Corporate Overview

MARCH 2021

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, FX301, 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, FX301, 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 expansion of the X-TOLE clinical trial and the anticipated timing of the topline data therefrom; the progress and potential of our other ongoing development programs; the potential receipt of milestone payments and royalties from our collaborators; and the timing of potential publication or presentation of future clinical data.

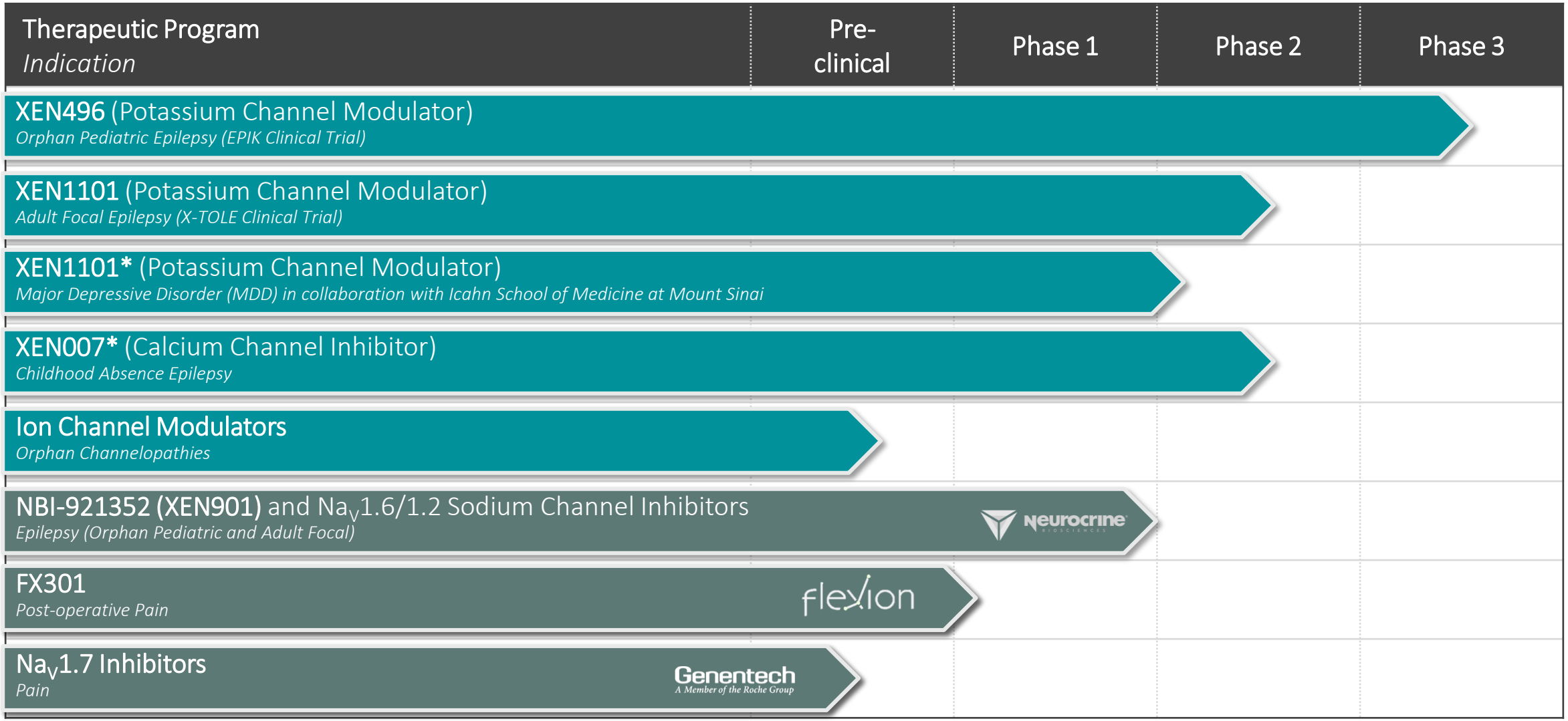
These statements are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many factors, including but not limited to: the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; 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 impose additional requirements or delay the initiation of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators' clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; impact of new or changing laws and regulations; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission and the securities commissions in British Columbia, Alberta and Ontario. Except as required by law, we assume no obligation and do not intend to update these forward-looking statements or to conform these statements to actual results or to changes in our expectations.

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
- Multiple mid- to late-stage clinical trials underway or being initiated in the near term
- Financial position as of Dec. 31, 2020
  - $177.0M in cash, cash equivalents and marketable securities
  - 35,012,125 common shares and 1,016,000 preferred shares
- Completed $115M public offering in March 2021
  - 5,135,135 shares at $18.50

Xenon's Ion Channel, Neurology-Focused Pipeline



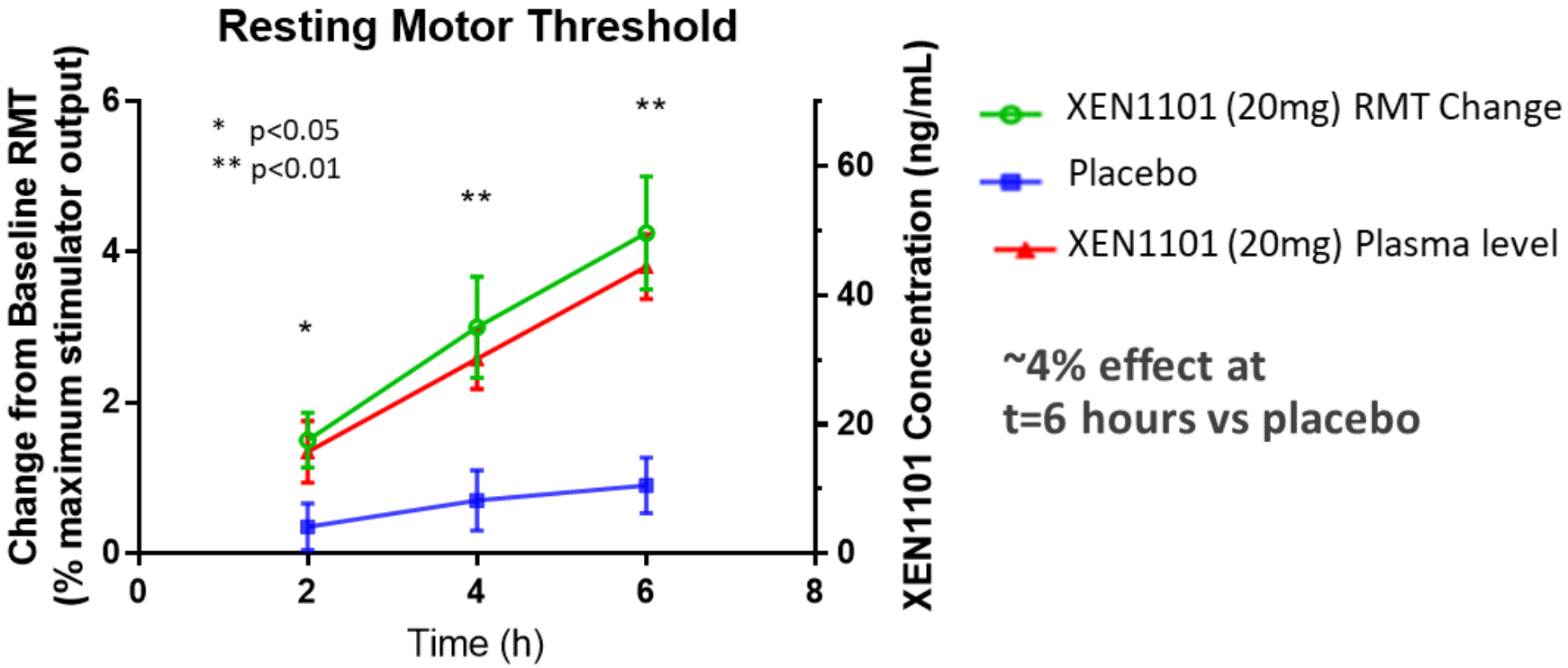
*Investigator Sponsored Phase 2 Proof-of-Concept Study

XEN1101: Potential "Next-Gen" K_V7 Channel Modulator

- Same proven MOA in adult focal seizures as ezogabine, but with potential 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 pigmented dimers and no predicted discoloration liability
- Phase 1 studies completed
  - 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
  - Robust TMS signal in Phase 1b study
- 300-patient Phase 2b "X-TOLE" clinical trial underway in Adult Focal Epilepsy
- Xenon is exploring the development of XEN1101 in major depressive disorder and other neurological indications

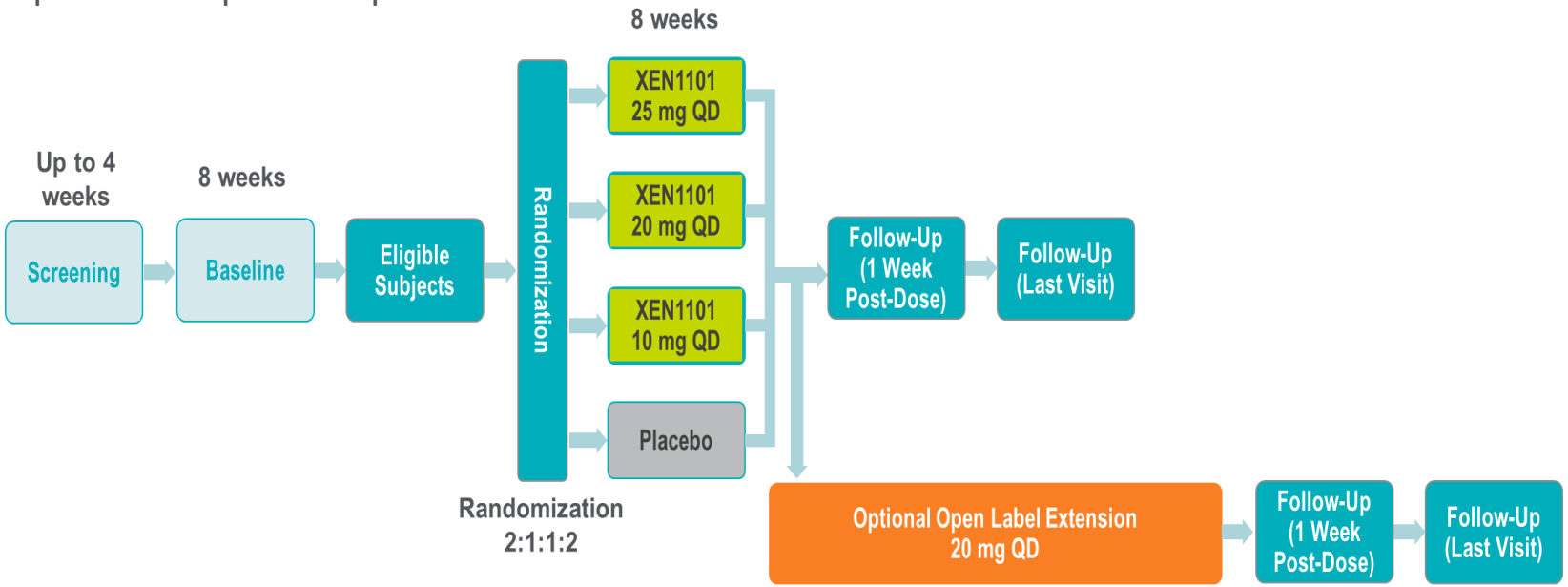
Summary of XEN1101 Phase 1b TMS Results

- 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



X-TOLE Phase 2b Clinical Trial Underway

- X-TOLE Study: Randomized, placebo-controlled Phase 2b clinical trial 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: median percent change (MPC) from baseline in monthly (28 days) focal seizure frequency in the 8-week double-blind treatment period compared to placebo



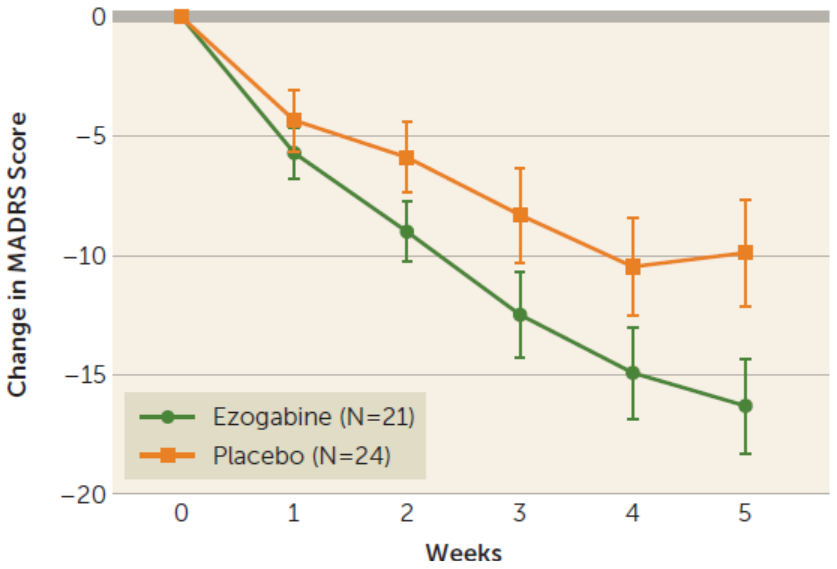
- Anticipate patient randomization will be completed in the first half of 2021, with topline data anticipated in the third quarter of 2021*

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

Other XEN1101 Indications: Phase 2 POC Study in MDD

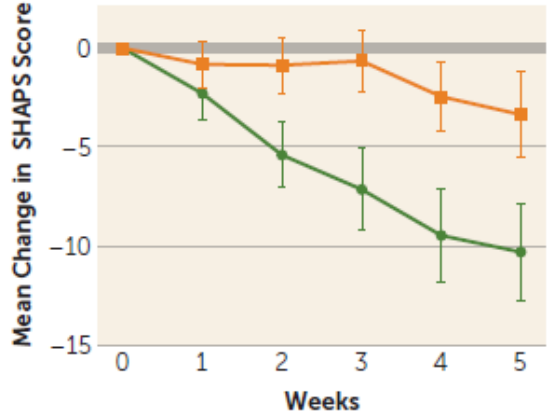
- In pre-clinical animal models, K_V7 channels mediate resilience to chronic stress related depression through blunting of VTA excitability within the reward system[1]
- Promising clinical results generated from both open-label study[2] and a randomized, placebo-controlled clinical trial[3] that explored the targeting of KCNQ channels as a treatment for MDD using ezogabine
- With academic collaborators at the Icahn School of Medicine at Mount Sinai, Phase 2 proof-of-concept clinical trial will study XEN1101 in major depressive disorder and anhedonia

Montgomery–Åsberg Depression Rating Scale



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

Snaith-Hamilton Pleasure Scale



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

[1] Mazarati, Brain 2008; Pineda, Epilepsia 2010; Sankar, Jasper's Basic Mechanisms of the Epilepsies 2012; Chen, Frontiers in Behavioural Neuroscience 2016; Medel-Matus, Epilepsia 2017; Boldt, Epilepsy & Behavior 2021.

[2] Tan et al 2018.

[3] 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.

Potential "Precision Medicine" Treatment of KCNQ2-DEE

- Severe neurodevelopmental disorder caused by dominant negative missense mutations in the KCNQ2 that presents during first week of life
- Recent epidemiology study from Europe reported KCNQ2 birth rate of ~1 in 17,000[1]

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 after) • 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

Summary of Published Case Reports of KCNQ2-DEE Patients Treated with Ezogabine

"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

[1]Symonds et al. "Incidence and phenotypes of childhood-onset genetic epilepsies: a prospective population-based national cohort." *Brain*, August 2019.

XEN496 Overview: Phase 3 Trial Initiated

- XEN496 is a pediatric-specific, granule formulation of ezogabine to be presented as sprinkle capsules
- Previously approved by FDA with MOA that potentiates K_V7-mediated potassium current
- Proven mechanism in adult focal seizures
- Potential for precision medicine approach to treat KCNQ2-DEE pediatric epilepsy
- Received Fast Track designation and Orphan Drug Designation for XEN496 for the treatment of seizures associated with KCNQ2-DEE from the FDA, as well as an orphan medicinal product designation from the European Commission

- A Phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter clinical trial, called the “EPIK” study has been initiated
  - To evaluate the efficacy, safety, and tolerability of XEN496 administered as adjunctive treatment in approximately 40 pediatric patients aged one month to less than 6 years with KCNQ2-DEE
  - Primary endpoint: the percent change from baseline in monthly countable motor seizure frequency during the blinded treatment period, as recorded by caregivers in a daily seizure diary

XEN007: Calcium Channel Modulator

- XEN007: active ingredient flunarizine
  - CNS calcium channel modulator (Cav2.1 and T-type calcium channels)
  - ~30 years' clinical use, including pediatrics; never developed in the U.S.
- Various development strategies and potential indications for XEN007 are under consideration

About Childhood Absence Epilepsy (CAE)

- CAE affects ~10-17% of children with epilepsy; onset generally between 4 to 10 years old, with a peak at 5 to 7 years old
- Characterized by an abrupt impairment of awareness with arrest in behaviour, staring, eye lid fluttering, and automatisms associated with generalized 3 Hz spike wave discharges (SWDs) on EEG
- Child may have one or many (up to 100) absence seizures per day and have problems with attention and learning

Orphanet; epilepsy.com; Killory et al., 2011; Shinnar et al., 2015; Masur et al., 2013

Physician-Led Phase 2 POC Study in CAE Underway

*Examining XEN007 as an adjunctive treatment in **pediatric patients** diagnosed with treatment-resistant **childhood absence epilepsy***

- Promising interim data collected from a small number of patients was presented at AES2020 in December 2020
- Topline results from a larger data set expected to be available in 2H:2021

Collaboration with Neurocrine Biosciences

NBI-921352 (formerly XEN901)

- Neurocrine Biosciences has exclusive license to XEN901 (now called NBI-921352) and other pre-clinical, selective $Na_V1.6$ inhibitors and dual $Na_V1.2/1.6$ inhibitors for development
- NBI-921352 is a clinical stage selective $Na_V1.6$ sodium channel inhibitor with potential in SCN8A-DEE and other forms of epilepsy
- Anticipate initiation of Phase 2 trial with NBI-921352 in adolescent patients in Q3:2021
  - The trial protocol will be amended to include younger pediatric patients (aged 2-11 years) with SCN8A-DEE as soon as the FDA has reviewed and approved additional non-clinical information
- In parallel, Neurocrine is advancing clinical plans to develop NBI-921352 for the treatment of adult focal epilepsy and expects to initiate a Phase 2 trial in 2021
  - Upon IND or equivalent regulatory acceptance for NBI-921352 in adult focal epilepsy, Xenon is eligible to receive a $10.0M milestone payment; upon FDA acceptance of a protocol amendment for NBI-921352 in pediatric patients (aged 2-11 years) with SCN8A-DEE, Xenon is eligible to receive a $25.0M milestone payment, or a $15.0M milestone payment if the IND acceptance for adult focal epilepsy occurs first. Both milestone payments are in the form of 45% cash and a 55% equity investment in Xenon at a 15% premium to Xenon's 30-day trailing volume weighted average price at that time

Neurocrine BIOSCIENCES

About SCN8A Developmental and Epileptic Encephalopathy (SCN8A-DEE)

- Rare form of early-onset epilepsy with occurrence of **seizures** beginning in the first 18 months of life
- **Physical and psychological symptoms** include recurrent seizures of all types, developmental delays, learning difficulties, muscle spasms, poor coordination, sleep problems, and autistic-like features
- **No approved treatments**

Collaboration with Flexion Therapeutics

FX301 (formerly XEN402)

- In September 2019, we entered into an agreement providing Flexion with the global rights to develop and commercialize XEN402, now known as FX301, a $Na_V1.7$ inhibitor
- Flexion's FX301 program consists of XEN402 formulated for extended release from a thermosensitive hydrogel
- Initial development of FX301 is intended to support administration as a peripheral nerve block for control of post-operative pain
- In February 2021, the FDA cleared an IND for FX301, resulting in a $1.0M milestone payment due to Xenon
- Flexion anticipates initiating a Phase 1b proof-of-concept clinical trial of popliteal fossa block with FX301 in patients undergoing bunionectomy in the first half of 2021
- Topline results could potentially be available in late 2021
- Pursuant to the terms of the agreement, we are eligible to receive up to an additional $7.0M in milestone payments through initiation of a Phase 2 clinical trial

Multiple Catalysts & Value-Creating Milestone Opportunities

XEN1101

- Phase 2b clinical trial (X-TOLE study) in adult focal seizures ongoing in Canada, U.S. and Europe
- Patient randomization to be completed in 1H:2021; topline results anticipated in Q3:2021
- Announced investigator-sponsored Ph2 POC in MDD with collaborators at Mount Sinai

XEN496

- Phase 3 clinical trial (EPIK study) in pediatric KCNQ2-DEE initiated

XEN007

- Physician-led Phase 2 open label study in CAE; topline results expected in 2H:2021

Partnered Programs

NBI-921352 (XEN901) / Neurocrine Biosciences

- Neurocrine anticipates initiation of Phase 2 clinical trial(s) in 2021, triggering cash + equity investment milestone payment

FX301 / Flexion Therapeutics

- FX301 expected to enter a Phase 1b POC clinical trial in 1H:2021, with topline results anticipated in late 2021

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