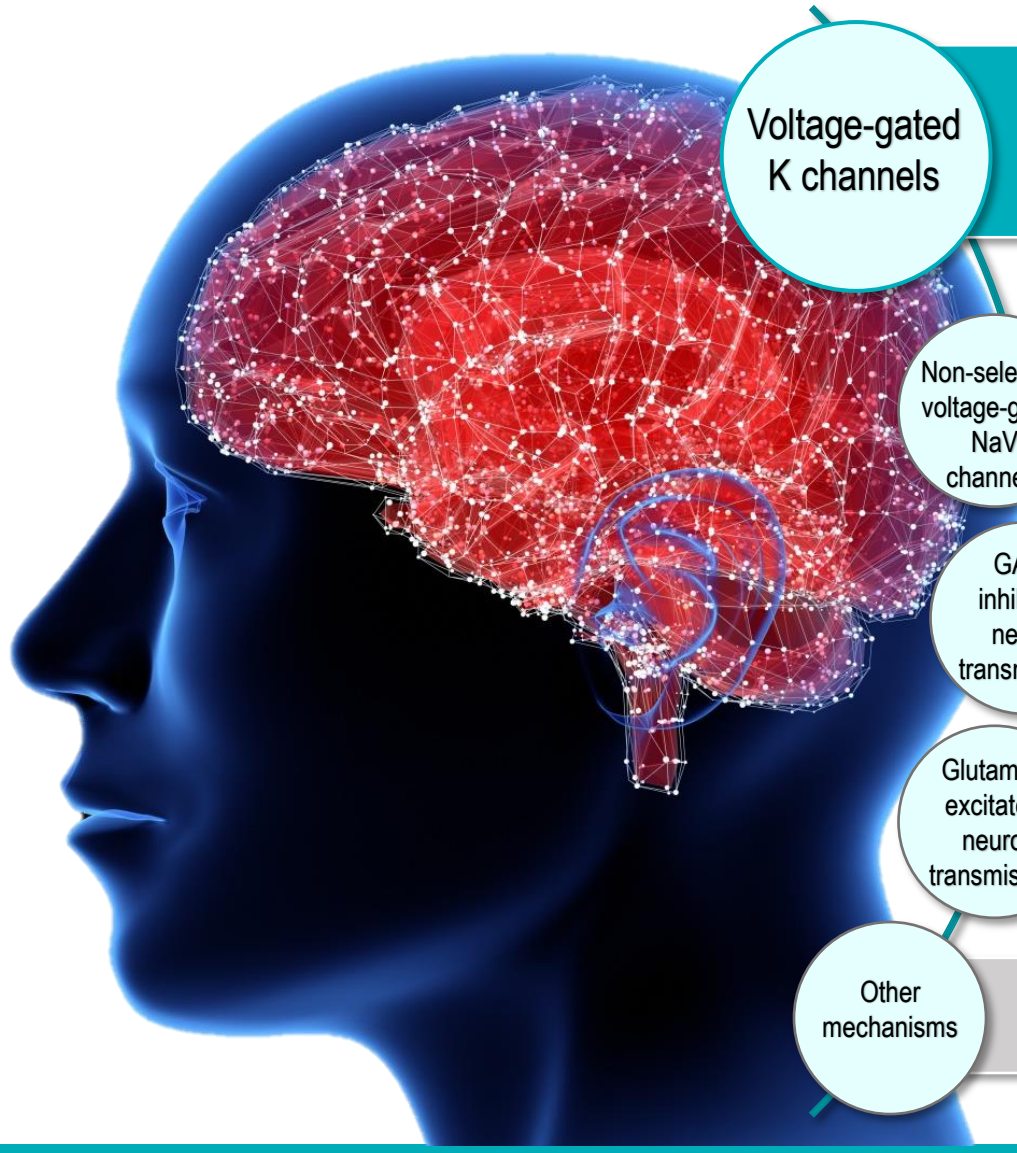
Clinical Development of XEN496

NEXT STEPS

- Initiate Phase 3 clinical trial in 2020*
- Randomized, double-blind, placebo-controlled study
  - ***Anticipated primary endpoint***: median % change in seizure frequency from baseline compared to treatment period of active versus placebo
- ~40 KCNQ2-DEE patients (infants up to six years old)

*Guidance is dependent upon the ability to initiate clinical sites and patient enrollment given the ongoing COVID-19 pandemic.

Xenon's K_V7 Channel Modulators for Adult and Pediatric Epilepsies



XEN1101 (K_V7) | XEN496 (K_V7)

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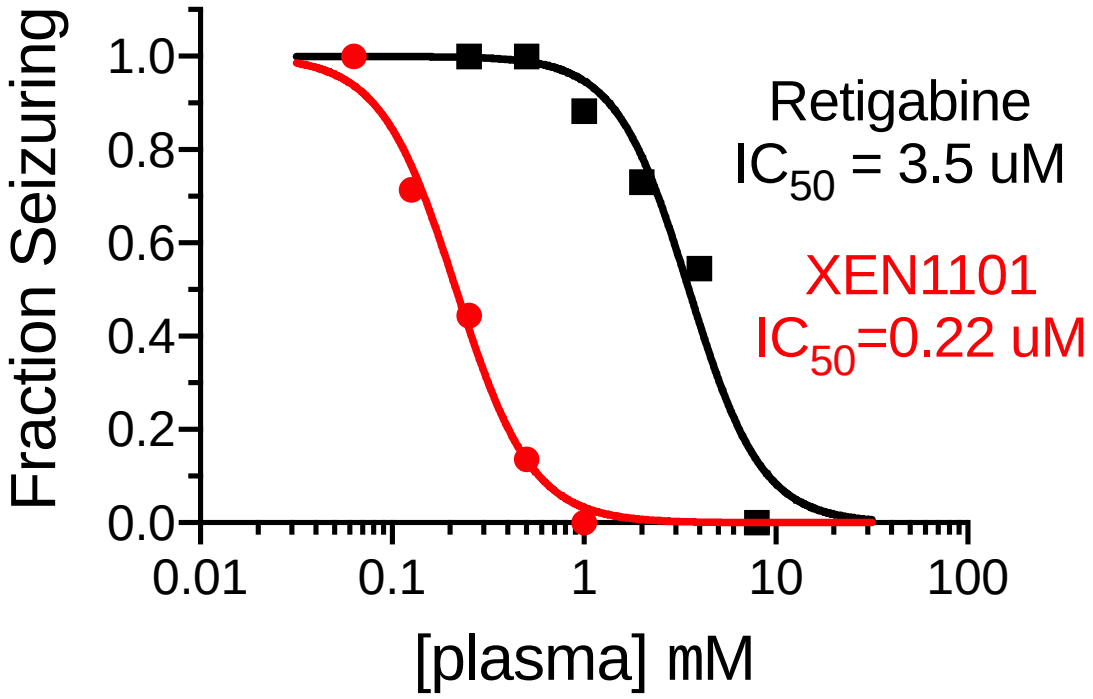
XEN1101: "Next-Gen" K_V7 Potassium Channel Modulator

- Proven MOA in adult focal seizures with ezogabine, but with significant improvements
  - More potent *in vitro* and *in vivo*
  - 3- to 4-fold selective for KCNQ2/3 over other KCNQ channels
  - Once daily dosing with evening administration
  - No potential to form chromophoric phenazinium dimers
- Phase 1 studies completed
  - PK supporting once-daily dosing
  - Transient, dose dependent AE profile consistent with MOA (e.g. dizziness, sedation, blurred vision)
  - No safety signals in ECG or Safety Labs; no SAEs
  - Robust TMS signal in Phase 1b study
- 300-patient Phase 2b clinical trial underway in Adult Focal Epilepsy (X-TOLE Trial)
- Planning indication expansion in other neurological indications

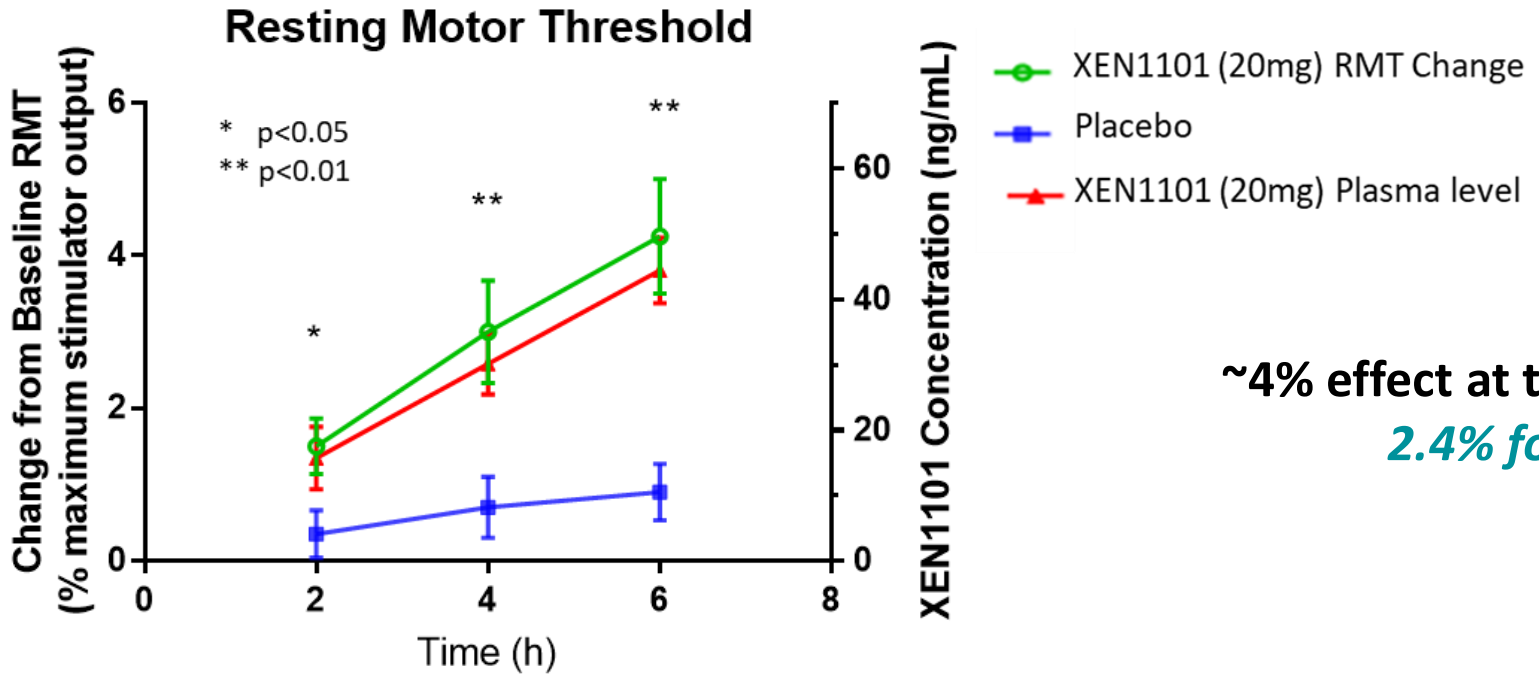
XEN1101: Anti-Seizure Activity vs Retigabine

- Maximal Electroshock Stimulus (MES) using 60 Hz bipolar stimulus with CF-1 mice
- Oral dosing, plasma concentration at time of efficacy measure.
  - Data binned by [plasma]
- XEN1101 16-fold more potent than retigabine
- 40% seizure reduction in humans (placebo, 16%) with plasma concentration of 3 µM retigabine (Gunthorpe, 2012).



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

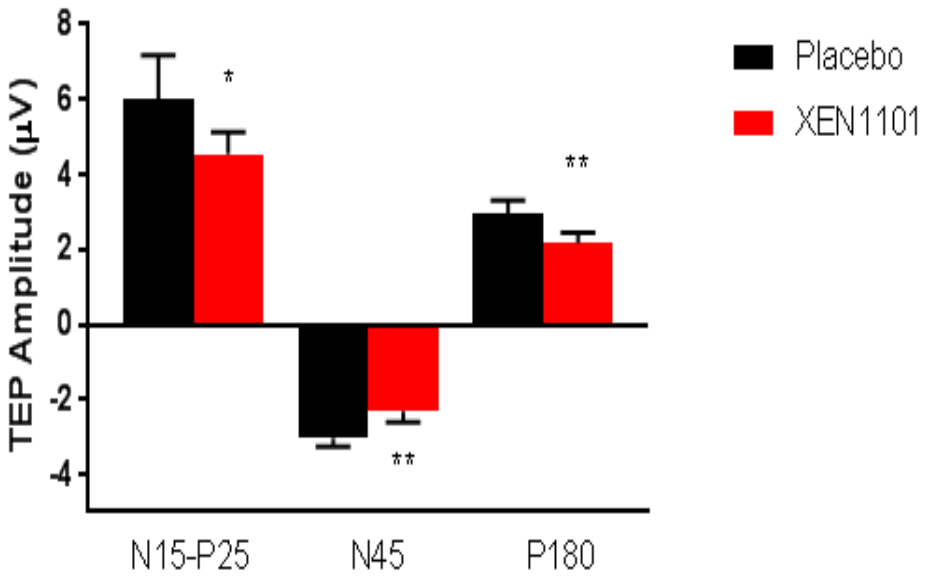


~4% effect at t=6 hours vs placebo

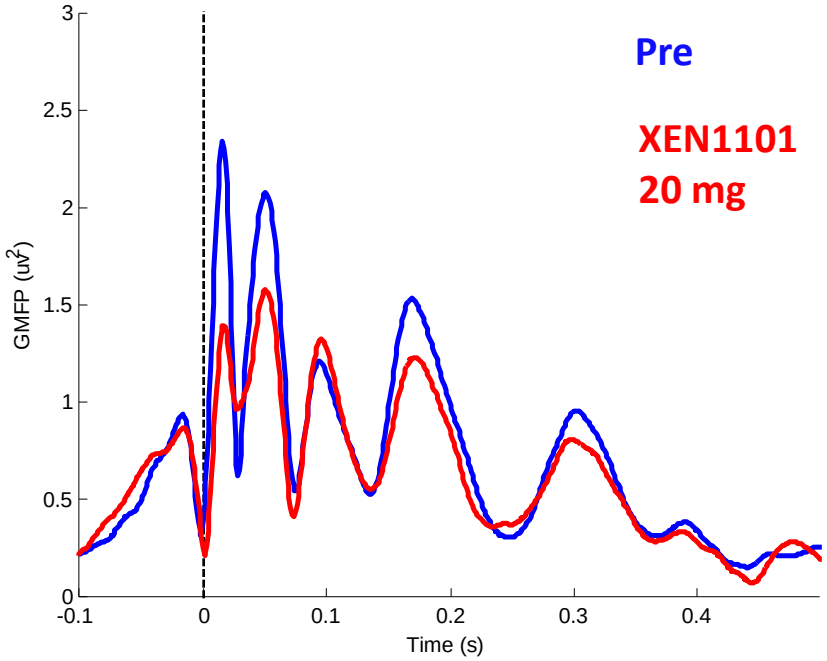
2.4% for retigabine

TMS-EEG: XEN1101 Reduced Cortical Excitability

TMS evoked potentials (TEPs)



Global Mean Field Power (GMFP)



Effects shown at time of maximum XEN1101 plasma level (~45 ng/mL) during assessments compared to time matched placebo.

- XEN1101 suppressed cortical excitability as evidenced by decreased TEP amplitudes and reduction in GMFP (XEN1101 reduced the overall amount of electrical activity induced by TMS)

XEN1101 Phase 2b Clinical Trial Underway

- Phase 2b clinical trial (called the X-TOLE Study) underway 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
  - Patient enrollment underway in U.S., Canada and Europe
  - Blinded safety data shows XEN1101 is well-tolerated
  - The rate of discontinuations in study are lower than modeled
  - To date, ~90% of subjects from double-blind portion have rolled into open-label extension
- Topline data expected in 1H:2021*

*Guidance is dependent upon feedback from the clinical sites and patient enrollment rates given the ongoing COVID-19 pandemic.

Summary

- Xenon has two potassium channel modulators for the treatment of epilepsy in late clinical development

XEN496

- Initiation of Phase 3 clinical trial in pediatric KCNQ2-DEE anticipated in 2020*

XEN1101

- Phase 2b X-TOLE Study in adult focal seizures ongoing in Canada, U.S. and Europe
- Top-line results anticipated in 1H:2021*
- Planning indication expansion for XEN1101

*Guidance given is dependent upon patient enrollment rates and/or the ability to initiate clinical sites given the ongoing COVID-19 pandemic.

For more information:

investors@xenon-pharma.com