Fourth Quarter and Full Year 2024 Earnings Presentation

March 2025

Lexicon pharmaceuticals

Forward-Looking Statements

- This presentation, including any oral presentation accompanying it, contains “forward-looking statements,” including statements about Lexicon’s strategy and operating performance and events or developments that we expect or anticipate will occur in the future, such as projections of our future results of operations or of our financial condition, the potential therapeutic and commercial potential of pilavapadin (LX9211), LX9851, sotagliflozin and our other drug programs, the success of our commercialization efforts with respect to INPEFA (sotagliflozin) and any other approved products, the results of and expected timing of the completion of ongoing and future clinical trials, the expected timing and outcome of discussions with regulatory authorities regarding such trials and any applications for approval based on such trials, our other research and development efforts, and the anticipated trends in our business.
- These forward-looking statements are based on management’s current assumptions and expectations and involve risks, uncertainties and other important factors that may cause our actual results to be materially different from any future results expressed or implied by such forward-looking statements.
- Information identifying such important factors is contained in our most recent annual report on Form 10-K and quarterly reports on Form 10-Q, including the sections entitled “Risk Factors,” as well as our current reports on Form 8-K, in each case filed with the Securities and Exchange Commission.
- Lexicon undertakes no obligation to update or revise any such forward-looking statements, whether as a result of new information, future events or otherwise.

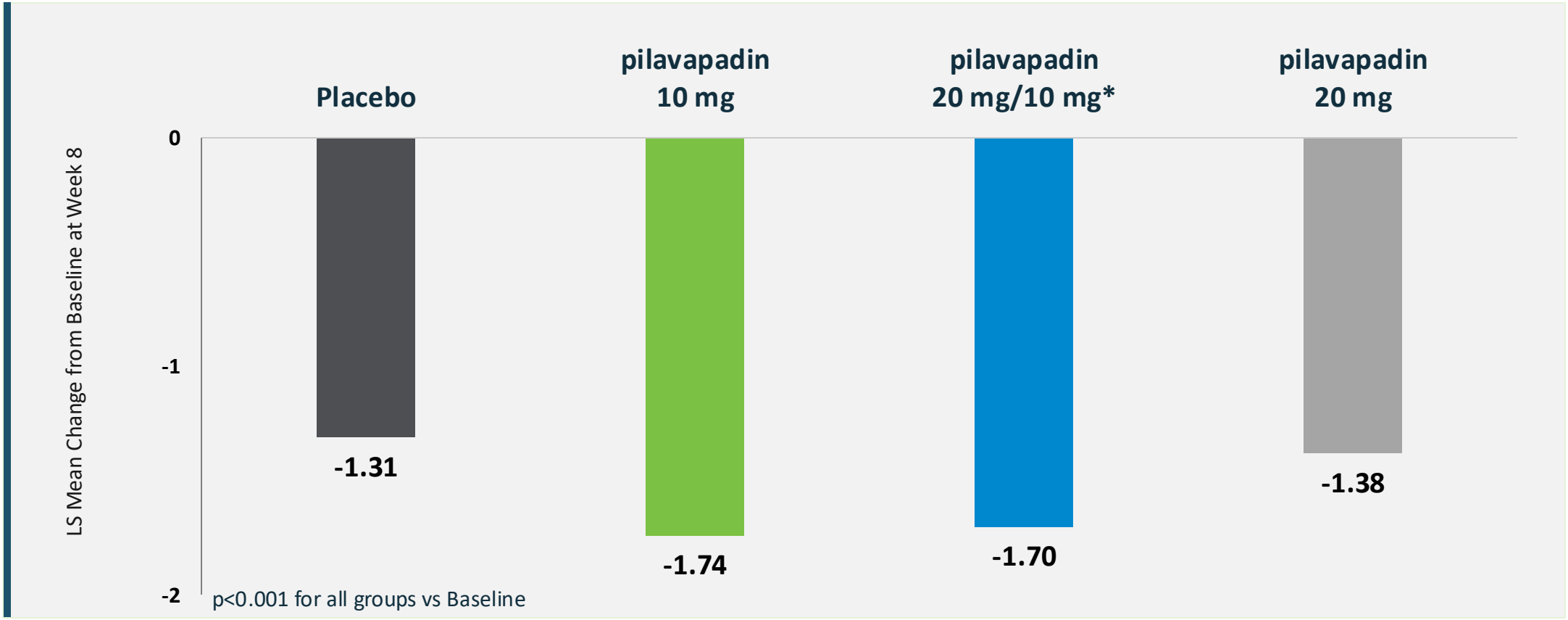
Business Overview

Mike Exton, PhD
Director and Chief Executive Officer

2024: Repositioned to focus on advancing strong R&D pipeline

- **Refocused resources where Lexicon has potential to Lead to Succeed as a clinical-development focused company**
- **Accelerated topline data readout of PROGRESS, Phase 2b dose optimization study of pilavapadin in DPNP to Q1 2025**
- **Continued enrollment in pivotal Phase 3 study of sotagliflozin in SONATA-HCM**
- **Advanced IND-enabling studies of LX9851 in obesity and related metabolic disorders**
- **Reinvigorated business development efforts, beginning with Viatris licensing agreement**

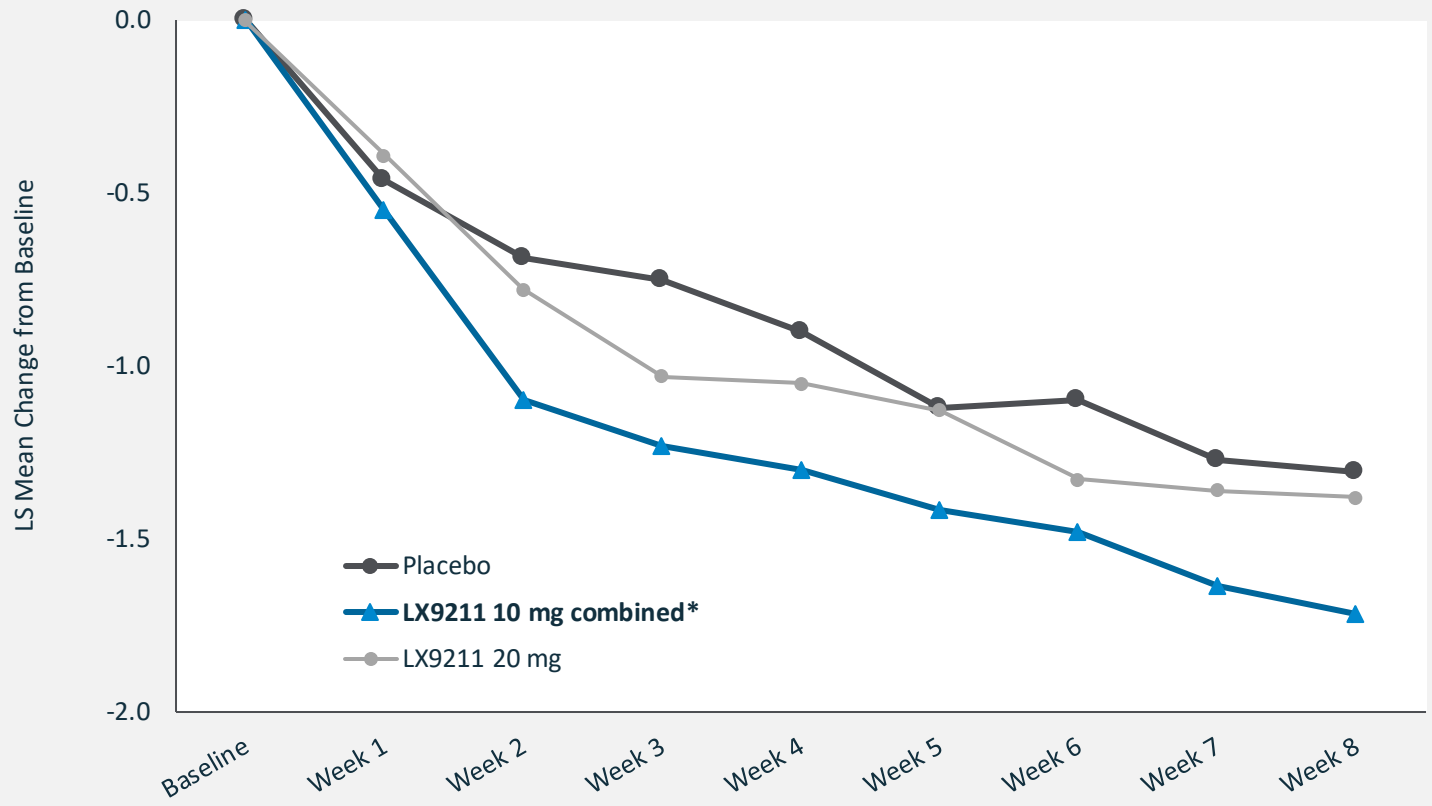
PROGRESS Phase 2b study evaluating pilavapadin (LX9211) in DPNP identified 10 mg dose as most clinically meaningful



*LX9211 20 mg for 7 days and then 10 mg thereafter

PROGRESS post-hoc analysis reaffirms 10 mg as most appropriate to advance into Phase 3 clinical development

Efficacy of pooled, 10 mg dosing arms *(post-hoc)*



Key Findings

- 10 mg dose demonstrated early and sustained separation from placebo (slide 20 Appendix)
- Post-hoc analysis of data in the 10 mg and 20+10 mg arms (without the 20 mg arm) was statistically significant (p = 0.04)

*LX9211 combined = LX9211 10 mg + LX9211 20 mg/10 mg

PROGRESS 10 mg dose had placebo-like study completion rate

	Placebo (N = 124) n (%)	10 mg (N = 123) n (%)	20 mg/10 mg (N = 124) n (%)	20 mg (N =125) n (%)	Total (N = 496)* n (%)
Number of patients completed	109 (87.9)	108 (87.8)	102 (82.3)	96 (76.8)	415 (83.7)
Number of patients discontinued	14 (11.3)	14 (11.4)	21 (16.9)	28 (22.4)	77 (15.5)

*Intent-to-treat (ITT) population: includes four patients (one in each study arm) who were randomized but never received study drug

A clear need and opportunity in the DPNP treatment landscape for new treatments

Sizable Market Opportunity for DPNP

~9 Million
U.S. patients with progressive DPNP

60%
of patients have tried multiple treatments

Majority of patients experience moderate-to-severe pain

High Unmet Need

Low Satisfaction
with current treatment options

Alternatives to Pain Act
physicians and legislators seeking non-opioids

- ✓ HCPs and patients seek pain relief balanced with tolerability and ease of use
- ✓ Potential for secondary symptom management to improve quality of life

CDC National Diabetes Statistics Report 2024. Du SH, Zheng YL, Zhang YH, Wang MW, Wang XQ. The Last Decade Publications on Diabetic Peripheral Neuropathic Pain: A Bibliometric Analysis. Front Mol Neurosci. 2022 Apr 13;15:854000. doi: 10.3389/fnmol.2022.854000. PMID: 35493329; PMCID: PMC9043347. Source: prevalence rate of DPNP in diabetics is based on primary and secondary research; DPNP: diabetic peripheral neuropathic pain

Based on pre-clinical studies, LX9851 has the potential to address unmet needs in obesity and related cardiometabolic disorders

LX9851 | First in class, potent and selective orally bioavailable, investigational small molecule ACSL5 inhibitor

Biology-based Mechanism to Address Obesity

Induces satiety

Decreases body weight

Reduces food consumption

Triggers Ileal Brake mechanism

Reduces steatosis

Potential Advantages of LX9851

- Oral agent / chronic use
- Reduction in body fat
- Improved metabolic profile
- Use alone or on top of GLPs
- Potential additional, related indications/benefits

On track for IND filling in 2025

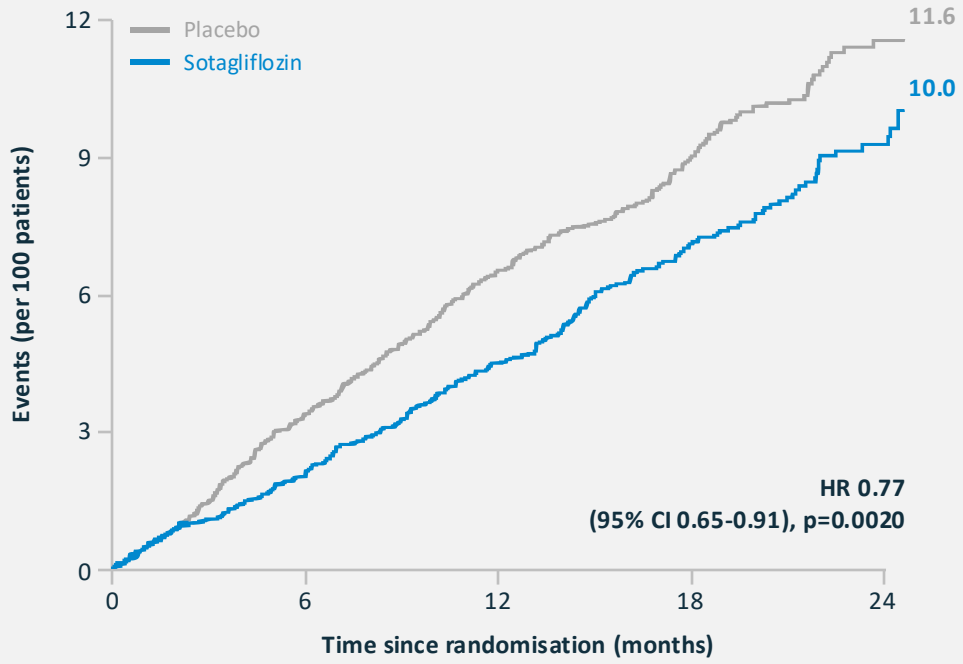
Focused on further differentiating sotagliflozin among SGLT class and maintaining a scientific presence in CV

2025 Focus: Bridging strategy to potential HCM indication

- INPEFA remains available on the market with continued commitment to maintain awareness and provide tools to support patients on therapy
- Ongoing trials designed to generate more evidence on unique CV and dual-inhibition benefits
- Ex-US, ex-EU registration and regional development by Viatris underway
- SONATA-HCM trial enrolling globally

The Lancet Diabetes & Endocrinology highlights unique efficacy benefits of sotagliflozin

Cumulative incidence of total MACE by treatment group



Number at risk (cumulative number censored)

THE LANCET
Diabetes & Endocrinology

- Reduced major adverse cardiovascular events (MACE), MI and stroke among patients with type 2 diabetes (T2D), chronic kidney disease (CKD), and high cardiovascular (CV) risk
- Benefit on both heart attack and stroke reduction
- Not demonstrated with SGLT2 inhibitors

Financial Overview

Scott Coiante
Chief Financial Officer

Q4 and FY 2024 Financial Summary

Note: $ in Millions except per share amounts

	Q4 2024	Q4 2023	FY 2024	FY 2023
Total revenues	$26.6	$.70	$31.1	$1.2
R&D	$26.7	$14.8	$84.5	$58.9
SG&A	$32.3	$32.6	$143.1	$114.0
Total operating expenses	$59.3	$47.4	$228.2	$173.0
Net loss	($33.8)	($49.8)	($200.4)	($177.1)
Net loss per common share	($0.09)	($0.20)	($0.63)	($0.80)

	As of December 31, 2024	As of December 31, 2023
Cash, cash equivalents and short-term investments	$238.0	$170.0
Total assets	$298.4	$229.4
Long-term debt	$100.3	$99.5

2025 guidance reflects significantly lower operating expenses

2H 2024 Key Financial Highlights

- Announced strategic restructuring to reduce operating costs
  - Reduction of number of employees by approximately 70 percent
  - Elimination of promotional activities for INPEFA
- Licensing agreement with Viatris for sotagliflozin for ex-U.S. and ex-EU included a $25 million upfront payment and future potential development and commercial milestones and royalties

Full Year 2025 Operating Expenses*

- Total operating expenses expected to be between $135 - $145 million
  - R&D expected between $100 - $105 million
    - Excludes clinical trial costs related to Phase 3 pivotal studies of pilavapadin
  - SG&A expected between $35 - $40 million

*As of March 6, 2025

Summary

Mike Exton, PhD
Director and Chief Executive Officer

Significant number of planned catalysts through 2025

Pipeline	Indication	Planned Catalyst 2025
Pilavapadin	• Diabetic Peripheral Neuropathic Pain	• Full PROGRESS data anticipated in Q2 • End of Phase 2 meeting planned in Q3 • Data at upcoming medical meetings, potentially including: ADA, Neuro Diab, EASD
LX9851	• Obesity and Weight Management	• IND filing in 2025 • Ongoing evaluation of potential partnerships
Sotagliflozin	• Hypertrophic Cardiomyopathy	• EU and LATAM sites enrolling • All Phase 3 study sites running by Q3
Sotagliflozin / Viatris License	• Heart Failure	• Regulatory submissions in key ex-U.S. markets in 2025

Q&A

Mike Exton, PhD

Director and Chief Executive Officer

Craig Granowitz, MD, PhD

Senior Vice President and Chief Medical Officer

Scott Coiante

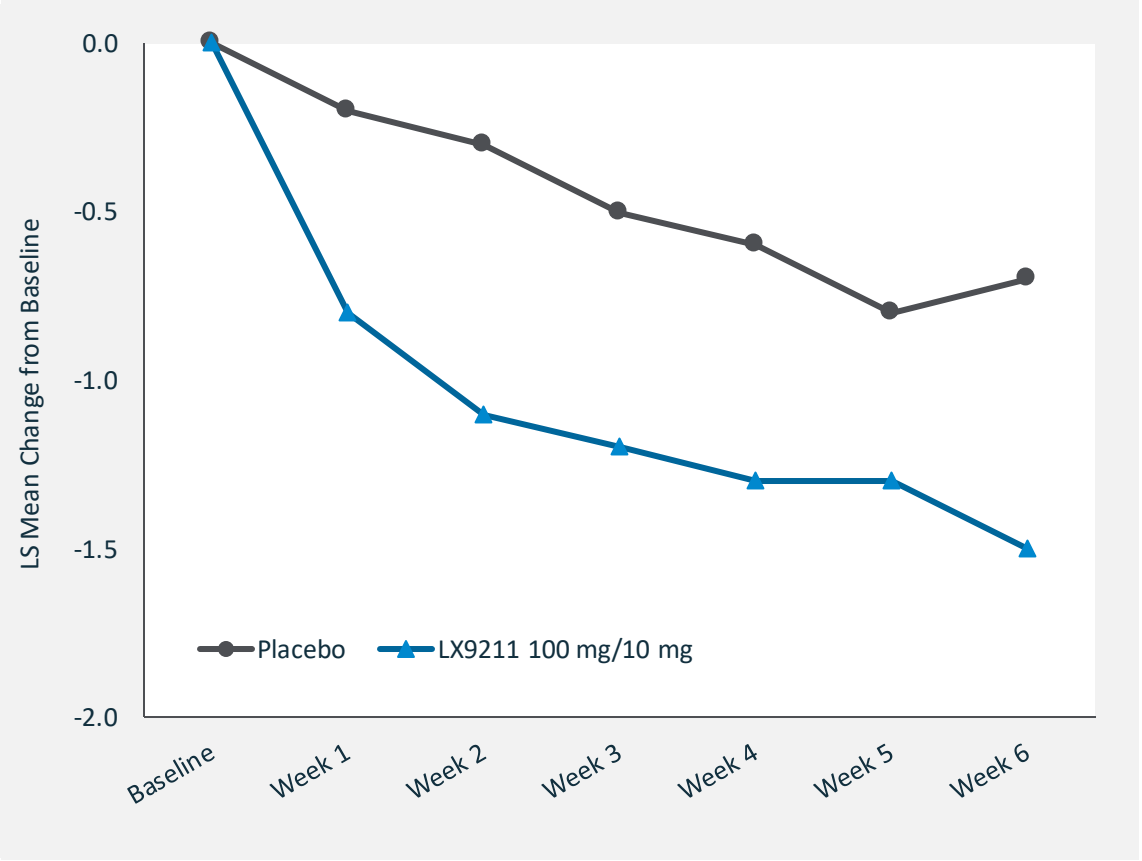
Chief Financial Officer

Thank You

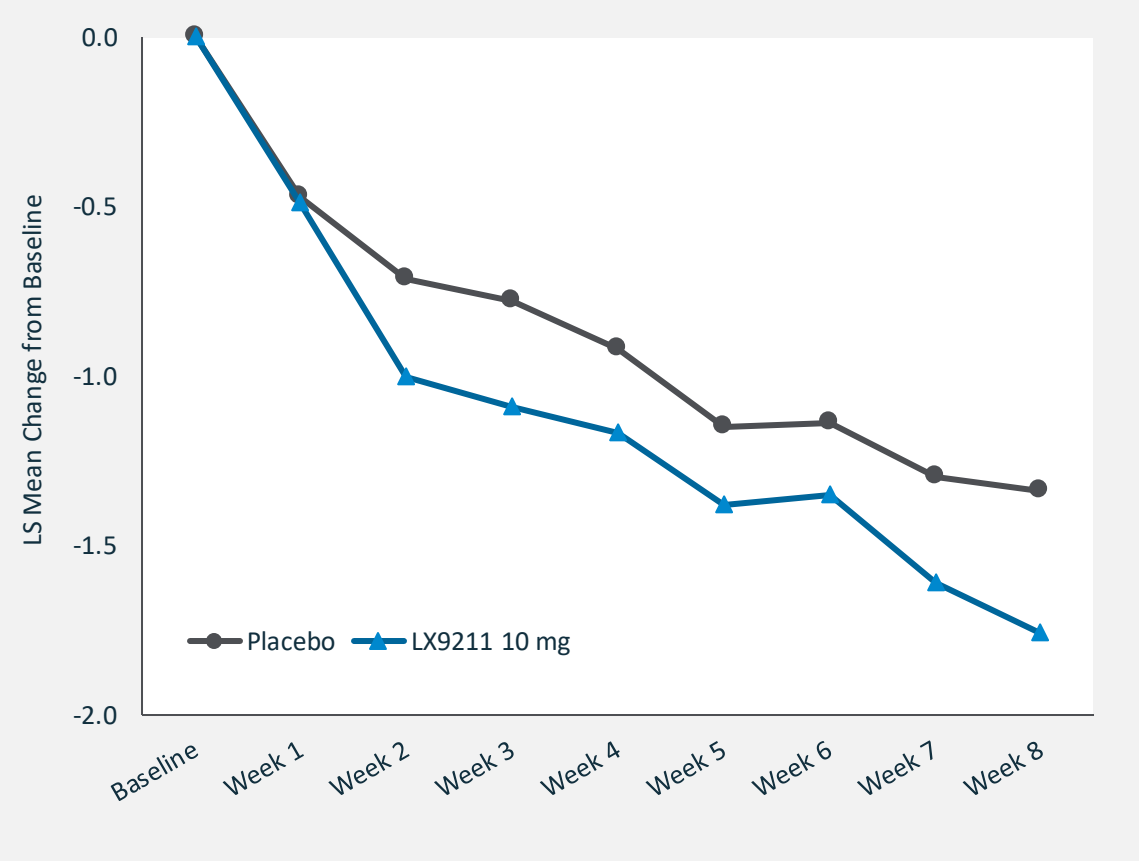
Appendix

10 mg demonstrated an early, sustained separation from placebo

RELIEF-DPN-1 Phase 2a



PROGRESS Phase 2b



*LX9211 100/10 mg: included 200 mg as day 1 loading dose
**200/20 mg: included 100 mg as day 1 loading dose

PROGRESS 10 mg dose was well-tolerated with few treatment discontinuations

	Placebo (N = 124) n (%)	10 mg (N = 122) n (%)	20 mg/10 mg (N = 122) n (%)	20 mg (N =124) n (%)	Total (N = 492)* n (%)
Subjects who discontinued who had a TEAE	2 (1.6)	9 (7.4)	14 (11.5)	22 (17.7)	47 (9.6)
Dizziness	0	3 (2.5)	1 (0.8)	5 (4.0)	9 (1.8)
Nausea	0	4 (3.3)	1 (0.8)	4 (3.2)	9 (1.8)

*Safety population: includes all patients who received study drug; excludes four patients (one in each study arm) who were randomized but never received study drug