CORPORATE OVERVIEW

NOVEMBER 2021

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, including, but not limited to, statements regarding the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN496, XEN1101, 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 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, 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, and other proprietary development programs; the timing and results of our interactions with regulators; 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 efforts to enhance our intellectual property portfolio 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.

Xenon Overview

- Neurology-focused biopharma company
  - A leader in small molecule, ion channel drug development
- Multiple mid- to late-stage clinical trials underway
  - Announced positive topline data from Phase 2b X-TOLE clinical trial (Oct. 2021)
- Strong financial position
  - $249.6 million in cash, cash equivalents and marketable securities (as of Sept. 30, 2021)
    - Subsequent to quarter-end, raised $324.3 million, net of underwriting discounts and commissions but before operating expenses, in an underwritten public offering

Xenon's Ion Channel, Neurology-Focused Pipeline

Therapeutic Program *Indication*	Pre-clinical	Phase 1	Phase 2	Phase 3
XEN496 (Potassium Channel Opener) *Orphan Pediatric Epilepsy (EPIK Clinical Trial)*				
XEN1101 (Potassium Channel Opener) *Adult Focal Epilepsy (X-TOLE Clinical Trial)*				
XEN1101* (Potassium Channel Opener) *Major Depressive Disorder (MDD) / Mount Sinai Collaboration*				
XEN1101 (Potassium Channel Opener) *Major Depressive Disorder (MDD)*				
Ion Channel Modulators *Orphan Channelopathies*				
NBI-921352 (XEN901) *Rare Pediatric Epilepsy: SCN8A-DEE / Neurocrine Biosciences*				
NBI-921352 (XEN901) *Focal-Onset Seizures in Adults / Neurocrine Biosciences*				
FX301 (Topical $Na_V1.7$ Inhibitor) *Post-operative Pain / Flexion Therapeutics*				

*Investigator Sponsored Phase 2 Proof-of-Concept Study

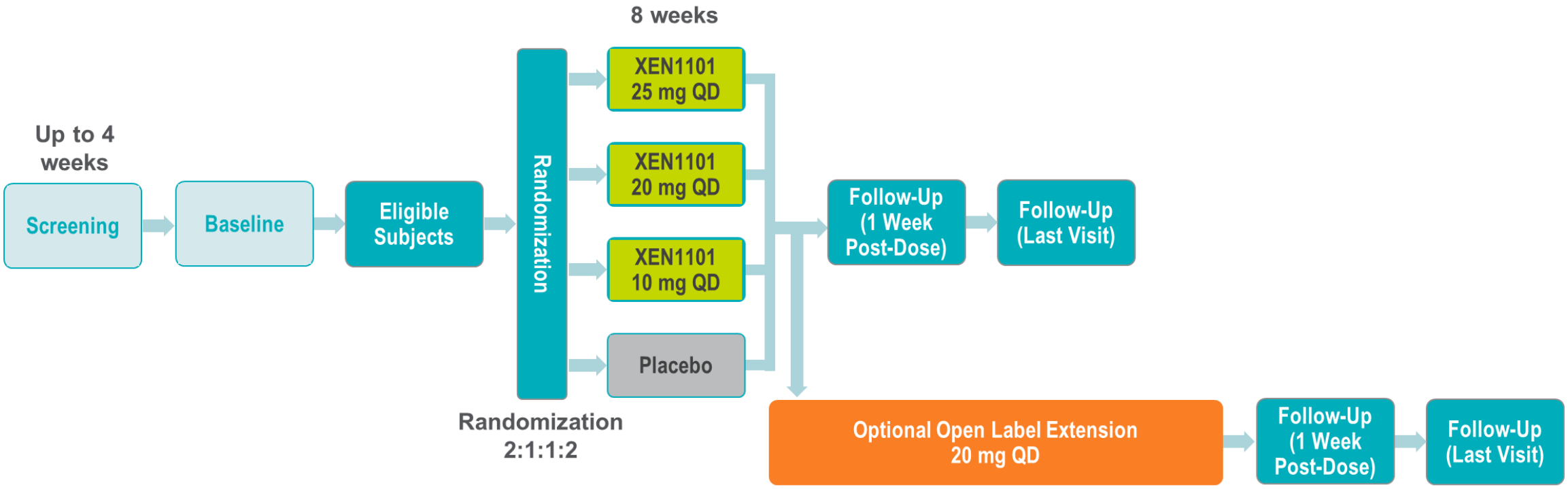
Topline Results from XEN1101 “X-TOLE” Phase 2b Clinical Trial

ANNOUNCED ON OCTOBER 4, 2021

Executive Summary

Summary of Key Findings	• X-TOLE primary efficacy endpoint with XEN1101 demonstrated a statistically significant dose-dependent reduction from baseline in monthly focal seizure frequency when compared to placebo (monotonic dose response; p<0.001) • The median percent reduction in monthly focal seizure frequency was 52.8% (2-sided p-value <0.001) in the XEN1101 25 mg group, 46.4% (2-sided p-value <0.001) in the XEN1101 20 mg group, and 33.2% (2-sided p-value = 0.035) in the XEN1101 10 mg group compared to 18.2% in the placebo group
Efficacy	• Efficacy demonstrated in X-TOLE suggests a highly CNS-active profile for XEN1101, meeting statistical significance in reduction from baseline in monthly focal seizure frequency compared to placebo and 50% reduction in monthly focal seizures versus placebo in all dosing groups • XEN1101 demonstrated clear and statistically significant dose response with consistency across endpoints • Statistically significant improvements in CGI-C and PGI-C were demonstrated for the 25 mg group
Safety / Tolerability	• XEN1101 was generally well-tolerated in this study with adverse events consistent with other commonly utilized ASMs • The most common treatment-emergent adverse events across all XEN1101 dose groups were dizziness, somnolence, fatigue, and headache • No TEAEs of pigmentary abnormalities reported during the double-blind phase of the study or in preliminary analysis during the ongoing open label extension to date with approximately 70 subjects now treated more than 12 months
Commercial Outlook / Next Steps	• The outcome of X-TOLE suggests that XEN1101 offers a clinical profile that could be highly competitive in the future adult focal seizure market • XEN1101 has the potential to offer compelling efficacy that when combined with other desirable attributes such as QD dosing, no titration, and broad-spectrum activity could make XEN1101 a highly attractive agent in the future adult focal epilepsy landscape

XEN1101 “X-TOLE” Phase 2b Study Design



Primary / Secondary Objectives of X-TOLE Study

A Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Safety, Tolerability, and Efficacy of XEN1101 as Adjunctive Therapy in Focal-onset Epilepsy, with an Open-label Extension

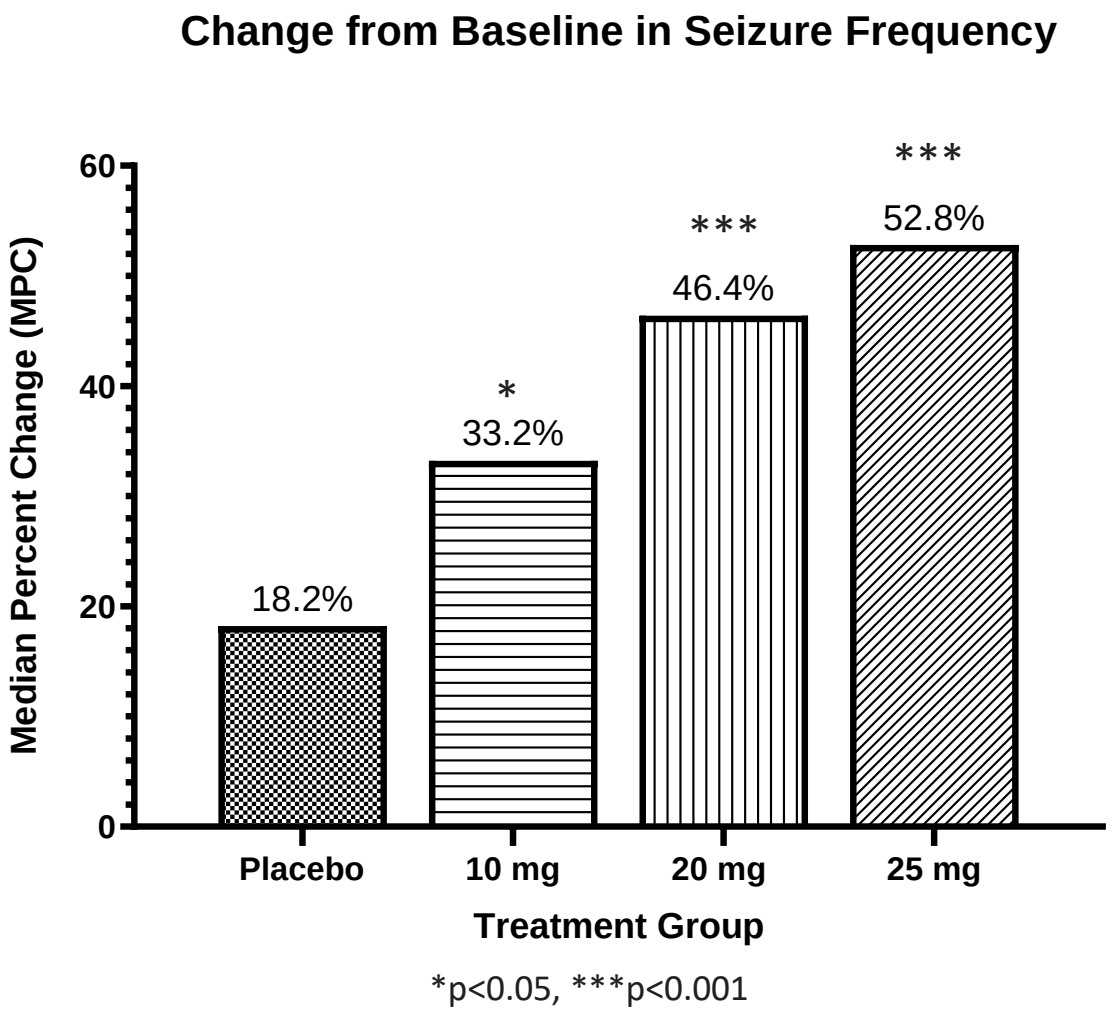
	OBJECTIVES	ENDPOINTS
Primary Objectives	To assess the efficacy of XEN1101 compared to placebo on focal seizure frequency in adults with focal epilepsy taking 1 to 3 ASMs in the double-blind period (DBP)	• Median percent change (MPC) in monthly (28 days) focal seizure frequency from baseline to DBP for XEN1101 versus placebo
	To assess the safety and tolerability of XEN1101 in adults with focal epilepsy taking 1 to 3 ASMs in the DBP	In the DBP: • Severity and frequency of associated adverse events (AEs)/serious adverse events (SAEs) • Clinically significant changes in clinical laboratory findings • Clinically significant changes in 12-lead ECG • Change in suicidality risk as assessed by the C-SSRS including increase in suicidal thoughts or an attempt • Clinically significant changes in vital signs including blood pressure, pulse, or weight • Clinically significant changes in urological symptoms including retention as measured by the American Urological Association (AUA) Symptom Index
Secondary Objectives	To evaluate the 50% XEN1101 response rates in comparison to placebo in the DBP	• Responders are defined as patients experiencing ≥50% reduction in monthly (28 days) focal seizure frequency from baseline compared to DBP
	To evaluate trends in focal seizure frequency over time in the DBP	• Percent change from baseline in weekly focal seizure frequency for each week of the DBP
	To assess the effect of XEN1101 vs placebo on seizure severity and impact in adults with focal epilepsy taking 1 to 3 ASMs in the DBP	• Clinical Global Impression of Change (CGI-C) and Patient Global Impression of Change (PGI-C) scores during the DBP

Demographics and Baseline Characteristics (Safety Population)

	Placebo (N=114)	XEN1101 10mg (N=46)	XEN1101 20mg (N=51)	XEN1101 25mg (N=114)	TOTAL (N=325)
Age in years, Mean (SD)	**42.9 (13.7)**	**40.0 (12.1)**	**41.7 (13.6)**	**38.7 (13.1)**	**40.8 (13.3)**
Age at study entry category					
≥ 65, n (%)	**5 (4.4)**	**2 (4.3)**	**4 (7.8)**	**1 (0.9)**	**12 (3.7)**
< 65, n (%)	**109 (95.6)**	**44 (95.7)**	**47 (92.2)**	**113 (99.1)**	**313 (96.3)**
Gender					
Female, n (%)	**61 (53.5)**	**27 (58.7)**	**26 (51.0)**	**54 (47.4)**	**168 (51.7)**
Male, n (%)	**53 (46.5)**	**19 (41.3)**	**25 (49.0)**	**60 (52.6)**	**157 (48.3)**
Region					
Europe, n (%)	**67 (58.8)**	**31 (67.4)**	**32 (62.7)**	**68 (59.6)**	**198 (60.9)**
North America, n (%)	**47 (41.2)**	**15 (32.6)**	**19 (37.3)**	**46 (40.4)**	**127 (39.1)**
Background ASM Use					
1, n (%)	**12 (10.5)**	**4 (8.7)**	**2 (3.9)**	**11 (9.6)**	**29 (8.9)**
2, n (%)	**46 (40.4)**	**18 (39.1)**	**20 (39.2)**	**47 (41.2)**	**131 (40.3)**
3, n (%)	**56 (49.1)**	**24 (52.2)**	**29 (56.9)**	**56 (49.1)**	**165 (50.8)**
Number of Pre-study ASMs failed					
Median [Q1, Q3]	**6.0 [3.0, 8.0]**	**5.0 [4.0, 9.0]**	**6.0 [4.0, 9.0]**	**5.5 [3.0, 9.0]**	**6.0 [4.0, 9.0]**

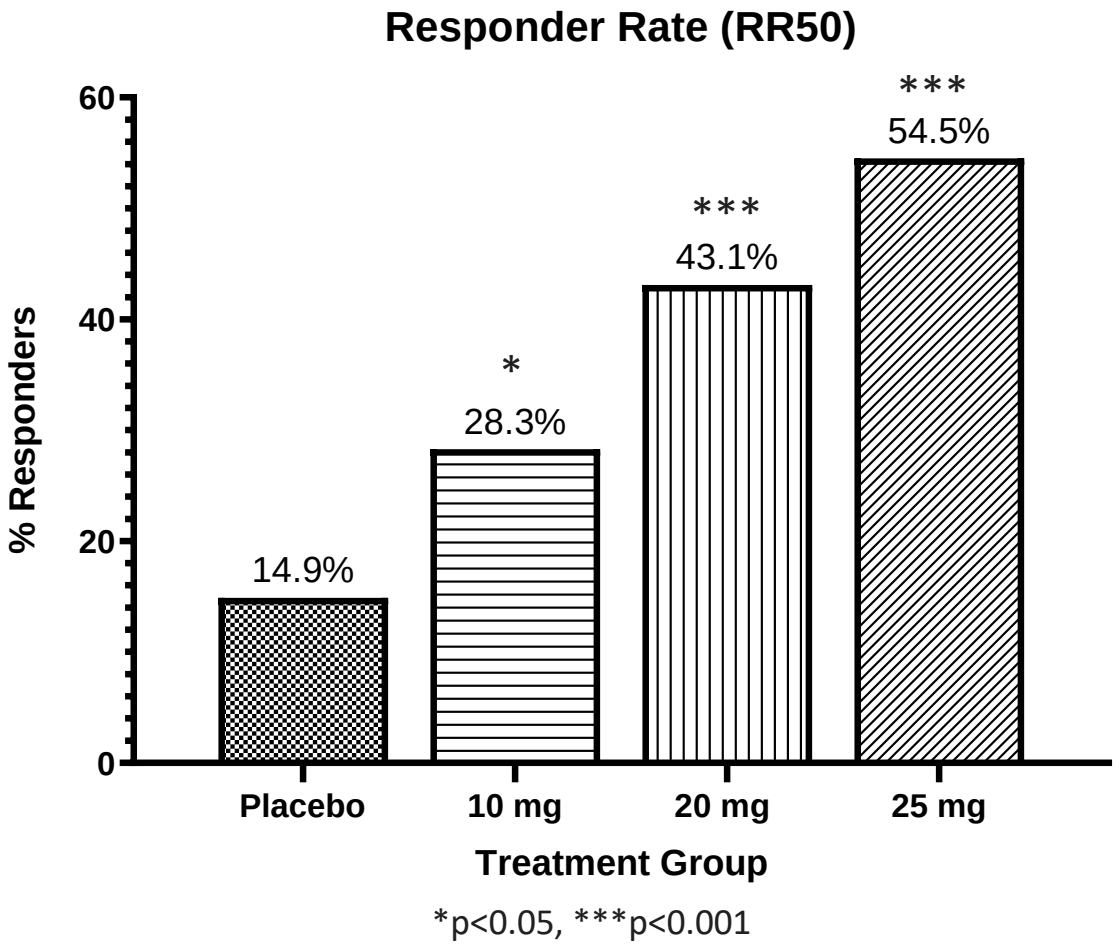
Arms well balanced and representative of a difficult to treat adult FOS patient population

Summary of Overall Efficacy Readout



- Data suggest a highly statistically significant dose-response relationship for XEN1101 in the adjunctive treatment of focal seizures in adult patients with focal epilepsy
- Primary efficacy endpoint highly statistically significant ($p<0.001$) in 20 mg and 25 mg dose groups
- Efficacy demonstrated in difficult to treat patient population with significant burden of disease
- Efficacy data signal activity of XEN1101 in the central nervous system

Secondary Endpoint: Response Rates and CGI-C/PGI-C



	XEN1101 25 mg (N=112)	Placebo (N=114)
CGI-C (Portion of Patients Much Improved or Very Much Improved)	46.4% (p<0.001)	22.8%
PGI-C (Portion of Patients Much Improved or Very Much Improved)	42.9% (p=0.001)	21.9%

Highly significant dose dependent increase in responder analysis in all dose groups and statistically significant improvements in CGI-C/PGI-C in the 25 mg dose group

Summary of All TEAEs* in the DBP (Safety Population)

Subjects with n(%)	Placebo (N=114)	XEN1101 10mg (N=46)	XEN1101 20mg (N=51)	XEN1101 25mg (N=114)	XEN1101 Any dose (N=211)
At least one TEAE	71 (62.3)	31 (67.4)	35 (68.6)	97 (85.1)	163 (77.3)
At least one serious TEAE	3 (2.6)	2 (4.3)	2 (3.9)	3 (2.6)	7 (3.3)
At least one TEAE leading to permanent treatment discontinuation	4 (3.5)	1 (2.2)	7 (13.7)	18 (15.8)	26 (12.3)
At least one serious TEAE leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

*TEAE: Treatment Emergent Adverse Event i.e. AEs started or worsened in Double Blind Phase including 6 weeks of follow-up

SAEs balanced across treatment groups

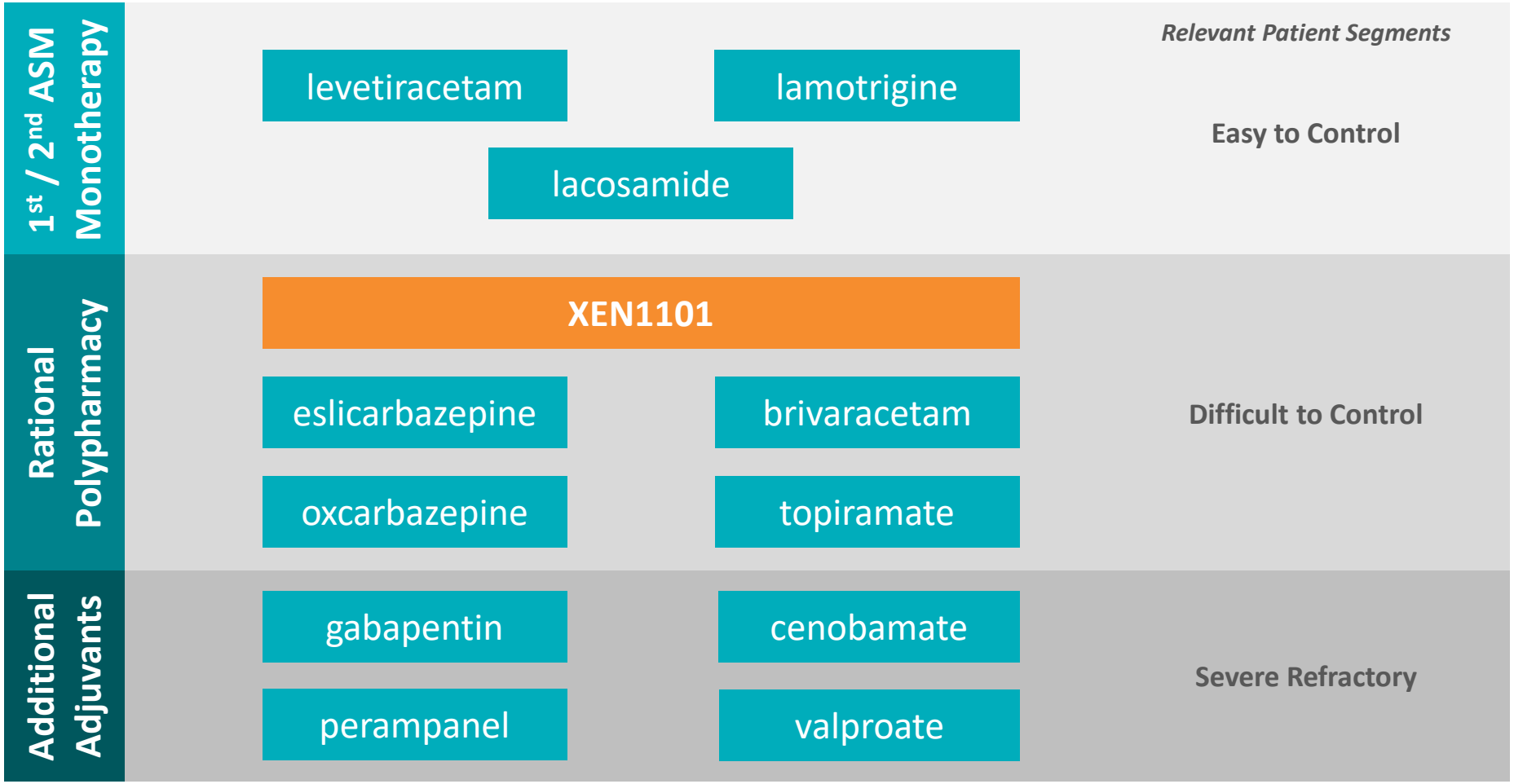
Overall Adverse Event Profile

- XEN1101 was generally well-tolerated in this study with AEs consistent with other commonly prescribed ASMs
- The most common treatment emergent adverse events across all XEN1101 dose groups were dizziness (n=52, 24.6%), somnolence (n=33, 15.6%), fatigue (n=23, 10.9%), and headache (n=21, 10.0%)
- Two TEAEs of urinary retention were reported in the active treatment groups, one of which required a dose reduction, and both subjects remained on drug with no other changes or intervention
- There have been no TEAEs of pigmentary abnormalities reported during the double-blind phase of the study or in preliminary analysis during the ongoing OLE to date
- Electrocardiogram changes were evenly balanced between placebo and active treatment groups

Safety and tolerability profile in line with commonly used ASMs

XEN1101 Clinical Positioning

Potential Future Treatment Paradigm



Source: Blinded Xenon Market Research

Summary

XEN1101 Value Proposition

Efficacy

- Compelling efficacy data in difficult to treat adult FOS patient population
- Strong combination data supporting polypharmacy use (50.8% of patients on 3 ASMs in trial)
- May provide mood benefit beyond seizure control

Ease of Use

- One pill, once-daily
- No titration required
- Unique and novel MOA can be leveraged in rational polypharmacy
- Forgiving PK provides coverage for missed doses[1]

Safety / Tolerability

- Well-tolerated with AE profile in line with other ASMs
- Evening dose results in C_{max} during sleep[1]
- No drug allergic reactions observed
- No TEAEs of pigmentary abnormalities

[1] Company Poster. 2018 American Epilepsy Society (AES) Annual Meeting: "A First-in-Human Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Pharmacodynamics of a Novel Small Molecule KV7.2/7.3 Positive Allosteric Modulator (XEN1101) in Healthy Subjects." December 3, 2018

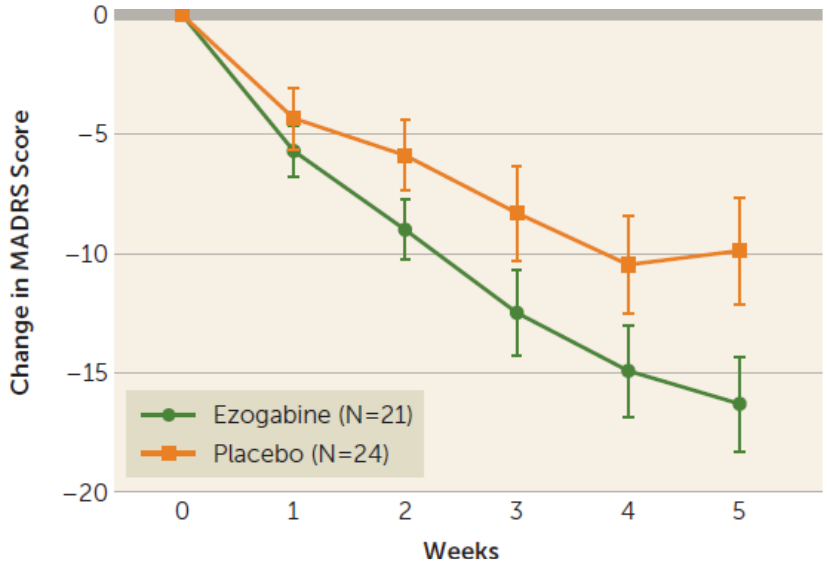
Other Proprietary and Partnered Programs

XEN1101 (MDD) | XEN496 | NBI-921352 | FX301

XEN1101 Phase 2 POC Studies in Major Depressive Disorder

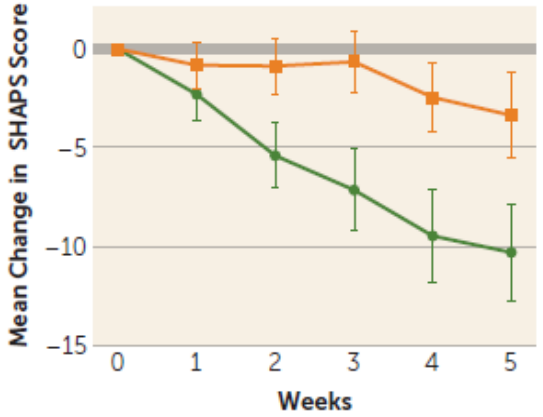
- Promising clinical results with ezogabine when targeting KCNQ channels as a treatment for Major Depressive Disorder (MDD)[1]
- Patient enrollment underway in investigator-sponsored Phase 2 proof-of-concept, multi-site, randomized, parallel-arm, placebo-controlled clinical trial of XEN1101 for the treatment of MDD with collaborators at the Icahn School of Medicine at Mount Sinai
  - ~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
- In addition, Xenon is planning a larger, company-sponsored XEN1101 clinical study in MDD; initiation anticipated in 1H:2022

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]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.

About KCNQ2-DEE

- Rare, severe neurodevelopmental disorder caused by dominant negative missense mutations in the KCNQ2 that presents during first week of life with estimated KCNQ2 birth rate of ~1 in 17,000 (Symonds et al. 2019)

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

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

Case studies suggest ezogabine is active in this often-refractory disease

XEN496: Potential Precision Medicine Approach for KCNQ2-DEE

Development of Proprietary XEN496

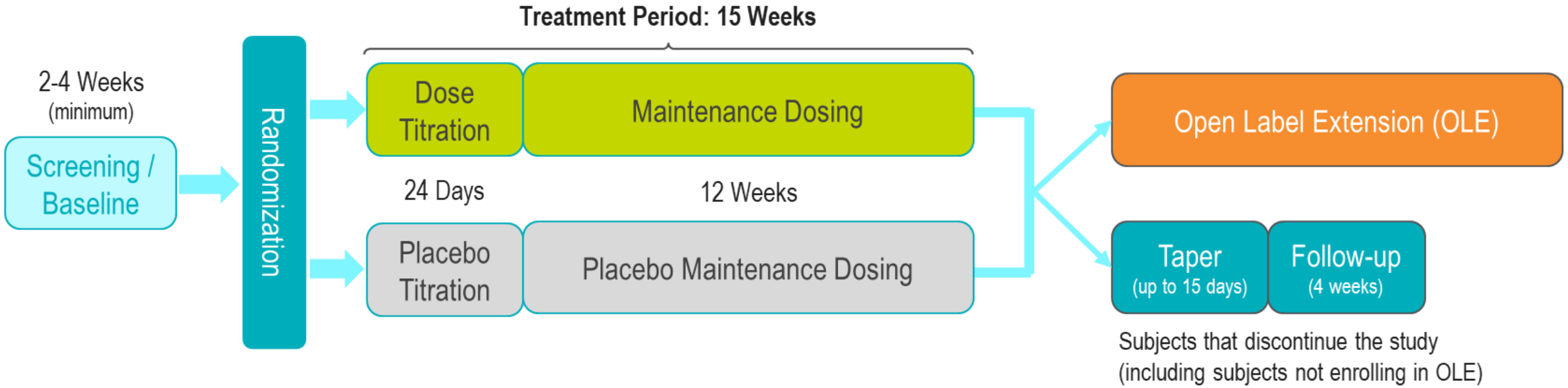
- XEN496 is pediatric-specific, granule formulation of ezogabine to be presented as sprinkle capsules
- MOA that potentiates Kv7-mediated potassium current
- Ezogabine previously approved by FDA with proven mechanism in adult focal seizures
- Potential for precision medicine approach to treat rare KCNQ2-DEE pediatric epilepsy
- Fast Track designation and Orphan Drug Designation in U.S. and Orphan Medicinal Product Designation (Europe) for KCNQ2-DEE

"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

Phase 3 Clinical Trial Underway

Primary Objective: evaluate the efficacy of XEN496 as adjunctive therapy in reducing seizure frequency from baseline, compared to placebo in pediatric subjects with KCNQ2-DEE



Study completion anticipated in 1H:2023

Partnered Programs

NBI-921352 (formerly XEN901)

- Clinical stage selective $Na_V1.6$ sodium channel inhibitor with potential in SCN8A-DEE and other forms of epilepsy
- Neurocrine Biosciences has exclusive license to NBI-921352 and other $Na_V1.6$ & dual $Na_V1.2/1.6$ inhibitors for development
- Two Phase 2 clinical trials underway in adolescent patients with SCN8A-DEE and adult patients with focal-onset seizures
- Xenon received $10M regulatory milestone in September 2021; potential for additional $15M upon FDA acceptance of a protocol amendment for NBI-921352 in pediatric patients (aged 2-11 years) with SCN8A-DEE, as well as other potential collaboration milestone payments and future sales royalties

FX301 (formerly XEN402)

- Flexion has the global rights to develop and commercialize XEN402, now known as FX301, a $Na_V1.7$ inhibitor 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
- Topline data anticipated in Q1:2022 from Phase 1b proof-of-concept clinical trial of popliteal fossa block with FX301 in patients undergoing bunionectomy
- Xenon is eligible to receive certain clinical, regulatory, and commercial milestone payments, as well as future sales royalties

Multiple Catalysts & Value-Creating Milestone Opportunities

XEN1101 (Epilepsy)

- Successful Phase 2b clinical trial (X-TOLE study) in adult focal seizures demonstrating statistical significance on primary and secondary seizure reduction endpoints, showing dose-dependent CNS activity
- End of Phase 2 meeting with FDA anticipated in Q2:22 to support Phase 3 XEN1101 clinical program in adult patients with focal epilepsy in 2H:22
- Currently evaluating other potential epilepsy indications for future development of XEN1101

XEN1101 (MDD)

- Mount Sinai investigator-sponsored Ph2 POC in MDD underway
- Plans for a larger, company-sponsored clinical study in MDD anticipated to begin in 1H:22

XEN496

- Phase 3 clinical trial (EPIK study) in pediatric KCNQ2-DEE underway; anticipated completion of study in 1H:23

Partnered Programs

NBI-921352 (XEN901) / Neurocrine Biosciences

- Two Phase 2 clinical trials underway with NBI-921352 in adult focal-onset epilepsy and pediatric SCN8A-DEE
- $10M regulatory milestone achieved in Sept. 2021 and potential $15M for next regulatory milestone

FX301 / Flexion Therapeutics

- Topline results for FX301 Phase 1b POC clinical trial anticipated in Q1:22

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