Pilavapadin
Phase 2b PROGRESS Topline Readout

Lexicon pharmaceuticals

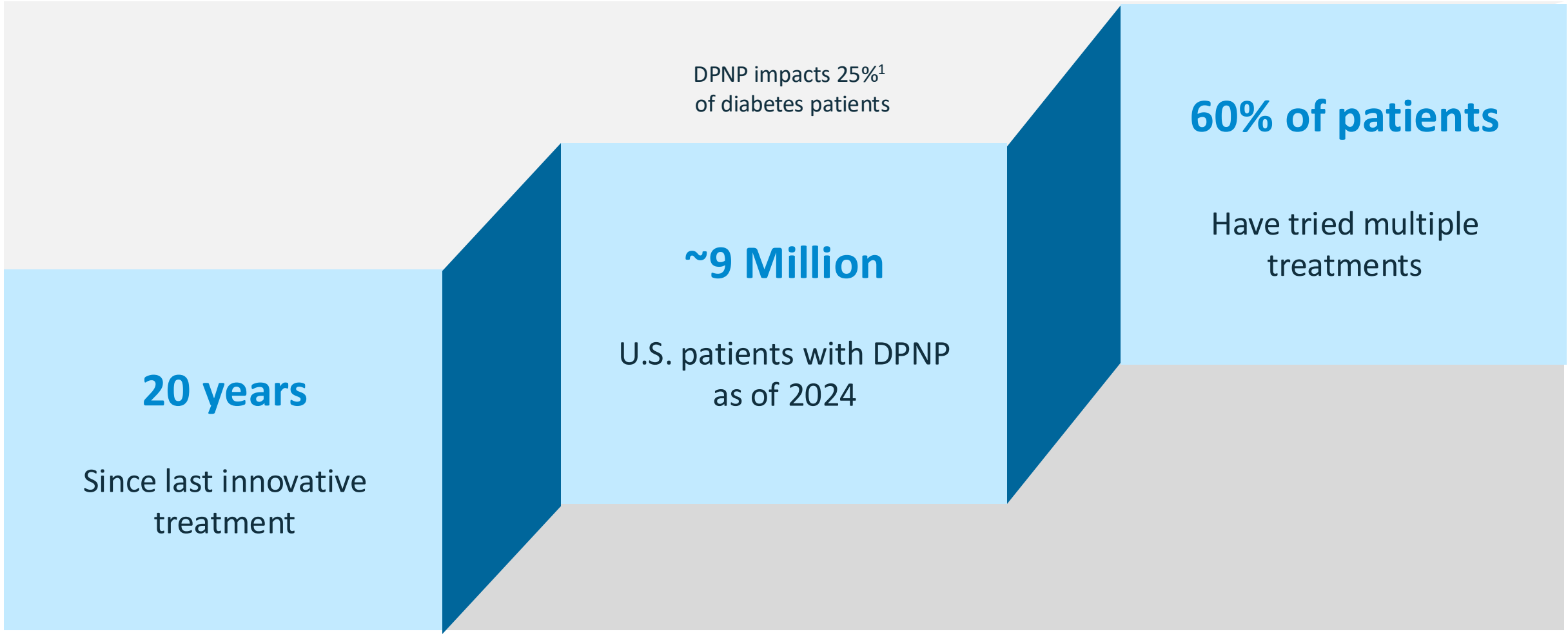
Forward-Looking Statements

- 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.

PROGRESS study met Company's objectives

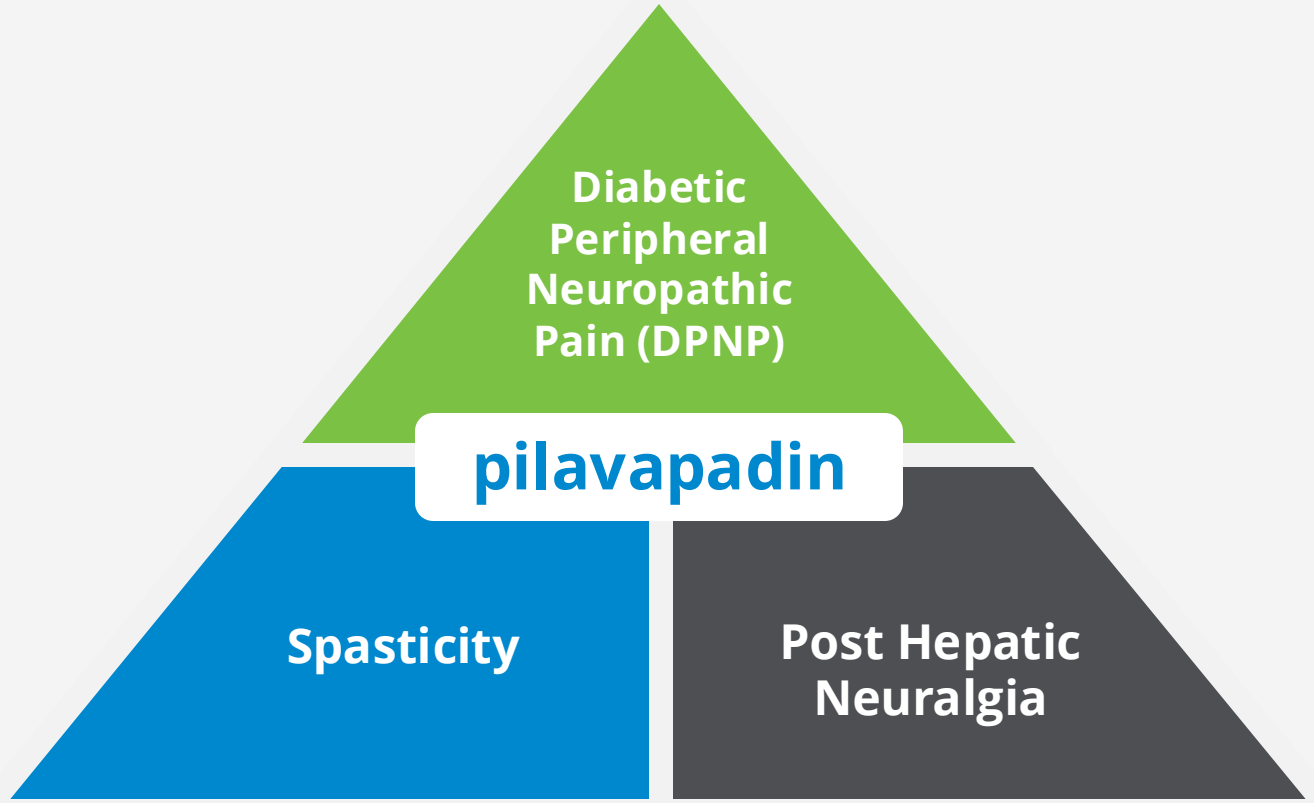
- Meaningful reduction in average daily pain score (ADPS) and separation from baseline and placebo in 10 mg dose
- 10 mg was well-tolerated and had placebo-like study completion rates
- Supports advancement of 10 mg dose into Phase 3 development

A clear need and opportunity in the DPNP treatment landscape



1) 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

Pilavapadin developed specifically for the treatment of neuropathic pain



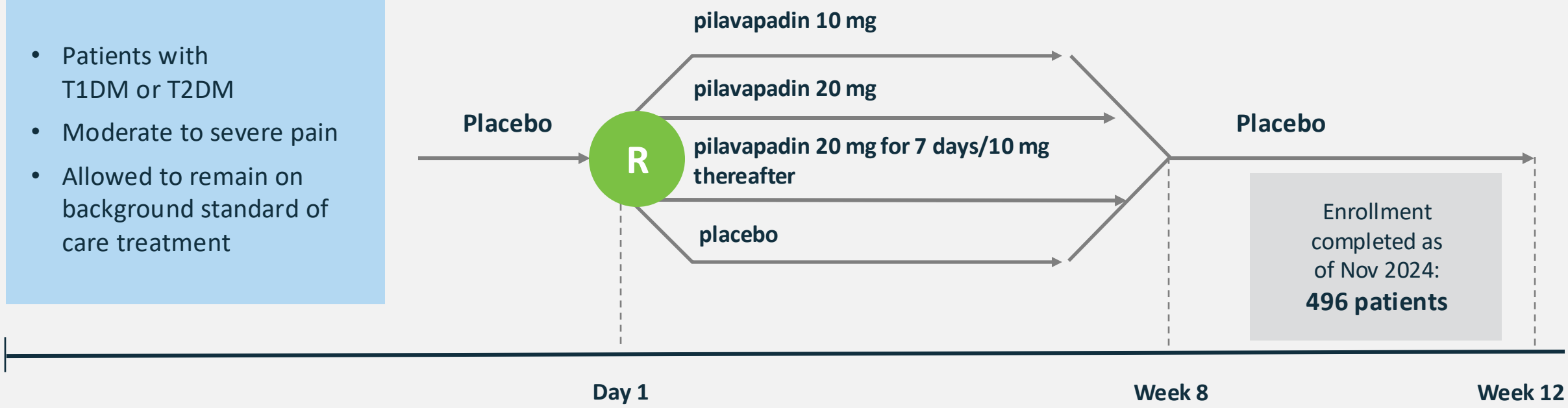
Potential advantages of pilavapadin (LX9211)

- Novel AAK1 mechanism
- Oral, once daily, non-opioid
- Nearly 600 DPNP patients treated with pilavapadin
- FDA Fast Track designation in DPNP

PROGRESS Phase 2b study design

Patient Population	Run in period 2-week	Treatment Period 8-week	Safety Follow-up 4-week

- Patients with T1DM or T2DM
- Moderate to severe pain
- Allowed to remain on background standard of care treatment

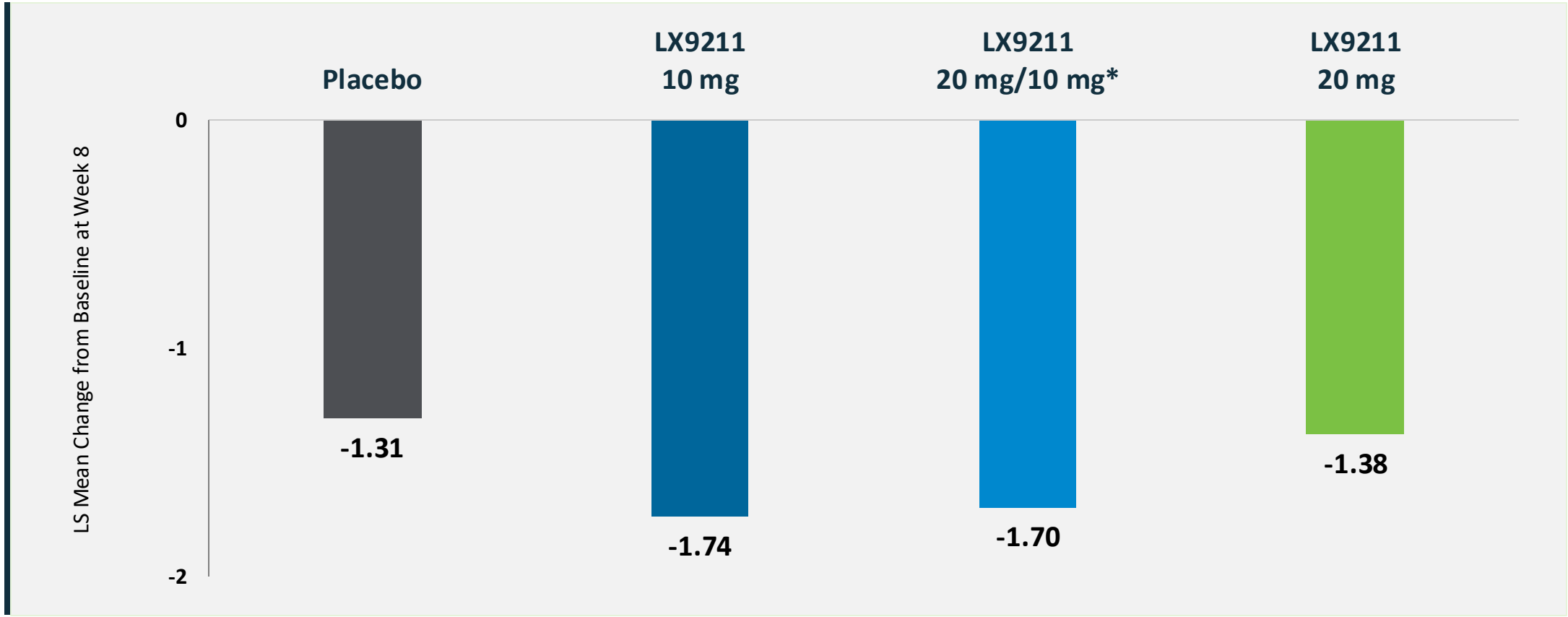


Full data anticipated in Q2

PROGRESS achieved main corporate objectives

- **Identify single dose to take into placebo-controlled Phase 3 studies**
- **Demonstrate meaningful pain reduction**
- **Achieve improved tolerability**

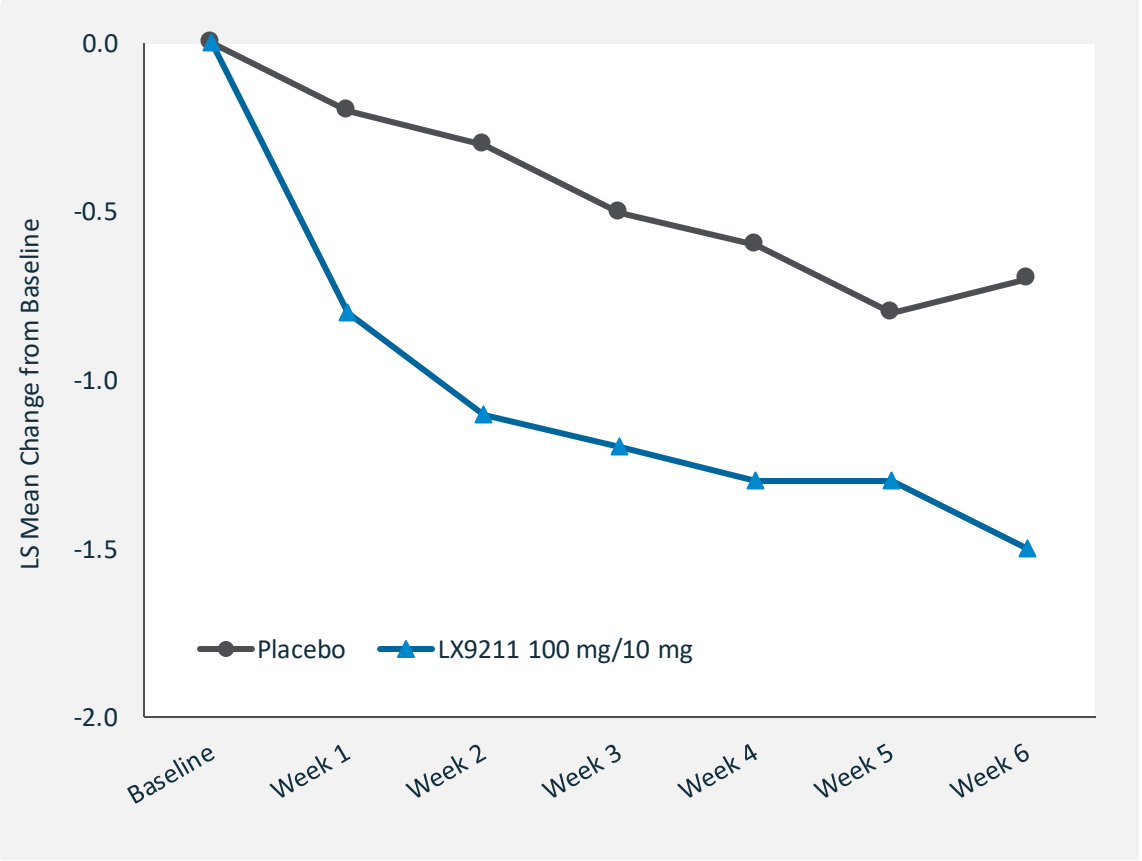
PROGRESS study identified 10 mg dose as most clinically meaningful



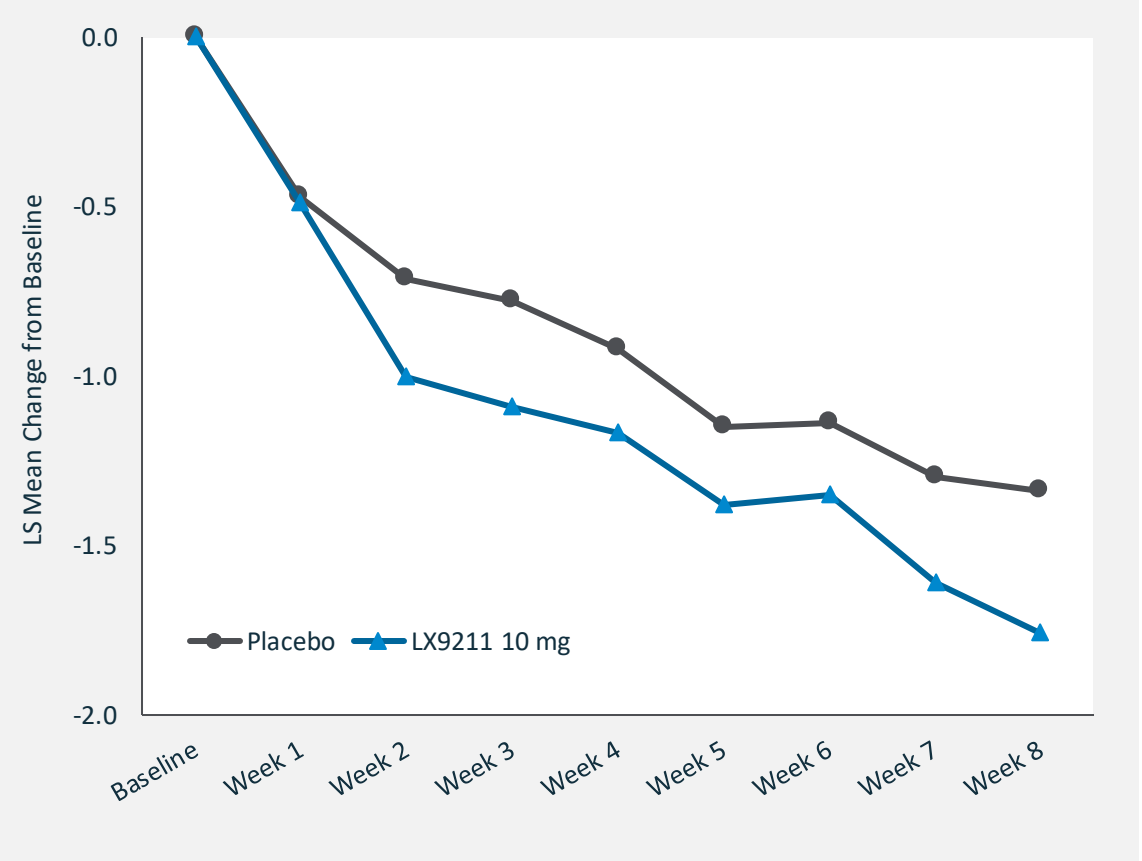
*LX9211 20 mg for 7 days and then 10 mg thereafter

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 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

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

Next steps in advancing pilavapadin

Present full results at upcoming medical meeting

Hold End-of-Phase 2 meeting with FDA

Prepare to initiate potential Phase 3 program in 2025

Q&A

Mike Exton, PhD

Craig Granowitz, MD, PhD

Suma Gopinathan, PhD

Scott Coiante

Thank You