

24th Annual Needham Virtual Healthcare Conference

April 2025



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.

Focusing on Science And Advancing Clinical Programs

Positioned for value creation



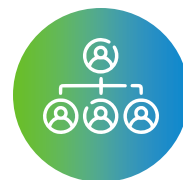
ATTRACTIVE ASSETS

- Diversified pipeline platform potential
- Partnership potential
- Earlier-stage opportunities in add'l indications



DEVELOPMENT EXPERTISE

- Clinical drug development expertise
- Adaptive, efficient trial designs
- Multiple late-stage candidates



LEAN, AGILE ORGANIZATION





- Full focus as a development company
- Minimum viable sotagliflozin support for patient access
- Strong cash runway



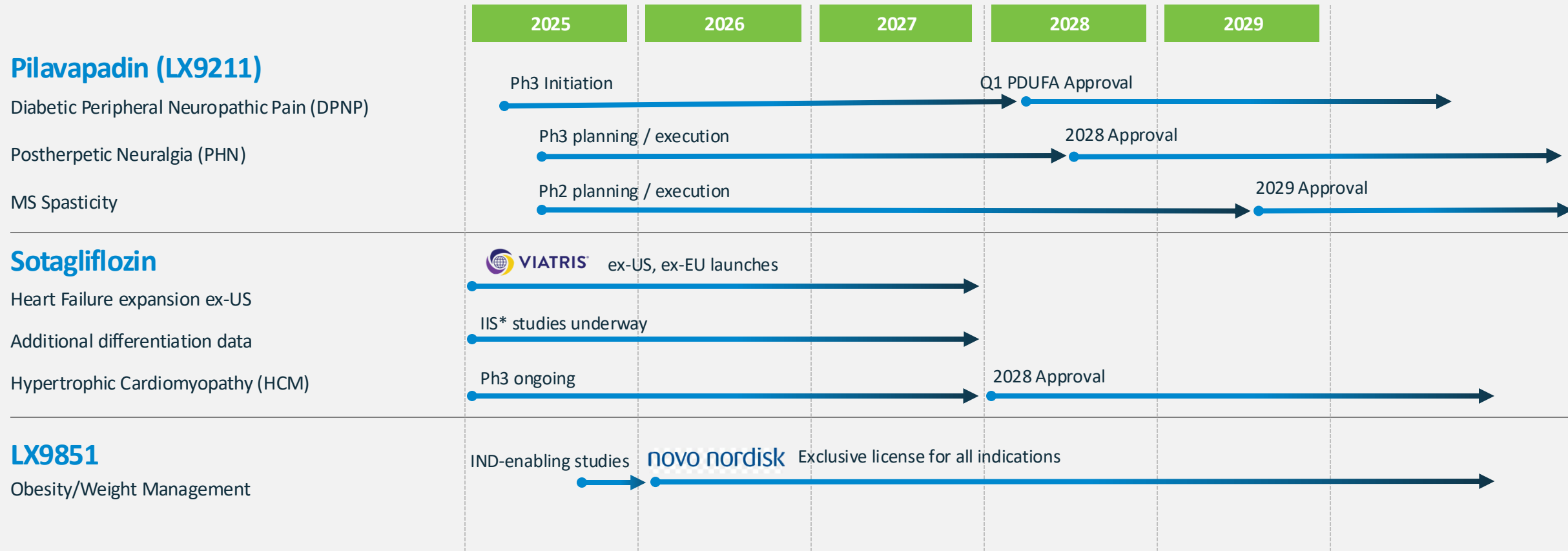
NEAR-TERM CATALYSTS

- **Pilavapadin** Ph. 2b full data readout in 2025
- **SONATA HCM** Ph. 3 enrollment underway
- **LX9851** IND enabling studies underway

Focused on advancing a strong R&D pipeline

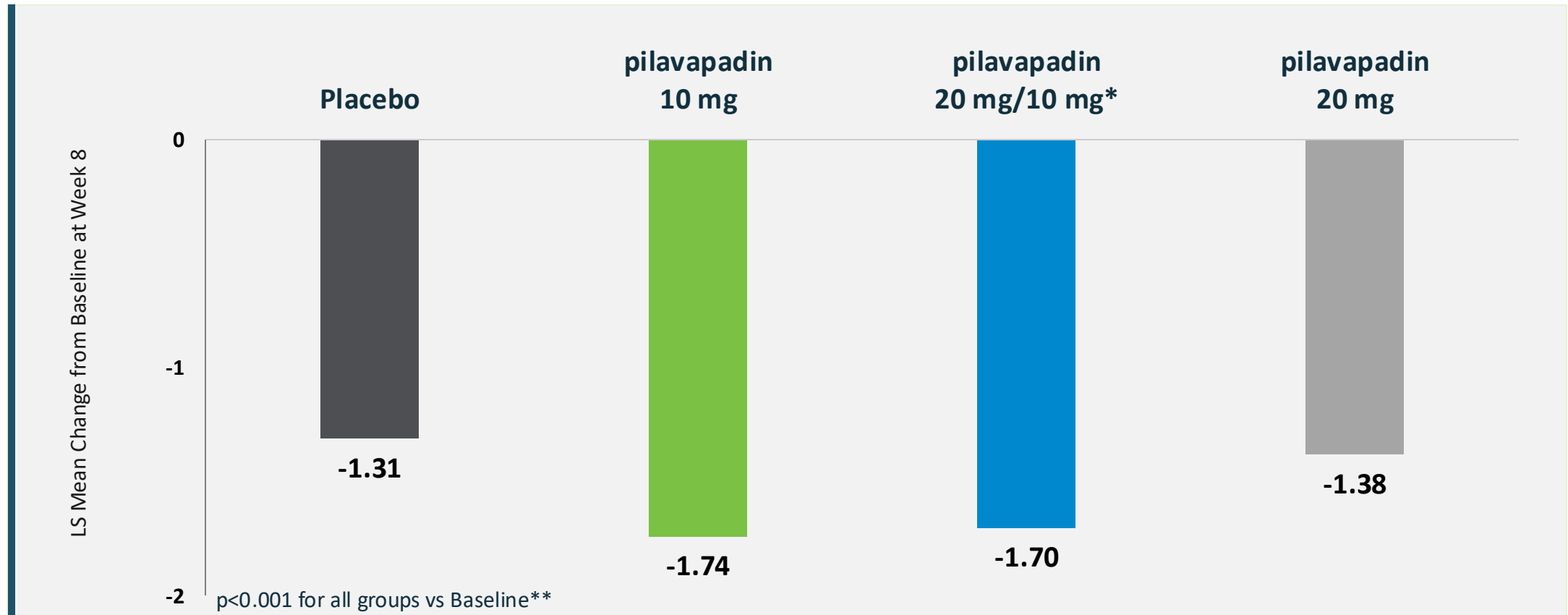
-  **Announced topline data from Phase 2b dose optimization PROGRESS study of pilavapadin in DPNP**
-  **Continued enrollment in pivotal Phase 3 study of sotagliflozin in SONATA-HCM**
-  **Advanced IND-enabling studies of LX9851 in obesity and related metabolic disorders**
-  **Reinvigorated business development efforts, including licensing agreements with Viartis for sotagliflozin and Novo Nordisk for LX9851**

A portfolio of potential “pipelines in a pill”



Timelines are illustrative and represent potential scenarios aligned to Lexicon’s overall strategy
 * IIS: Investigator-initiated studies

PROGRESS study identified 10 mg dose as most clinically meaningful and reaffirms 10 mg as most appropriate to advance into Phase 3 clinical development

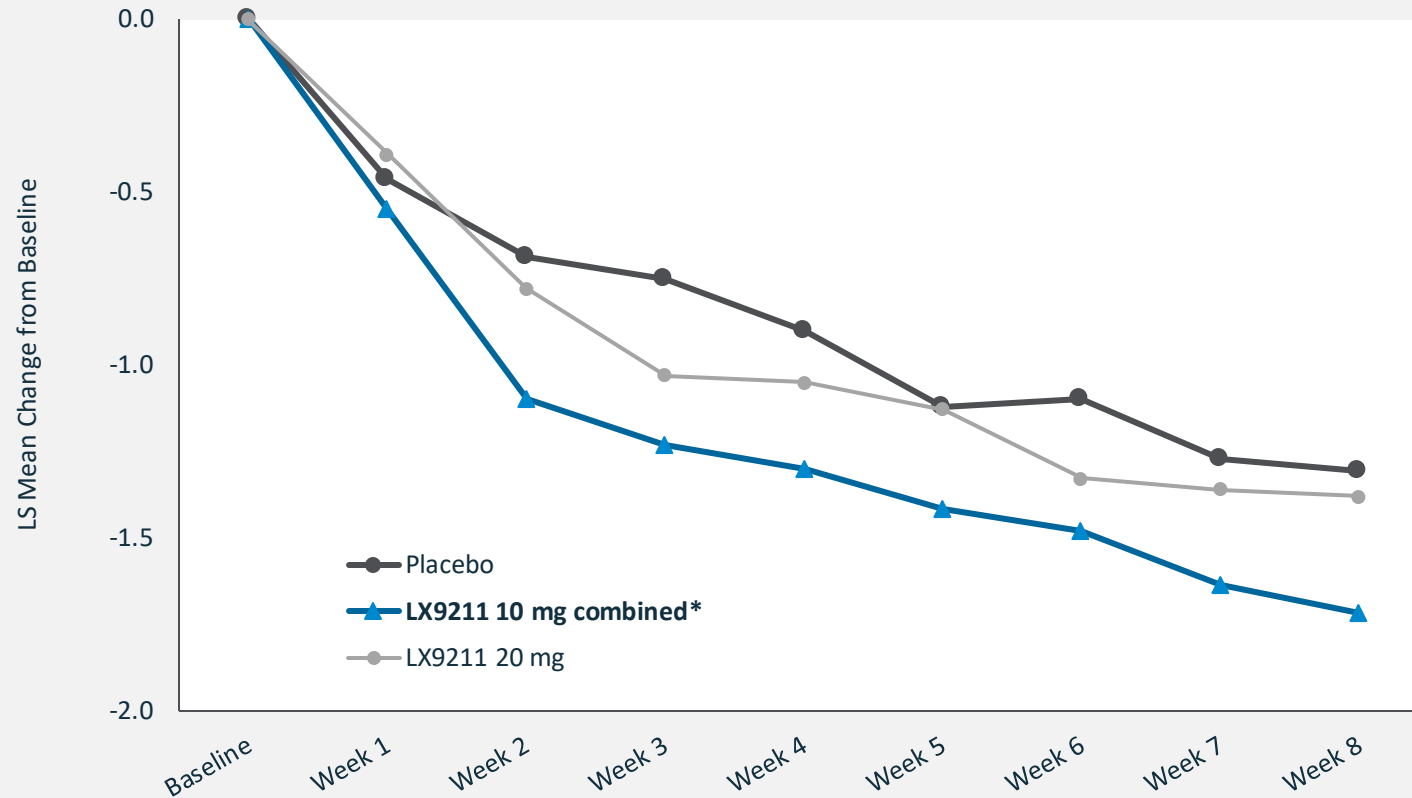


*LX9211 20 mg for 7 days and then 10 mg thereafter

**Post-hoc analysis

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*)



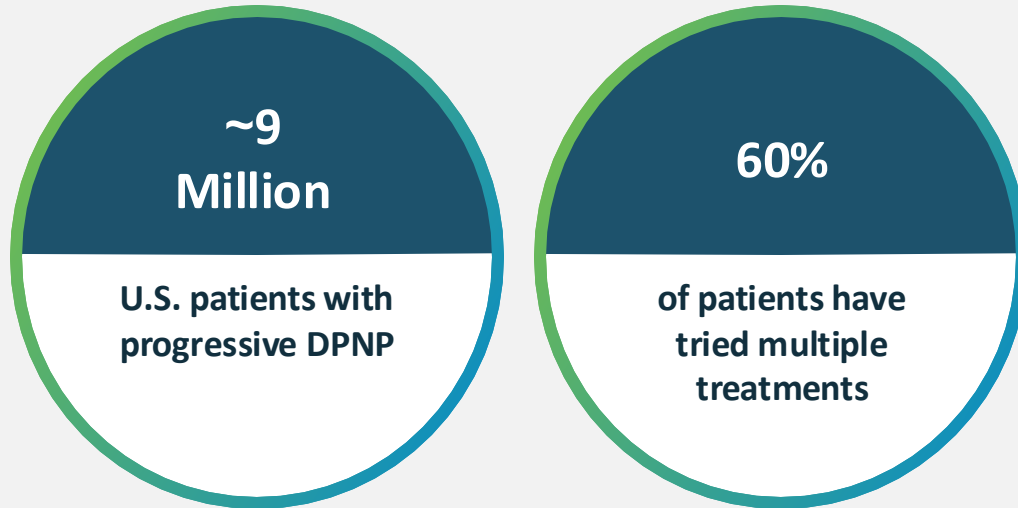
Key Findings

- 10 mg dose demonstrated early and sustained separation from placebo
- Post-hoc analysis of the 10 mg and 20+10 mg arms (without the 20 mg arm) showed statistically significant pain reduction as compared to placebo ($p = 0.04$)

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

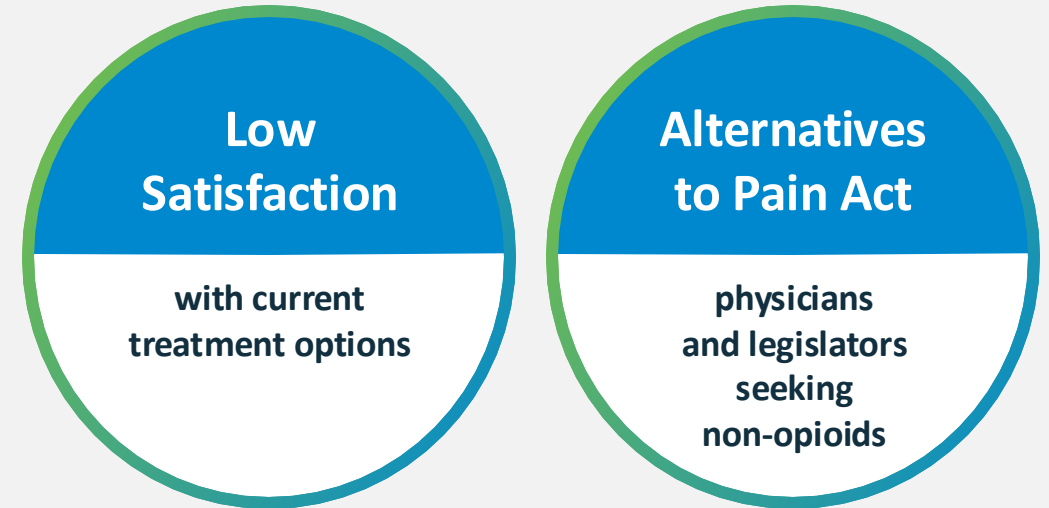
A clear need and opportunity in the DPNP treatment landscape for new treatments

Sizable Market Opportunity for DPNP



Majority of patients experience moderate-to-severe pain

High Unmet Need



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

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



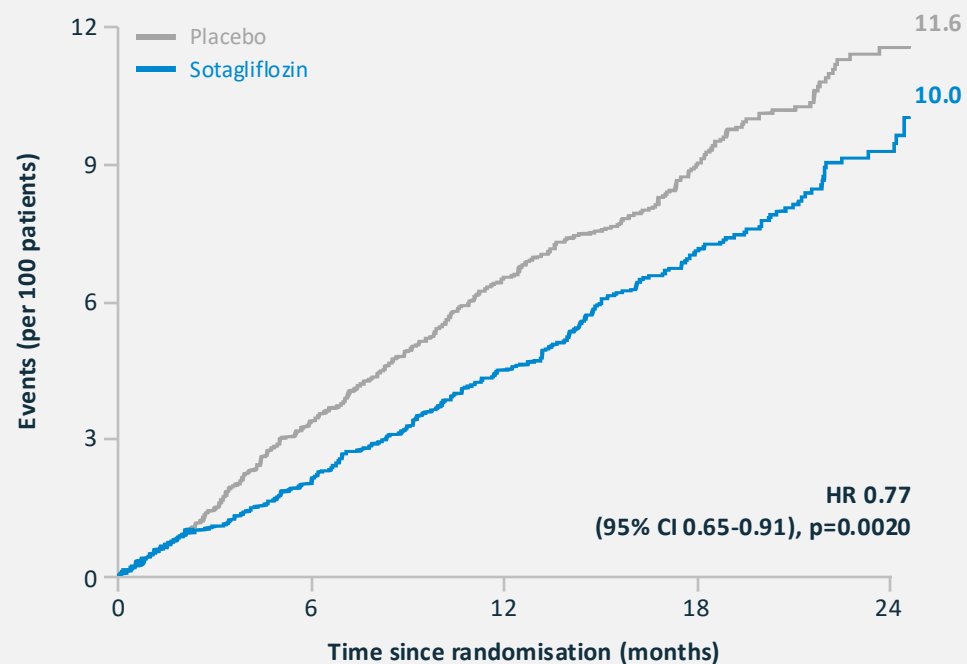
Ex-US, ex-EU registration and regional development by Viatrix underway



SONATA-HCM trial enrolling globally

The Lancet Diabetes & Endocrinology highlights unique efficacy benefits of sotagliflozin

Cumulative incidence of total MACE by treatment group



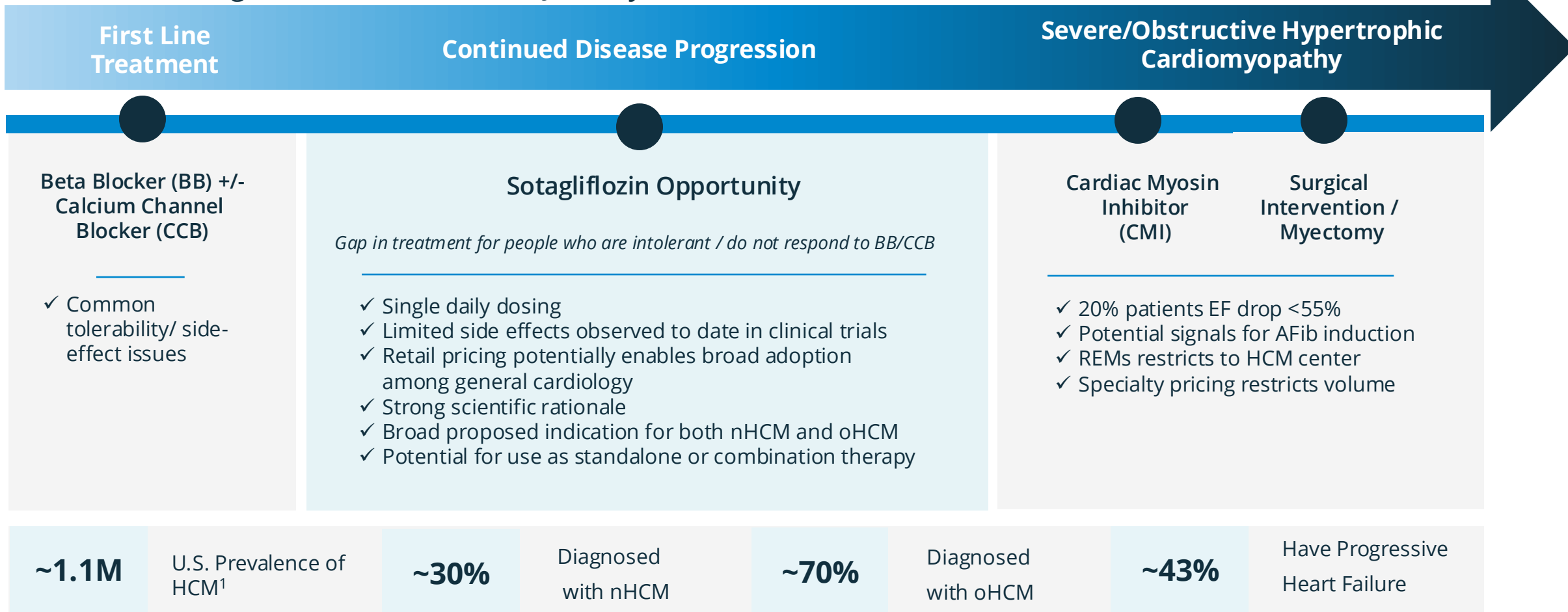
Number at risk (cumulative number censored)

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

Sotagliflozin has Potential to Occupy a Unique Position in Symptomatic HCM

HCM Disease Progression and Treatment Journey



Source: 1. CVrg Market Strategies. Cardiovascular Resource Group, Oct. 2023.

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

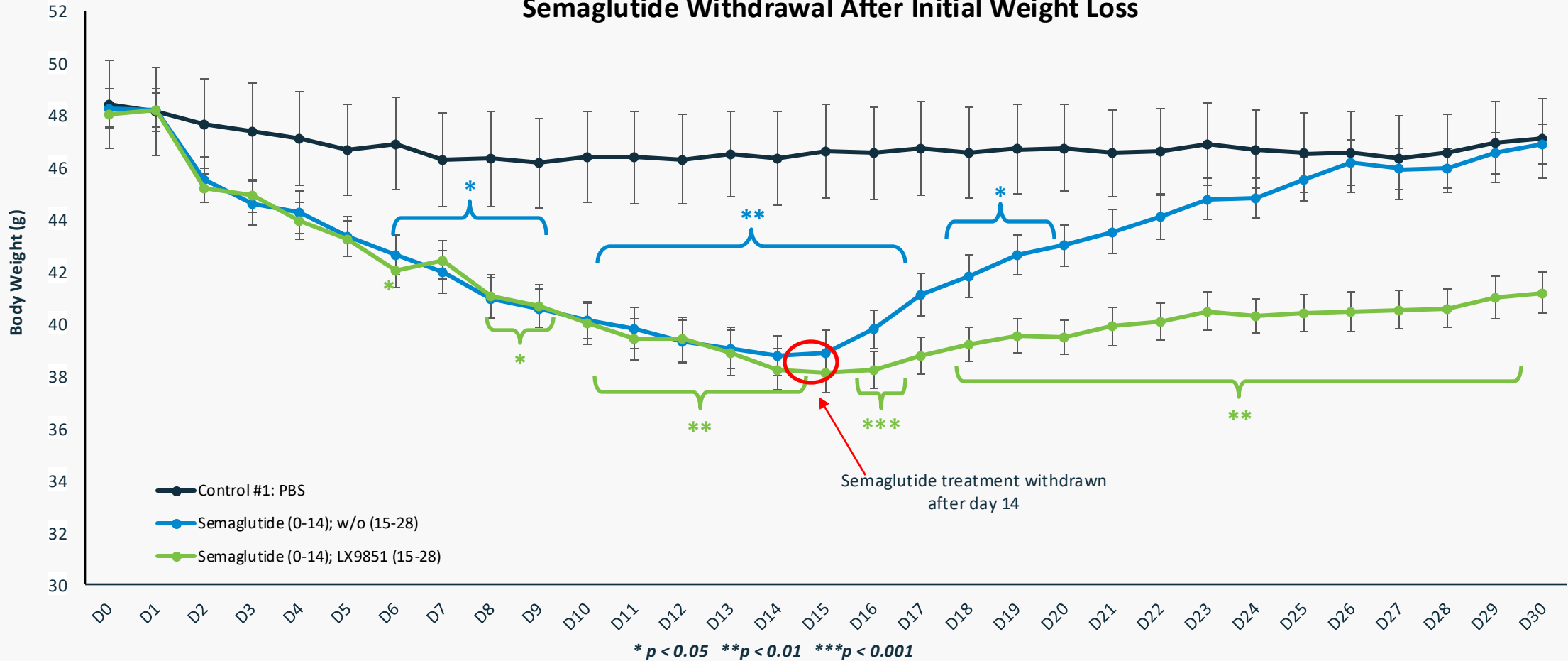
Potential Advantages of LX9851

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

LX9851: Weight loss maintained after semaglutide discontinuation in HFD-fed DIO mice



Semaglutide Withdrawal After Initial Weight Loss



Recent collaborations designed to unlock long-term value in areas of high opportunity



Exclusive licensing agreement for **LX9851** in obesity and all other indications

Global markets

\$75M in upfront and near-term milestones; eligible for up to \$1B in aggregate upfront and milestone payments



Exclusive licensing agreement for **sotagliflozin** in cardiometabolic and all other indications

All markets outside of the U.S. and Europe

\$25M upfront; eligible for up to almost \$200M in milestone payments

Significant number of planned catalysts through 2025

Pipeline	Indication	Planned Catalyst 2025
Pilavapadin	<ul style="list-style-type: none"> Diabetic Peripheral Neuropathic Pain 	<ul style="list-style-type: none"> Full PROGRESS data anticipated in Q2 End of Phase 2 meeting planned in Q3 Data at upcoming medical meetings Partnership discussions ongoing
LX9851	<ul style="list-style-type: none"> Obesity and Weight Management 	<ul style="list-style-type: none"> Ongoing collaboration with Novo Nordisk on IND-enabling studies
Sotagliflozin	<ul style="list-style-type: none"> Hypertrophic Cardiomyopathy 	<ul style="list-style-type: none"> EU and LATAM sites enrolling All Phase 3 study sites running by Q3
INPEFA[®] (sotagliflozin)	<ul style="list-style-type: none"> Heart Failure 	<ul style="list-style-type: none"> Regulatory submissions by Viatris in key ex-U.S. markets Potential Type C meeting re: MACE data in Q3
ZYNQUISTA[™] (sotagliflozin)	<ul style="list-style-type: none"> Type 1 Diabetes (with CKD) 	<ul style="list-style-type: none"> End of review meeting scheduled in Q2

Thank You