

# Second Quarter 2025 Earnings Presentation

August 6, 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<sup>®</sup> (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

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**Mike Exton, Ph.D.**

Director and Chief Executive Officer

## Strong execution against strategic pivot to R&D focused company



**Pilavapadin full Phase 2 results to be presented September 2025; partnership discussions ongoing**



**On track to complete IND-enabling studies of LX9851 in 2025**



**Accelerated site initiations in Phase 3 SONATA-HCM study of sotagliflozin in HCM**



**Excellent progress with Viartis to make sotagliflozin available outside the U.S. and EU**

**Well positioned to continue advancing and investing in innovative R&D pipeline**

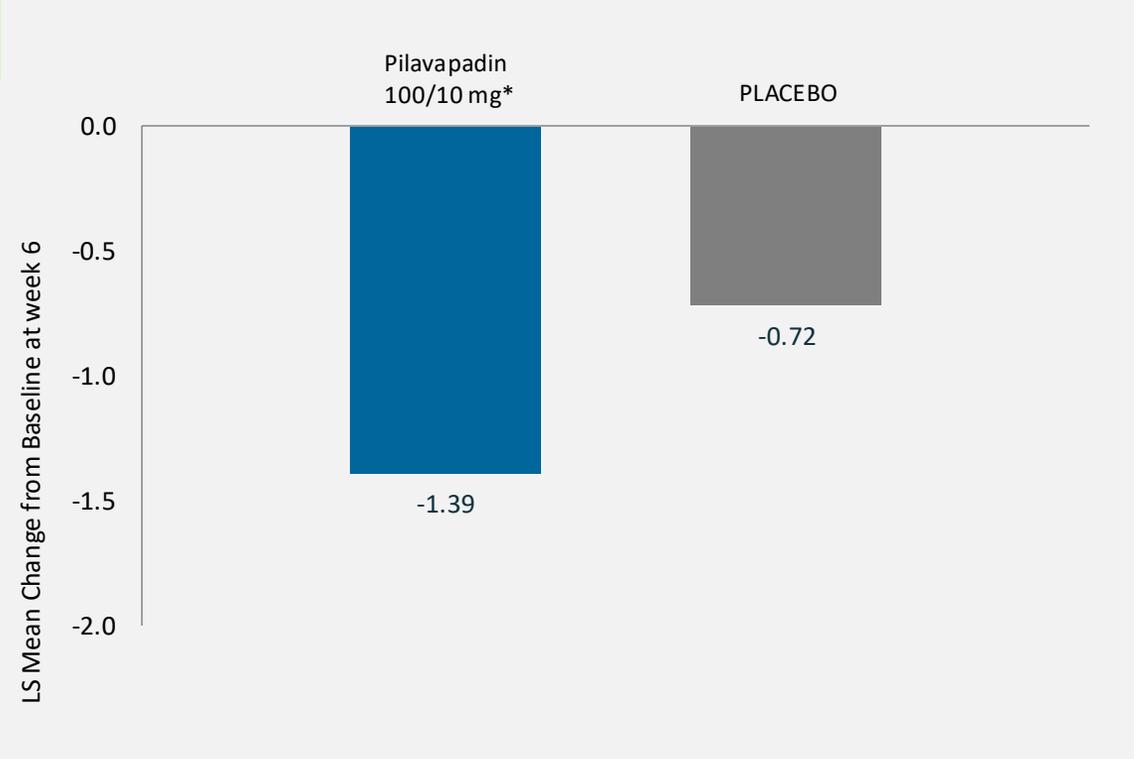
# Pipeline Overview

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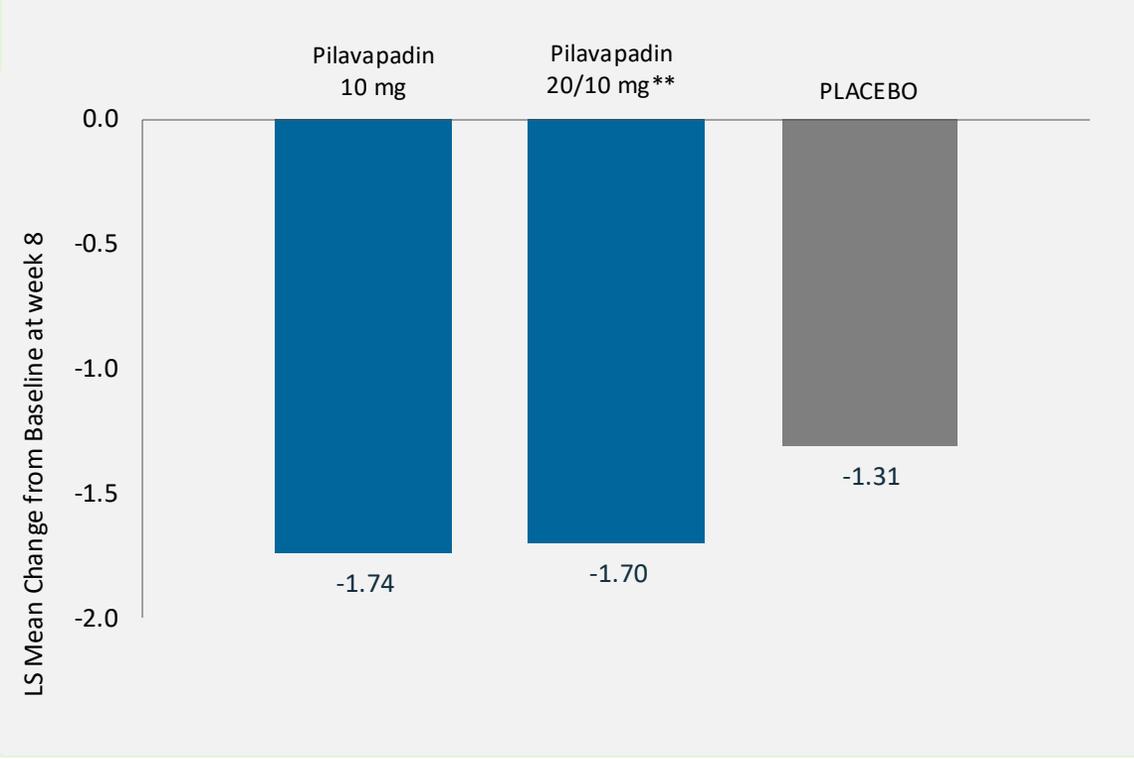
**Craig Granowitz, M.D., Ph.D.**  
Senior Vice President and Chief Medical Officer

# Pilavapadin 10 mg has consistently delivered clinically meaningful pain reduction

### RELIEF Phase 2a ADPS Reduction



### PROGRESS Phase 2b ADPS Reduction



ADPS: average daily pain score  
\*Pilavapadin (LX9211) 100/10 mg: included 100 mg as day 1 loading dose  
\*\*Pilavapadin (LX9211) 20 mg for 7 days and then 10 mg thereafter

# Advisory board supported key findings in PROGRESS topline data

## Secondary data analysis of comprehensive Phase 2 program ongoing



Pilavapadin demonstrated clinically meaningful efficacy



10 mg identified as the appropriate dose for registrational studies



Pilavapadin demonstrated acceptable safety and tolerability profile



Provided considerations for continued improvement of study design to lower placebo response and improve adherence

# Pilavapadin: Validated MOA, compelling profile, and broad applicability

## A portfolio in a pill with multiple near-term catalysts



Clinically meaningful pain reduction demonstrated across three Phase 2 trials\*



A full portfolio with a Phase 3-ready lead indication in DPNP and additional indications ready for Phase 2



IND-enabling work complete in multiple neuroscience indications



Extensive safety and tolerability experience with >600 pilavapadin-treated patients



Long patent life through 2040 when including anticipated five-year patent term extension

\*2 Phase 2 studies in DPNP, 1 Phase 2 study in PHN

# HCM: A significant and underpenetrated market with high disease burden

**~1.1 million people**

in the U.S. have either obstructive or non-obstructive HCM\*

Common signs include **altered cardiac energetics, fibrosis, and diastolic dysfunction**

Common symptoms **shortness of breath, fatigue, dizziness\*\***

HCM can lead to **heart failure, atrial fibrillation, and stroke**



**70%**

Diagnosed with oHCM

**30%**

Diagnosed with nHCM

**~1%**

CMI total market penetration

**43%**

Progress to heart failure

\*CVrg Market Strategies. Cardiovascular Resource Group, Oct. 2023.

\*\* Zaiser, Erica, et al. "Patient Experiences with Hypertrophic Cardiomyopathy: A Conceptual Model of Symptoms and Impacts on Quality of Life." Journal of Patient-Reported Outcomes, vol. 4, no. 1, Dec. 2020

## Broad potential for sotagliflozin within HCM treatment landscape

- ✔ Only HCM agent that ***works inside and outside the heart*** to reduce symptoms of HCM as well as to ***reduce*** HF and MACE events
- ✔ Also acts directly on the ***myocardium***
- ✔ ***Once-daily oral*** dosing enables broad potential adoption with no REMS
- ✔ ***Approved for heart failure*** with no observed increased risk of Afib to date

**Broad proposed indication for both nHCM and oHCM with potential for use alone or in combination**

# Significant data support sotagliflozin as only SGLT inhibitor to work inside and outside the heart for HCM



## Animal models in HCM\* and HFpEF\*

- Improved diastolic function
- Reduced
  - Wall thickness
  - Fibrosis
  - Cardiac inflammation



## Ex vivo in HCM myocardial slices\*

- Reduced stroke work
- Increase metabolites associated with improved cardiac energetics



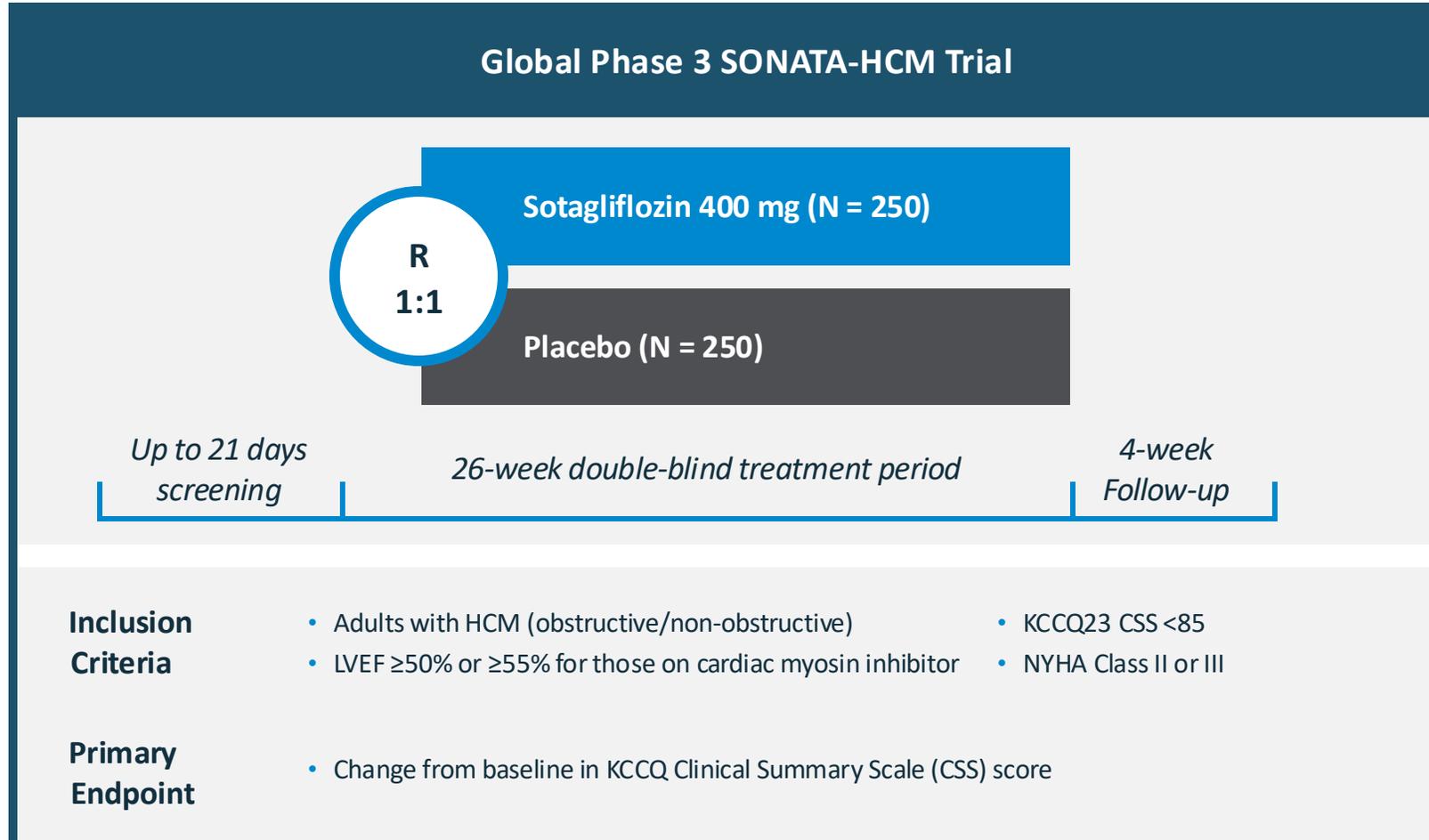
## Lexicon and IIS clinical studies

- SONATA-HCM
- SOTA-CROSS (nHCM)\*
- SOTA-P-CARDIA (HFpEF)\*

**Data generated validate use of dual SGLT1 and SGLT2 inhibition with sotagliflozin in HCM**

*\*IIS: Investigator-initiated studies*

# SONATA-HCM Phase 3 study for oHCM and nHCM



**Enrollment accelerating – on track for all sites active by end of Q3 2025**

**Sites opened in U.S., EU, Israel, and LATAM**

**Only ongoing trial to evaluate both obstructive and non-obstructive HCM**

**Potential for supplemental new drug application (sNDA) with broad label**

# Investigator-initiated studies complement registrational study and may support sotagliflozin use in HCM



## SOTA-P-CARDIA

- **Readout late 2025/early 2026**
- Investigate cardiorenal mechanistic benefits of sotagliflozin in **HFpEF**
- 6-month, placebo-controlled study
- 88 patients



## SOTA-CROSS

- **Readout mid-to-late 2026**
- Evaluate sotagliflozin in **symptomatic nHCM**
- 12-week, placebo-controlled, crossover study
- 26 patients



## SONATA-HCM

- Evaluate sotagliflozin in patients with **symptomatic HCM**
- 26-week, placebo-controlled study
- 500 patients
- Key endpoints include change in KCCQ and NYHA class improvement

**Endpoints include measures related to cardiac function, exercise performance, and quality of life (KCCQ)**

HFpEF: heart failure with preserved ejection fraction; nHCM: non-obstructive hypertrophic cardiomyopathy; \*KCCQ: Kansas City Cardiomyopathy questionnaire

# IND-enabling studies under strategic license with Novo Nordisk for LX9851 remain on track

**LX9851**

First-in-class, potent, selective, orally bioavailable, investigational small molecule ACSL5 inhibitor



Exclusive, worldwide license to develop, manufacture, and commercialize LX9851 in all indications



Positioned to benefit from Novo Nordisk size, scale and capabilities – IND-enabling studies on track to complete by end of 2025



\$75 million in upfront and potential near-term milestone payments (\$45 million upfront payment received in April); up to \$1 billion in total upfront and potential milestones; tiered royalties



Potential differentiation in the obesity market with shift in focus to orals, combinations, and improved weight-loss maintenance

ACSL5: Acyl-CoA synthetase 5

# Financial Overview

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**Scott Coiante**  
Chief Financial Officer

# Q2 2025 Financial Summary

\$ (in millions except per share amounts)

	As of June 30, 2025*	As of December 31, 2024
Cash, cash equivalents, short-term investments and restricted cash	\$168.0	\$238.0
Total assets	\$225.6	\$298.4
Total debt	\$56.1	\$100.3

	Q2 2025	Q2 2024
Revenue:		
Net product revenues	\$1.3	\$1.6
Licensing revenue	\$27.5	---
Total revenues	\$28.9	\$1.6
Operating expenses:		
R&D	\$15.7	\$17.6
SG&A	\$9.4	\$39.2
Total operating expenses	\$25.1	\$57.0
Net income / (loss)	\$3.3	(\$53.4)
Net income / (loss) per common share	\$0.01	(\$0.17)

Revenue includes \$27.5 million of revenue upfront payment for exclusive licensing agreement of LX9851 with Novo Nordisk

# Q2 2025 Financial Highlights

## Q2 2025 Key

### Financial Highlights



- The \$45 million upfront payment (received in April) under licensing agreement with Novo Nordisk was used to improve balance sheet by reducing long-term debt.
- Quarter over quarter operating expenses were down \$31.9 million primarily due to the strategic repositioning as R&D focused company in late 2024.

## Full Year 2025

### Operating Expenses\*



- Total 2025 operating expenses now expected to be between \$105 - \$115 million (previously \$135 - \$145 million)
  - R&D is now expected between \$70 - \$75 million (previously \$100 - \$105 million)
    - Excludes clinical trial costs related to Phase 3 pivotal studies of pilavapadin
  - SG&A remains expected between \$35 - \$40 million

\*As of June 30, 2025

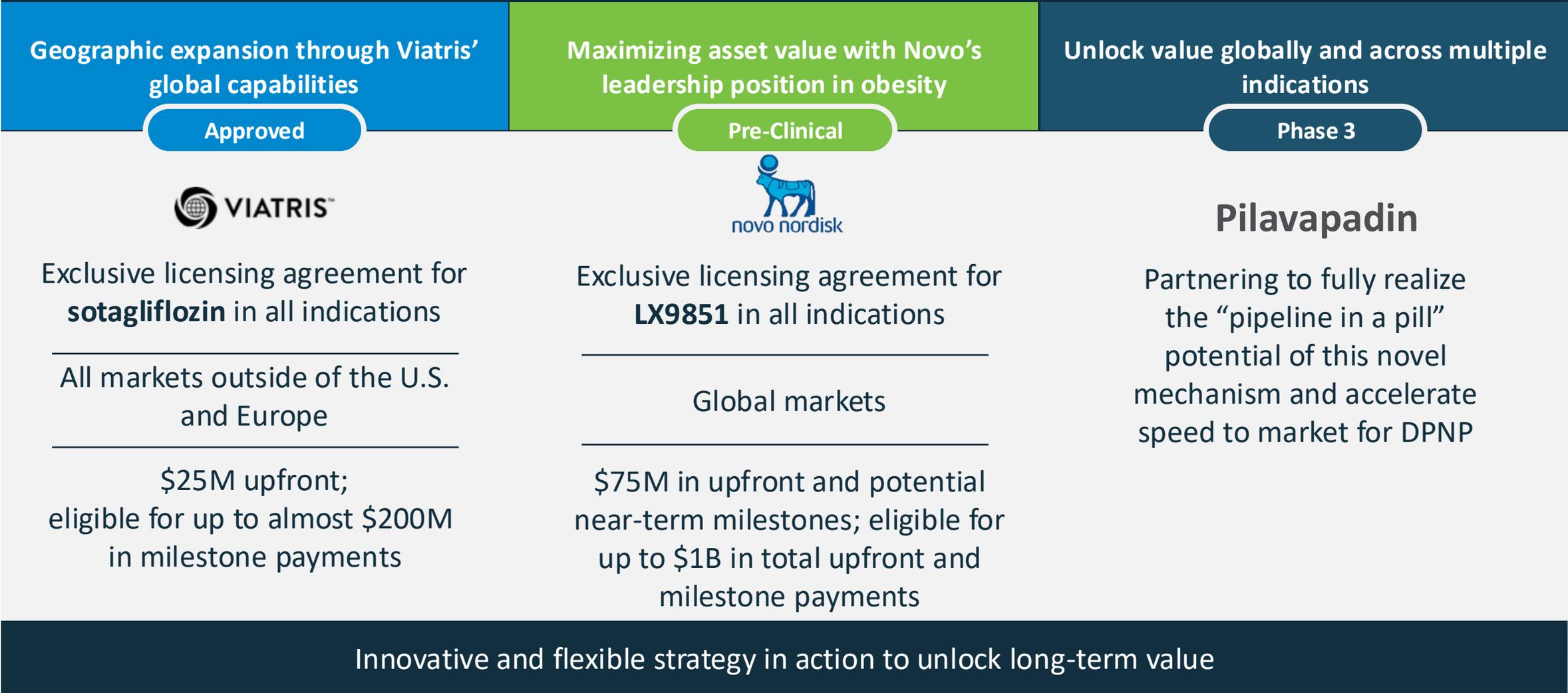
# Summary

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**Mike Exton, PhD**

Director and Chief Executive Officer

# Partnership strategy intended to enable focus on core cardiometabolic expertise



# Well-positioned with a portfolio of potential “pipelines in a pill”

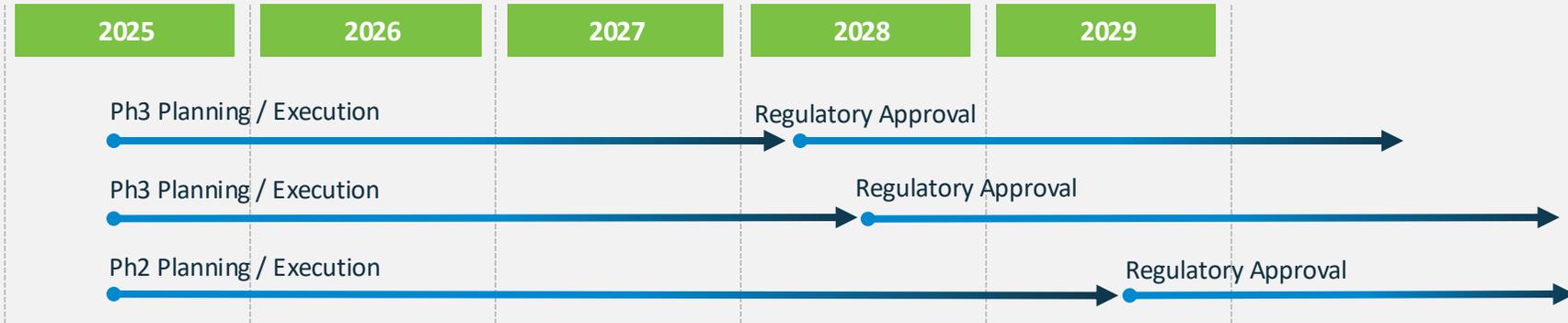
*Exploring opportunities across multiple therapeutic areas*

## Pilavapadin\*

Diabetic Peripheral Neuropathic Pain (DPNP)

Postherpetic Neuralgia (PHN)

Spasticity

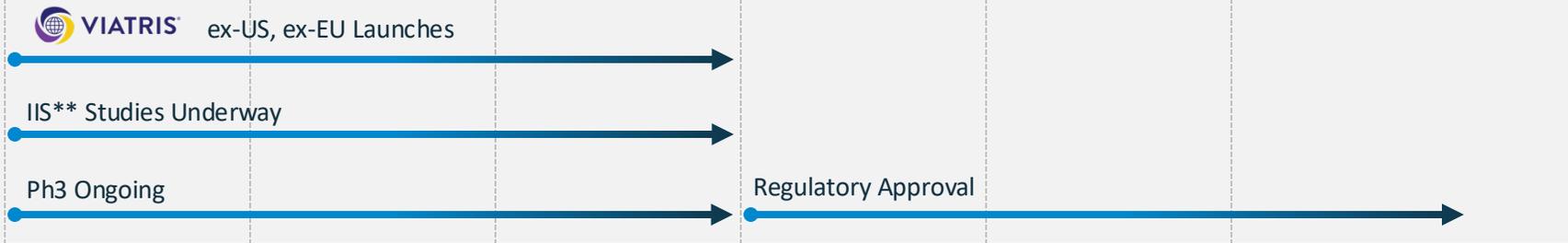


## Sotagliflozin

Heart Failure expansion ex-US

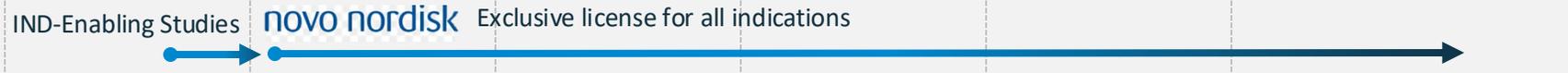
Additional differentiation data

Hypertrophic Cardiomyopathy (HCM)



## LX9851

Obesity/Weight Management



*Timelines are illustrative and represent potential scenarios aligned to Lexicon’s overall strategy*  
 \*Execution of trials and subsequent regulatory support would require partnership or additional funding  
 \*\* IIS: Investigator-initiated studies

# Well positioned for continued progress across all programs throughout 2025

<p><b>Pilavapadin</b></p>	<ul style="list-style-type: none"> <li>• Diabetic Peripheral Neuropathic Pain (DPNP)</li> </ul>	<ul style="list-style-type: none"> <li>• Full PROGRESS data anticipated in Q3</li> <li>• End of Phase 2 meeting before year-end</li> <li>• Ongoing partnership discussions</li> </ul>
<p><b>Sotagliflozin</b></p>	<ul style="list-style-type: none"> <li>• Hypertrophic Cardiomyopathy</li> </ul>	<ul style="list-style-type: none"> <li>• US, EU, Israel and LATAM sites enrolling</li> <li>• All Phase 3 study sites running by Q3</li> <li>• Data from IIS beginning late 2025 readout</li> </ul>
<p><b>INPEFA<sup>®</sup> (sotagliflozin)</b></p>	<ul style="list-style-type: none"> <li>• Heart Failure</li> </ul>	<ul style="list-style-type: none"> <li>• Regulatory submissions and approvals by Viatrix ex-U.S. and EU – ongoing</li> </ul>
<p><b>ZYNQUISTA<sup>®</sup> (sotagliflozin)</b></p>	<ul style="list-style-type: none"> <li>• Type 1 Diabetes</li> </ul>	<ul style="list-style-type: none"> <li>• End of review evaluation process ongoing</li> <li>• Patients continue to strongly advocate for approval</li> </ul>
<p><b>LX9851</b></p>	<ul style="list-style-type: none"> <li>• Obesity and Weight Management</li> </ul>	<ul style="list-style-type: none"> <li>• Ongoing collaboration with Novo Nordisk; IND-enabling studies on track for completion by end 2025</li> </ul>

# Q&A



**Mike Exton, Ph.D.**

*Director and Chief  
Executive Officer*



**Craig Granowitz, M.D., Ph.D.**

*Senior Vice President and Chief  
Medical Officer*



**Scott Coiante**

*Senior Vice President  
and Chief Financial  
Officer*

# Thank You