Corporate Presentation

November 2026

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 sotagliflozin, pilavapadin, LX9851 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.

Three Decades of Gene Science Now Power a Focused Cardiometabolic Portfolio

A leading cardiometabolic biopharmaceutical company built on a legacy in genetic target discovery

Discovery heritage, translated into focused patient impact



CREATING CONTINUED VALUE

DISCOVER

Leveraging foundational genome work to identify novel drug targets

DEVELOP

Advancing the most promising targets through clinical development

DELIVER

Thoughtfully partnering or commercializing to maximize each medicine's reach

Continued Progress on Our Objectives for 2026



Advance our late-stage sotagliflozin programs

- SONATA-HCM
- ZYNQUISTA® for T1D



Expand internationally and through collaborators

- Support of existing Viatris and Novo licensees
- Evaluate strategic options for pilavapadin in neuropathic pain, obesity and other indications



Remain operationally disciplined and focused

Support long-term growth and value

LEAD TO SUCCEED

Year-to-Date 2026 Highlights

Advancing our pipeline of novel therapies for serious cardiometabolic diseases

SOTAGLIFLOZIN

HCM

- Phase 3 SONATA-HCM enrollment complete; supports potential broad label
- Topline data expected Q1 2027

T1D

- STENO1 (third-party IIS) data package received & supports NDA resubmission
- DKA rates are low and comparable to standard of care in STENO1

Heart Failure — Global Expansion

- Viatris launch underway; approved in UAE and Bahrain
- Additional regulatory submissions in ex-US and ex-Europe markets

LX9851

Obesity

- Phase 1 study ongoing by Novo Nordisk
- Three $10M milestone payments received in 2026

PILAVAPADIN

Diabetic Peripheral Neuropathic Pain

Clear regulatory path to Phase 3 pivotal studies

Obesity & Additional Indications

Preclinical studies across multiple non-pain indications including recent data in obesity

CONTINUED COMMITMENT TO OPERATIONAL EXCELLENCE

STRATEGIC HIRING TO SUPPORT PRE-COMMERCIAL AND CLINICAL PLANNING

Sotagliflozin

Improving Cardiac Metabolism in HCM by Working Directly on the Heart

Enabled by unique SGLT1 mechanistic benefits

nHCM

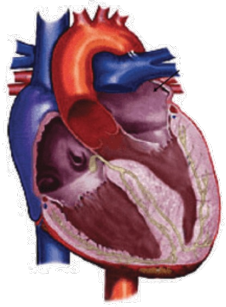
Characterized by global or localized thickening without a significant outflow tract pressure gradient.

LVOT Gradient
< 30 mmHg

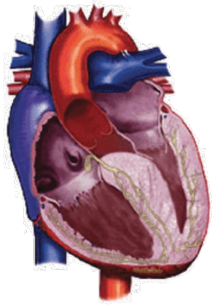
Many presentations… one disease

HYPERTROPHIC CARDIOMYOPATHY

Without Obstruction



With Obstruction



oHCM

The hallmark of obstructive disease is a physical blockage in the Left Ventricular Outflow Tract (LVOT).

LVOT Gradient
≥ 30 mmHg

Mechanistic Benefits of SGLT1 in HCM

Works directly on the heart, improving diastolic dysfunction and cardiac metabolism in HCM

Source: HCMAi, Hypertrophic Cardiomyopathy Association

Significant Need Remains for Patients with HCM

>800K

diagnosed HCM patients in the U.S.[1]

POPULATION MOMENTUM

nHCM population is growing strongly with rising levels of obesity and diabetes

~2/3

of symptomatic patients are nHCM – many more remain undiagnosed[2]

TREATMENT GAP

Currently no FDA-approved therapies for nHCM patients

SAFE + SIMPLE

Strong need for an option that is safe with simple dosing

ACCESS BARRIERS

REMS complexity and cost-associated restrictions limit penetration of new medicines

1: JACC, https://www.jacc.org/doi/10.1016/j.jacadv.2025.102552. 2: JACC, https://www.jacc.org/doi/10.1016/j.jacadv.2025.102552.

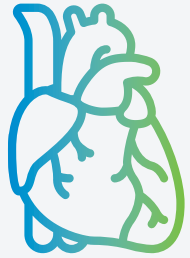
Sotagliflozin Predominantly Improves Diastolic Dysfunction By Improving Cardiac Metabolism

Mechanistic Benefits of SGLT1 in HCM

- **Enhanced calcium handling for myocardial relaxation**
- **Improved energy utilization of ketones versus glucose**
- **Reduced inflammation and fibrosis**
- **Reduced epicardial fat**

SGLT1i

expressed predominantly in the myocardium[1] and increased in ventricular hypertrophy



Works directly on the heart, improving cardiac **metabolism** in HCM

1. Li Y, Xu G. Sodium glucose cotransporter 1 (SGLT1) inhibitors in cardiovascular protection: Mechanism progresses and challenges. Pharmacological Research 176 (2022). doi.org/10.1016/j.phrs.2021.106049
2. Fonseca-Correa JI, Correa-Rotter R.Sodium-Glucose Cotransporter-2 Inhibitors Mechanisms of Action: A Review. Frontiers in Medicine. 2021;8:777861.

Potential to be a First-line Therapy in Symptomatic HCM

- The only HCM agent that **works inside and outside the heart** to reduce symptoms of HCM, as well as reduce HF and MACE events
- Novel MOA, with SGLT1 inhibition acting directly on the myocardium to **modify cellular energetics**
- Anticipated ease of adoption for patients and prescribers would enable broad uptake, **as a potential first-line agent** with no REMS
- **Designed to treat both types of HCM** by addressing cellular stiffness (diastolic dysfunction) and energy starvation, which happen in all HCM hearts

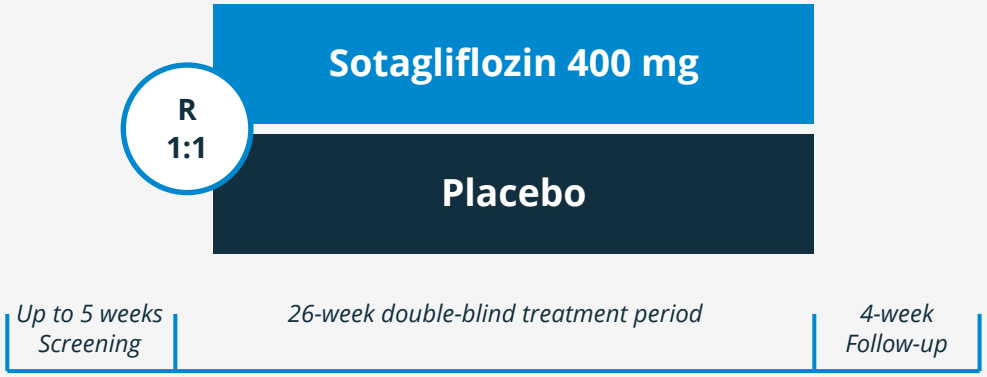
Sotagliflozin is both a hemodynamic and metabolic agent in HCM

SONATA-HCM Phase 3 Study for Symptomatic HCM

Baseline characteristics reflect broad and clinically relevant HCM population

Enrollment Complete; Topline Results Anticipated in Q1 2027

- Patient demographics **consistent with prior studies of other agents in HCM** and reflect real-world clinical practice
- Average **KCCQ score of 59**, signaling meaningful room to demonstrate a clinically relevant treatment benefit
- Evaluation in **broad HCM population, emphasizing nHCM**, where currently no FDA-approved treatment option exists
- 542 patients randomized; **substantial over-enrollment** strengthens statistical power
- Inclusion of background CMI therapy (~9%) supports **potential complementary positioning**



Primary endpoint:

Change from baseline in KCCQ CSS

KCCQ CSS = Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; R = randomization.

Growing Body of Recent Evidence Supports Sotagliflozin in HCM

Highlights differentiation of dual inhibition compared to SGLT2 alone

PRECLINICAL BIOLOGY

J Mol Cell Cardiol Plus 2026 | HCM Society 2025

HCM mouse model

Improved cardiac structure and function: normalized diastolic function, reversed hypertrophy progression and reduced fibrosis, with lower oxidative stress.

J Clin Invest 2026

Platelets and thrombosis

Sotagliflozin, but not SGLT2-selective empagliflozin, reduced platelet activation and thrombus formation without adversely affecting hemostasis.

CLINICAL READTHROUGH

AHA 2026 | University of Pennsylvania

Human myocardial slices

In living HCM heart tissue, SGLT inhibitors directly reduced myocardial work, with sotagliflozin showing greater potency at high afterload.

AHA 2026 | Ichan School of Medicine

Thrombus formation

In healthy adults, sotagliflozin significantly reduced thrombus formation vs. baseline; empagliflozin did not reach significance.

HCM CLINICAL PROGRAM

Investigator-initiated | University of Pennsylvania

SOTA-CROSS: nHCM

26 patients, 12-week crossover study; evaluating cardiac function, exercise performance and KCCQ. Completion expected 1H2027.

Phase 3 registrational

SONATA-HCM: oHCM and nHCM

>500 patients with both subtypes of HCM, 26 weeks: key endpoints include change in KCCQ and NYHA class.

Topline data expected Q1 2027

HCM: hypertrophic cardiomyopathy; oHCM/nHCM: obstructive/nonobstructive HCM; KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; SGLT: sodium glucose co-transporter. Qin F, et al. J Mol Cell Cardiol Plus. 2026;100873. Stanger L, et al. J Clin Invest. 2026. Taichman RB, et al. AHA Scientific Sessions 2026. Zafar MU, et al. AHA Scientific Sessions 2026; SOTA-CROSS: University of Pennsylvania (NCT06433050).

Clinical Data Support ZYNQUISTA's Resubmission

Patient-years of exposure achieved; DKA rates support positive benefit:risk profile

Zynquista™ (sotagliflozin) tablets 200 mg

~1M U.S. adults with T1D, with no approved treatment options beyond insulin

If approved, the first and only oral adjunct to insulin for glycemic control in T1D

inTandem clinical program

FDA-RECOGNIZED OUTCOMES IN T1D

1. HbA1c reduction
2. Increased time in range
3. Reduced hypoglycemic events
4. Reduced body weight
5. Lower blood pressure

STENO1 investigator-initiated study

FDA RESUBMISSION CRITERIA ACHIEVED

1. **Prospective study**
   FDA confirmed STENO1 is adequate to support resubmission
2. **Patient exposure**
   Achieved the years of exposure discussed with FDA
3. **DKA rates**
   Similar to standard of care in STENO1 and below rates in the inTandem studies

DKA: diabetic ketoacidosis; NDA: new drug application; T1D: type 1 diabetes. STENO1: Multifactorial Intervention to Reduce Cardiovascular Disease in Type 1 Diabetes, Steno Diabetes Center Copenhagen (NCT06082063), a third-party funded investigator-initiated study. InTandem: Lexicon's Phase 3 clinical program of sotagliflozin in T1D.

STENO1 DKA Rates are Low and Comparable to Standard of Care

ENROLLMENT SNAPSHOT

Group	Randomized patients, n	DKA rate per 100 patient years
Historic Rate in Denmark T1D Patients[1]	n/a	~1.0
Sotagliflozin	496	~1.0
Standard of Care	708	~1.0

Enrollment Summary as of August 30, 2026

NDA resubmission anticipated in Q1 2027

[1]Stougaard EB, et al. Diabetes Care. 2023;46:1897–1902. doi:10.2337/dc23-0475.

LX9851

Lexicon pharmaceuticals

Phase 1 Trial of LX9851 Ongoing by Novo Nordisk

First-in-class, non-incretin, oral, small molecule ACSL5 inhibitor in development for obesity and associated metabolic disorders

Phase 1 study of LX9851 initiated in March 2026

$30 million

in development milestones achieved year-to-date

Potential to achieve up to $1 billion in milestone payments plus tiered royalties on future net sales

ACSL5: Acyl-CoA Synthetase 5

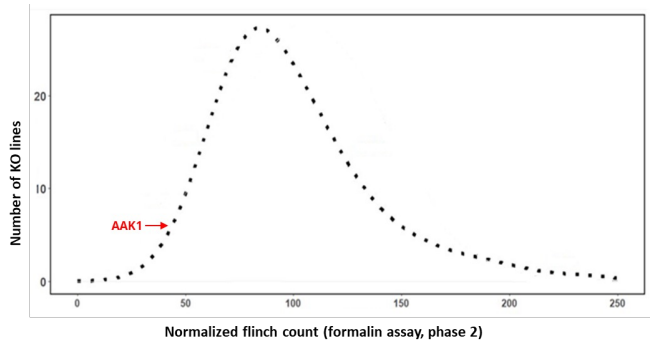
Pilavapadin

Lexicon pharmaceuticals

AAK1 Identified as a Leading Neuropathic Pain Target out of Nearly 5,000 Genes

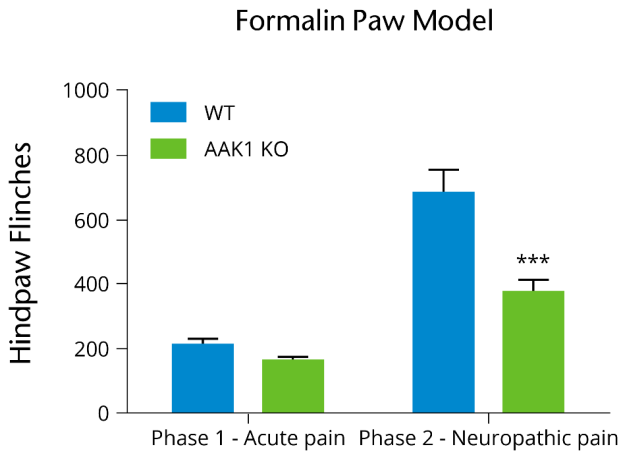
Genetic knockouts of AAK1 demonstrated…

…a highly potent effect on pain



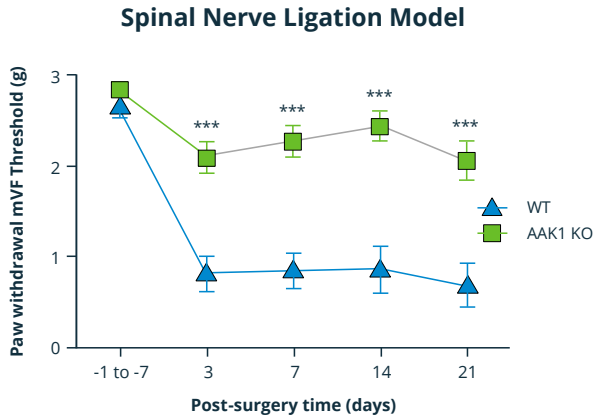
Characteristics of *Aak1* KO Phenotype Compared to Genome5000™ Assessment of Nearly 5,000 Genes – Formalin Paw, Phase 2 Results

… effects primarily on chronic pain rather than acute pain



Assessment of Chronic Pain – Formalin Paw, Phase 2 Results – Relevant to Neuropathic Pain

…resistance to neuropathic pain



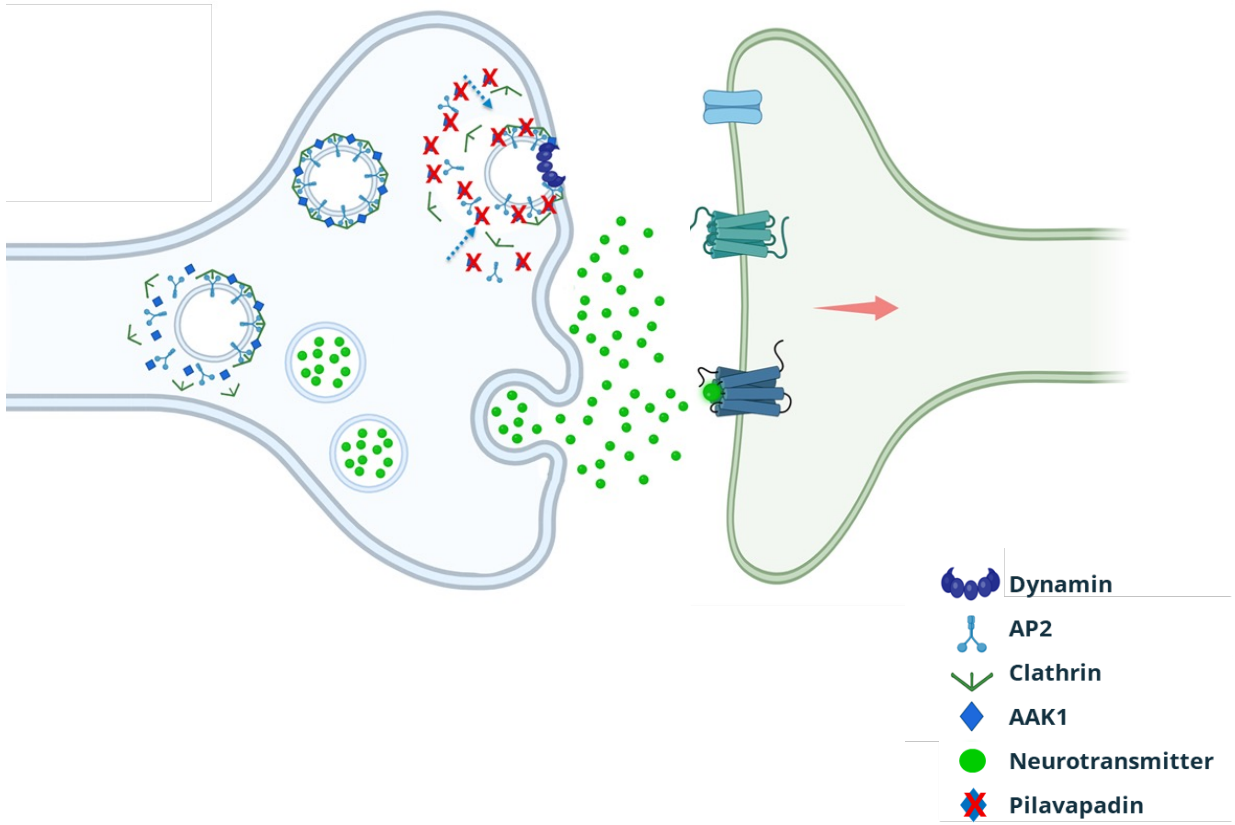
Spinal Nerve Ligation Model Is Key Assessment Specific to Neuropathic Pain

Clinical Data Reiterates Conviction for Pilavapadin 10 mg Dose for Diabetic Peripheral Nerve Pain (DPNP)

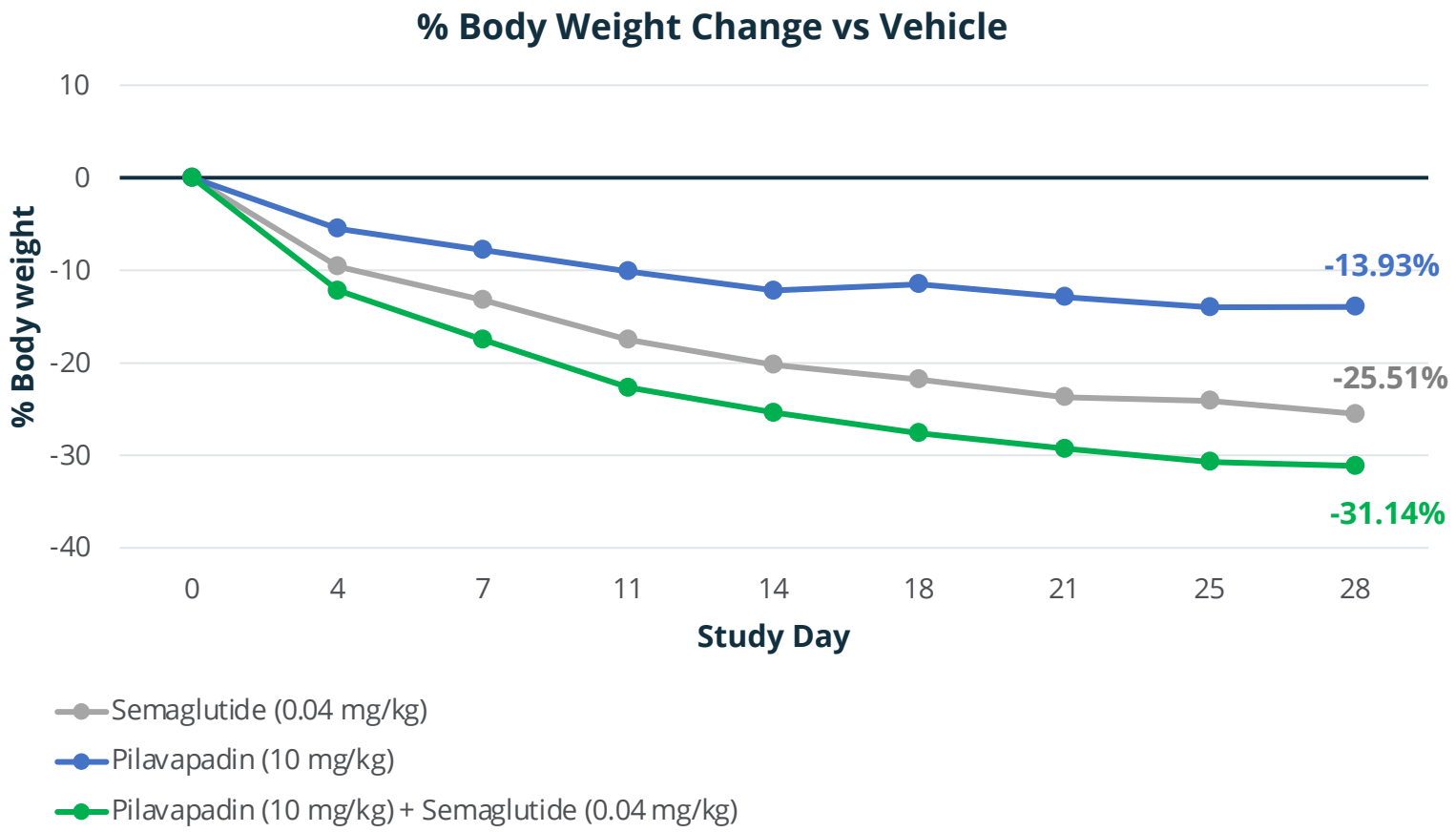
Novel, non-opioid target for treating neuropathic pain

Inhibits reuptake and recycling of neurotransmitters involved in pain signaling and spasticity

Phase 2b PROGRESS study **demonstrated reductions in average daily pain scores**; 10 mg dose ready for Phase 3 development



Significant Reduction in Body Weight from Baseline, Alone and in Combination With Semaglutide



- Pilavapadin drove a 13.9% reduction alone
- Combined with semaglutide, body-weight reduction reached 31.1% by Day 28

Broad and Significant Potential of AAK1 Target

DPNP

- PROGRESS Phase 2b results supporting selection of pilavapadin 10 mg for Phase 3 development in DPNP

Oral Presentation

Additional Efficacy Data Support Selection of Pilavapadin 10mg for Phase Three Development in DPNP: Results From PROGRESS

Suma Gopinathan, Ph.D., SVP of Discovery, Lexicon

American Academy of Neurology

Spasticity

- Evaluation of pilavapadin on spasticity-related endpoints in preclinical models of multiple sclerosis and spinal cord injury.

Poster Presentation

Preclinical Evidence Supporting Pilavapadin as a Novel Oral Therapy for Spasticity

Suma Gopinathan, Ph.D., SVP of Discovery, Lexicon

American Academy of Neurology

Obesity

- Pilavapadin drove significant body-weight reduction in a preclinical model, alone and in combination with semaglutide

Preclinical Data | Day 28

–13.9%
Pilavapadin alone
body-weight change

–31.1%
Pilavapadin + semaglutide
body-weight change

EVALUATING STRATEGIC OPTIONS

Financial Overview

Q3 2026 Financial Summary

$ (in millions except per share amounts)

	Q3 2026	Q3 2025
Total revenues	$11.3	$14.2
R&D	($16.2)	($18.8)
SG&A	($9.5)	($7.6)
Total operating expenses	($25.7)	($26.4)
Net loss	($14.0)	($12.8)
Net loss per common share	($0.03)	($0.04)

	As of September 30, 2026	As of December 31, 2025
Cash, cash equivalents, short-term investments and restricted cash	$183.2	$125.2
Total assets	$242.0	$185.0
Total debt	$51.9	$54.0

Q3 2026 Financial Highlights and FY 2026 Guidance

Q3 2026 Key
Financial Highlights



- Recognized $11.3 million in total revenue
  - Includes third $10 million payment from Novo Nordisk license agreement
  - Total of $30 million of milestone payments received from Novo Nordisk in 2026
  - $1.2 million in net sales of INPEFA

Full Year 2026 Guidance
Operating Expenses*



- Total 2026 operating expenses expected to be between $100 - $110 million
  - R&D expected between $63 - $68 million
    - Excludes expenses related to Phase 3 pilavapadin trials
  - SG&A expected between $37 - $42 million
    - Includes targeted investment in pre-commercialization activities

*As of November 5, 2026

Summary

Lexicon is Well Positioned for a Transformational Next 12 Months

OUR VISION

A future where people living with serious cardiometabolic diseases have more opportunities to live longer, healthier lives

01	SOTAGLIFLOZIN	HCM HEART FAILURE	• Pivotal Phase 3 readout Q1 2027 • **Potential broad HCM label path** • Pre-commercial planning and readiness ongoing • Ex-U.S. HF launch progressing
02	ZYNQUISTA	TYPE 1 DIABETES	• NDA resubmission anticipated Q1 2027 • Pending approval, poised to be **first and only** adjunct to insulin for glycemic control in decades
03	LX9851	OBESITY	• Phase 1 program advancing • **Potential path into later-stage development** • Additional milestones possible
04	PILAVAPADIN	PAIN OBESITY AAK1	• Phase 3 ready pain program • **Obesity investigation advancing** • Broader AAK1 opportunities under evaluation

Multiple potential value-creation paths across a broad cardiometabolic portfolio

Appendix

HCM Background

1. Sotagliflozin, a First-in-Class SGLT1/2 Inhibitor, Inhibits Clotting Potential in the Vessel via Inhibition of Platelet Activation, Integrin Activation, and Aggregation in Human Platelets
2. Sotagliflozin, a Dual SGLT 1 and 2 Inhibitor, Modulated Expression of Glucose Transport and Inflammatory Proteins in Endothelial Cells Following Angiotensin II Stimulation
3. Sotagliflozin Reduces Stroke Outcomes in Patients with Diabetes and Chronic Kidney Disease
4. SGLT1/2 inhibitor sotagliflozin, but not SGLT2-selective inhibitor empagliflozin, attenuates platelet activation and thrombosis
5. Effects of Sotagliflozin and Empagliflozin on Thrombus Formation in Healthy Volunteers: A Randomized Crossover Trial

Sotagliflozin MOA in HCM

SOLOIST-WHF	Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure
SCORED	Effect of sotagliflozin on major adverse cardiovascular events: a prespecified secondary analysis of the SCORED randomized trial
MOUSE MODEL	Sotagliflozin corrects myocardial phenotype, mitochondrial gene expression and oxidative stress in mice with hypertrophic cardiomyopathy
HUMAN TISSUE	Load-Dependent Effects of Sodium Glucose Co-Transporter Inhibitors on Work in Human Hypertrophic Cardiomyopathy Living Myocardial Slices

Landmark Studies Supporting HCM Evaluation

1. Patient Experiences with Hypertrophic Cardiomyopathy: A Conceptual Model of Symptoms and Impacts on Quality of Life
2. Diagnosis and Evaluation of Hypertrophic Cardiomyopathy: JACC State-of-the-Art Review
3. Stroke and Embolic Events in Hypertrophic Cardiomyopathy
4. Clinical Diagnosis of Hypertrophic Cardiomyopathy over Time in the United States (a Population-Based Claims Analysis)