May 2026 Investor Presentation

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.

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 licenses
- Establishment of new pilavapadin collaboration

Remain operationally disciplined and focused

to support long-term growth and value

Lead to Succeed

Year-to-Date 2026 Highlights

Advancing our pipeline of novel targeted therapies in cardiometabolic and pain

Cardiometabolic

SOTAGLIFLOZIN

HCM
Enrollment on track for mid-year enrollment completion

T1D
Preparing for NDA resubmission mid-year with STENO1 IIS data

Global Expansion – Heart Failure
Viatris launch underway in UAE; submitted applications for regulatory approval in an increasing number of ex-US and ex-Europe markets

LX9851

Obesity
Phase 1 study initiated by Novo Nordisk

Two $10 million milestone payments received

Chronic Pain

PILAVAPADIN

Neuropathic Pain
Regulatory path to Phase 3 pivotal studies clear

IND enabling work in multiple neuroscience indications

Engaging potential collaborators

CONTINUED COMMITMENT TO OPERATIONAL EXCELLENCE

HCM: hypertrophic cardiomyopathy; T1D: type 1 diabetes; STENO1: Multifactorial Intervention to Reduce Cardiovascular Disease in Type 1 Diabetes, Steno Diabetes Center Copenhagen (https://clinicaltrials.gov/study/NCT06082063)

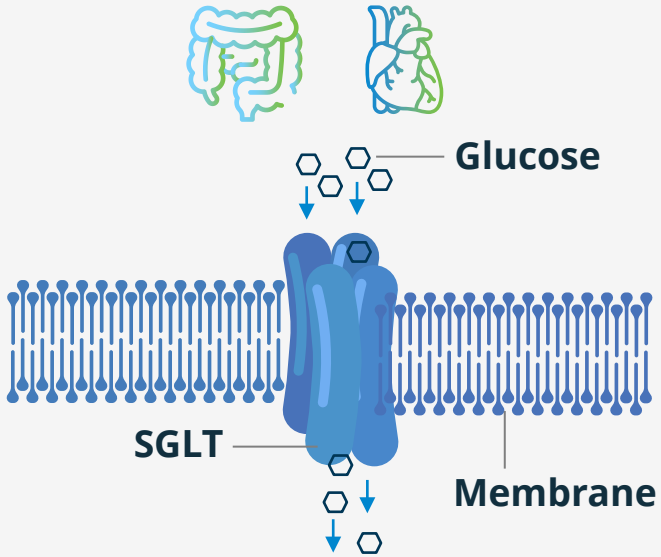
Cardiometabolic

SOTAGLIFLOZIN

Late-stage development programs in HCM and type 1 diabetes

Sotagliflozin Inhibits Two Targets With Important Cardiometabolic Profiles

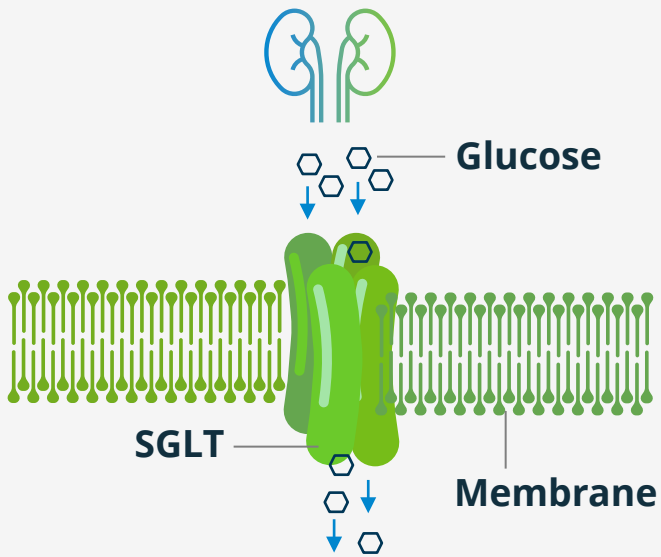
SGLT1 inhibitors work mainly in the gut and heart[1]



to slow sugar absorption from food

and to reduce work strain of the heart

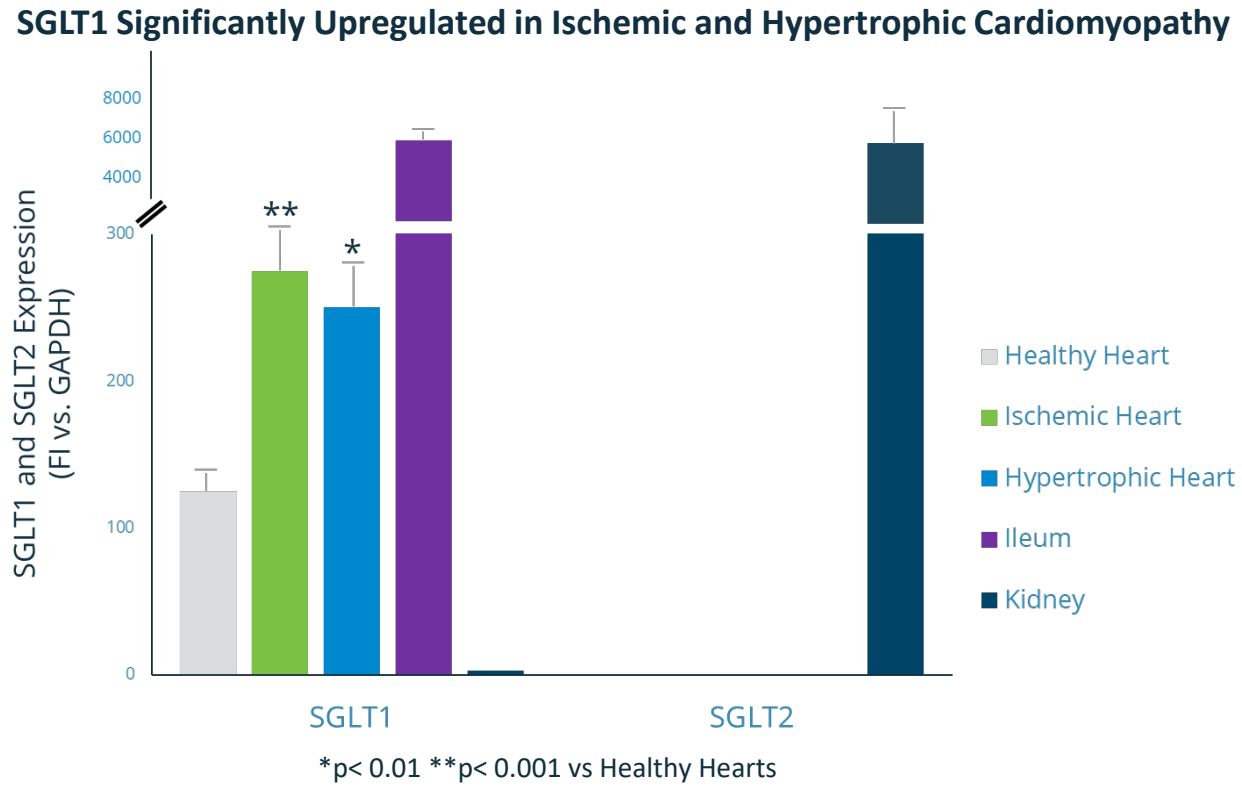
SGLT2 inhibitors work mainly in the kidneys[2]



to remove extra sugar from the body, which releases a small amount of salt and water, reducing the work strain on the heart

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.

SGLT1 is uniquely expressed in the intestine and in the heart



SGLT1 and *SGLT2* gene expression was assessed by QRT-PCR in ischemic and hypertrophic hearts compared to healthy hearts. Ileum and kidney were used as positive controls for *sglt1* and *sglt2* expression, respectively, viceversa representing negative controls for *SGLT1* and *SGLT2*. Data are expressed as mean ± SE target gene expression vs the housekeeping gene *gapdh*. Figure drawn for illustrative purposes; not to scale.

Only SGLT1 is expressed in cardiac tissue and is upregulated in hypertrophic hearts

Supports biological advantage **across a range of indications** where SGLT1 and SGLT2 are present

Figure drawn for illustrative purposes; not to scale.

Di Franco A et al. Int J Cardiol. 2017;243:86–90. doi:10.1016/j.ijcard.2017.05.032

Upcoming Milestones for Late-Stage Sotagliflozin Programs

HCM

- SONATA-HCM Phase 3 study, evaluating approximately 500 patients with **symptomatic HCM**
- Enrollment completion anticipated mid - 2026
- Patients now randomized across 130 active sites in 20 countries
- Topline data expected Q1 2027

Type 1 Diabetes

- On track for mid-2026 resubmission of the NDA for ZYNQUISTA as an adjunct to insulin for **glycemic control in adults with type 1 diabetes**
- Resubmission to include clinical data from the STENO1 investigator-initiated study
- Anticipate a six-month review with potential for approval this year

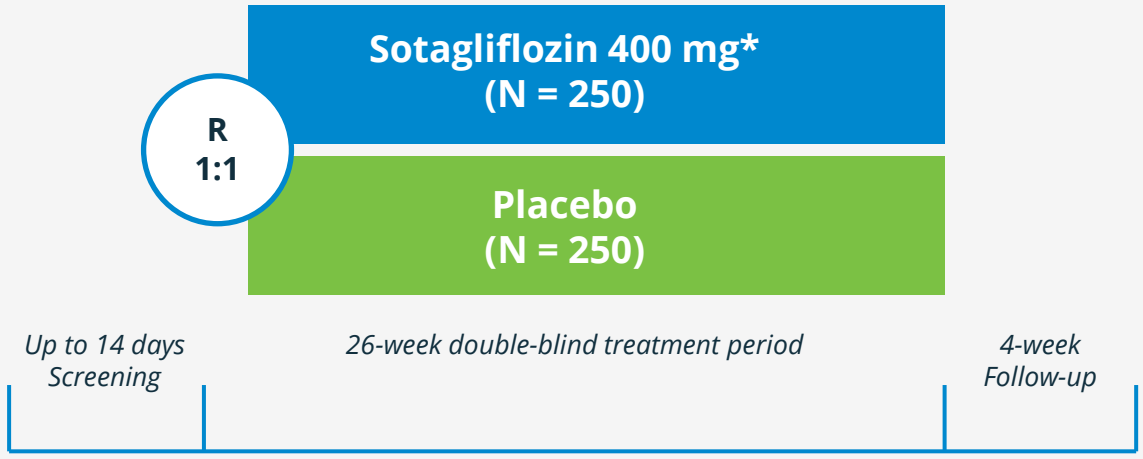
SONATA-HCM Phase 3 study for oHCM and nHCM

Primary endpoint:

Change from baseline in KCCQ CSS

Key Eligibility Criteria

- Adults with HCM (oHCM or nHCM)
- KCCQ23 CSS <85



For patients not tolerating treatment, sotagliflozin (and matching placebo) down-titrated to 200 mg starting at Week 4.

LVOT = left ventricular outflow tract; NYHA = New York Heart Association; KCCQ = Kansas City Cardiomyopathy Questionnaire; R = randomization.

Sotagliflozin is both a hemodynamic and metabolic agent in 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**
- Once-daily oral dosing enables broad potential adoption, **potentially as a first-line agent** with no REMS

Potential to be a first line therapy for treatment of symptomatic HCM

Continuing to generate data demonstrating mechanistic benefits of SGLT1 and SGLT2 inhibition

ATTD Advanced Technologies & Treatments for Diabetes 11-14 MARCH 2026 BARCELONA & ONLINE

Oral Presentation

Effect of Kidney Function on Efficacy and Safety of Sotagliflozin After 1 Year in Adults With Type 1 Diabetes

Michael Davies, Ph.D., Vice President, Clinical Development, Lexicon

March 2026

ACC.26

Moderated Poster

Sotagliflozin Improves Symptoms and Functional Capacity in Non Diabetic Patients With HFpEF: Results from the SOTA-P-CARDIA Trial

Dr. Juan Antonio Requena Ibanez, Icahn School of Medicine at Mount Sinai, NY

Moderated Poster

Epicardial and Hepatic Fat Reduction as a Potential Mechanism Of Sotagliflozin Benefit in Non-diabetic HFpEF

Dr. Juan J. Badimon, Icahn School of Medicine at Mount Sinai, NY

Moderated Poster

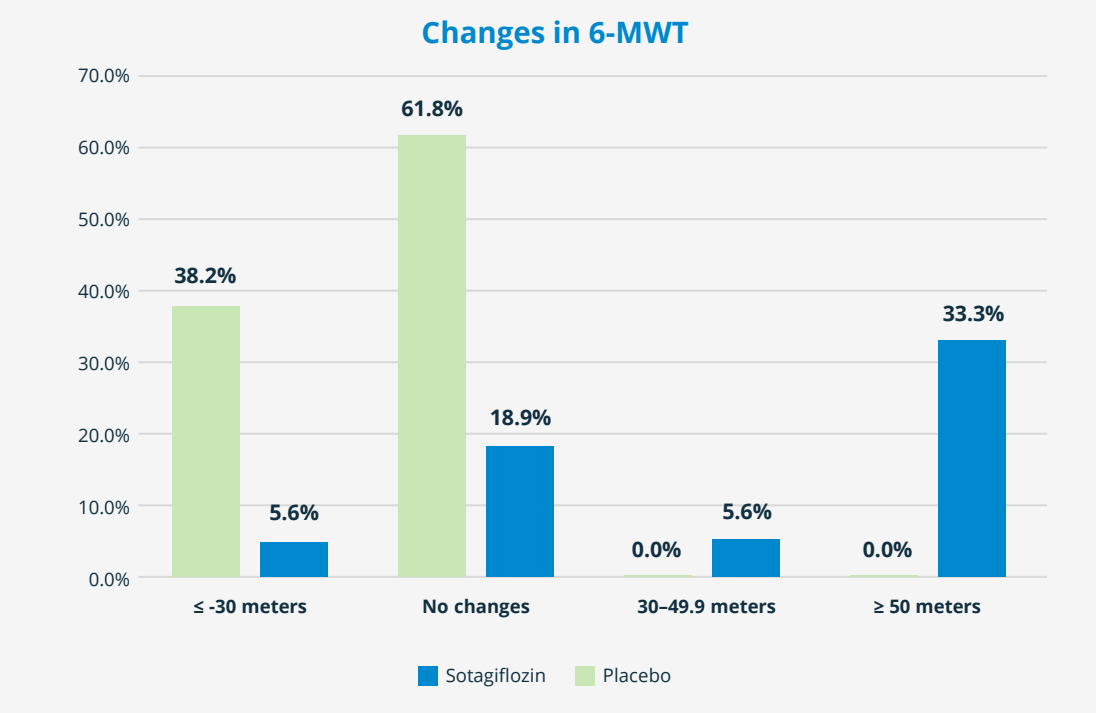
Efficacy of Sotagliflozin for Heart Failure and Major Adverse Cardiovascular Events by Body Mass Index: A Prespecified Analysis of SCORED

Dr. Deepak L. Bhatt, Director of Mount Sinai Fuster Heart Hospital

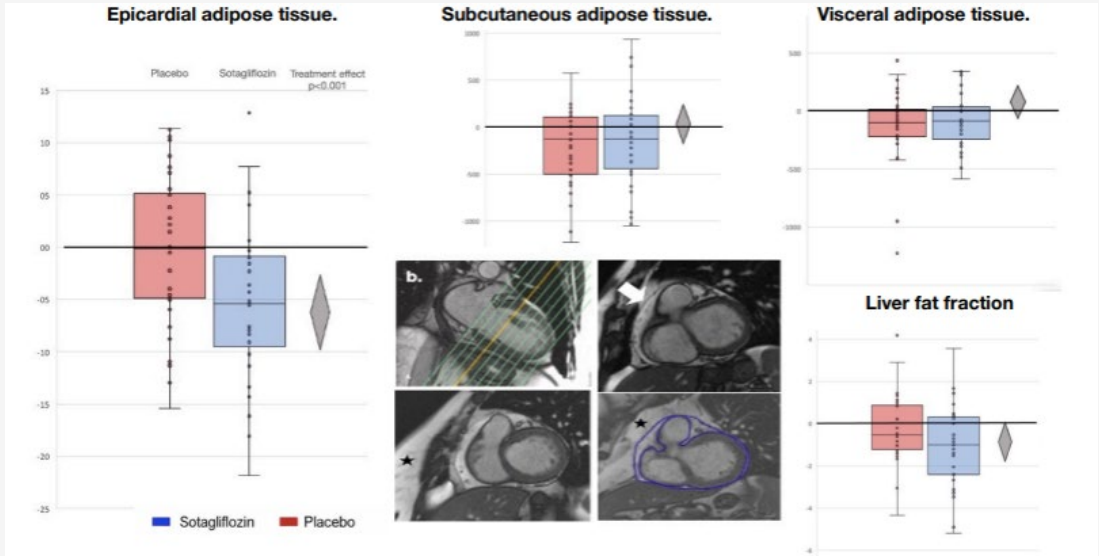
March 2026

SOTA-P-CARDIA provides evidence of benefits related to sotagliflozin's dual inhibition of SGLT 1 and 2

Significant improvements to health-related quality of life and physical limitations and reductions in epicardial fat



In non-diabetic HFpEF patients, sotagliflozin **significantly improved health-related quality of life and physical limitation** compared with placebo



In non-diabetic HFpEF patients, sotagliflozin **reduced epicardial adipose tissue** volume.

- Requena Ibanez, J et al. 26-A-20982-ACC SOTAGLIFLOZIN IMPROVES SYMPTOMS AND FUNCTIONAL CAPACITY IN NON DIABETIC PATIENTS WITH HFPEF: RESULTS FROM THE SOTA-P-CARDIA TRIAL. *JACC*. 2026 Mar, 87 (13_Supplement) A647. https://doi.org/10.1016/j.jacc.2026.02.1702
- Requena Ibanez, J et al. 26-A-16559-ACC EPICARDIAL AND HEPATIC FAT REDUCTION AS A POTENTIAL MECHANISM OF SOTAGLIFLOZIN BENEFIT IN NON-DIABETIC HFPEF. *JACC*. 2026 Mar, 87 (13_Supplement) A609. https://doi.org/10.1016/j.jacc.2026.02.1615

Preparing for ZYNQUISTA NDA resubmission in T1D with new clinical data

Zynquista™ (sotagliflozin) tablets 200 mg

- FDA confirmed **IIS study (STENO1) adequate** to support resubmission of NDA
- On track for **NDA resubmission mid-year**; expect a 6-month review, with **potential approval in 2026**
- **High unmet need remains** for adjunctive glycemic control in **1M adults in the US with T1D**, with no currently approved oral therapies
- **Overwhelming support for approval** from the T1D community

Phase 1 trial of LX9851 initiated by Novo Nordisk

- First-in-class, non-incretin, oral, small molecule inhibitor of ACSL5 in development for obesity and associated metabolic disorder
- Phase 1 study of LX9851 initiated in March
- Two $10 million development milestones achieved year-to-date, with potential to achieve a third $10 million milestone in 2026

Phase 1 program expected to be completed in Q1 2027

ACSL5: Acyl-CoA Synthetase 5

Chronic Pain

PILAVAPADIN

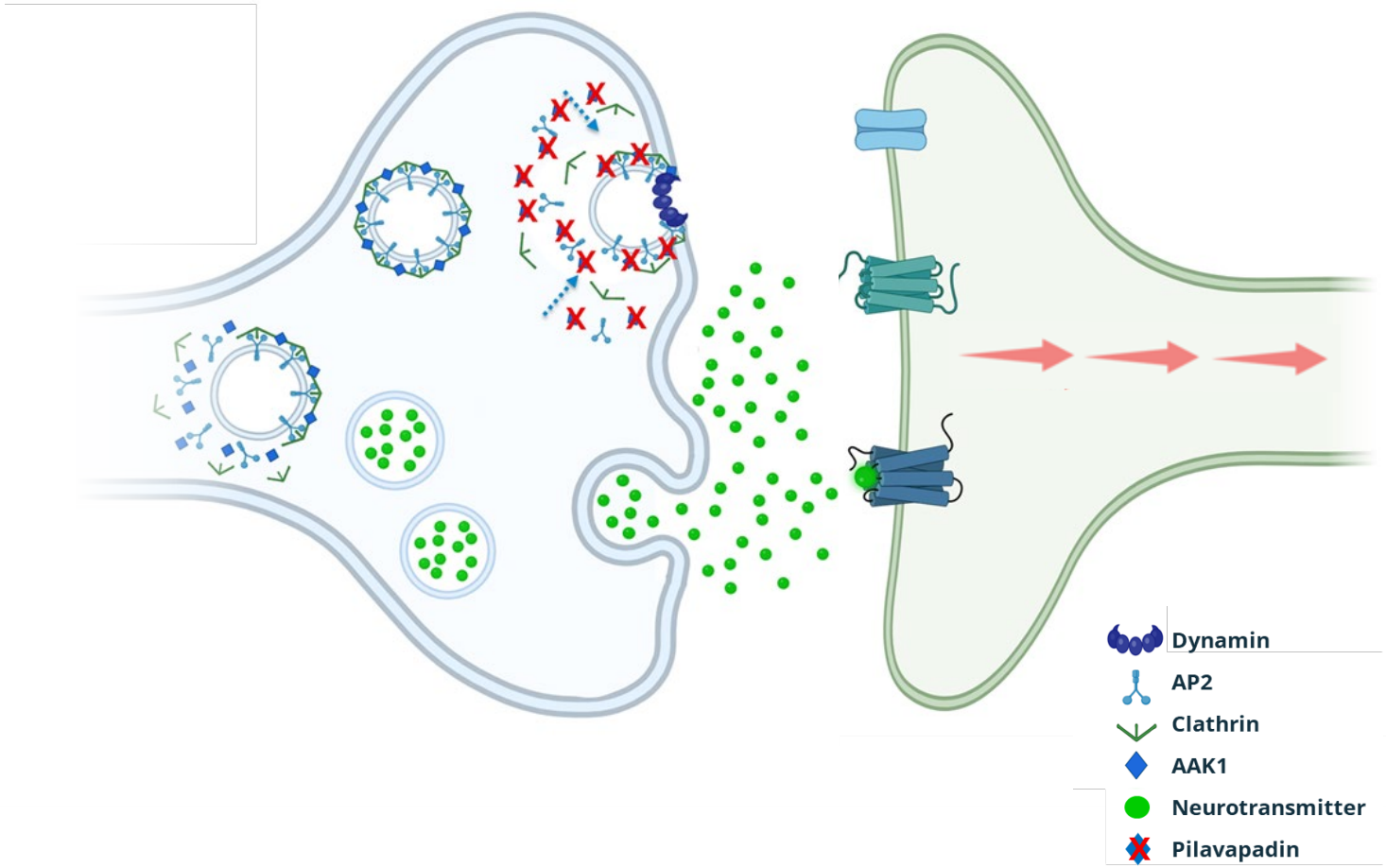
novel, non-opioid neuropathic pain investigational therapy

AAK1 is a novel target for neuropathic pain

Novel, non-opioid target
for treating neuropathic pain

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

Validated using a genetic knock-out model, preclinical studies, and **human clinical trials**



Clinical data reiterates conviction for pilavapadin 10 mg dose for DPNP and supports broad potential of novel AAK1 target

DPNP

- Additional 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

Neuropathic pain: A highly prevalent chronic condition with significant unmet need and opportunity for new treatments

Sizable market potential for DPNP

~9M

U.S. patients with progressive DPNP[1]

60%

of patients have tried multiple treatments[2]

- Majority of DPNP 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

1. Includes diagnosed patients only, CDC National Diabetes Statistics Report 2024. Source: prevalence rate of DPNP in diabetics is based on primary and secondary research; Source: Clearview Analysis. 2. Veeva Compass data; based on internal Lexicon claims analysis.

Environment supportive of non-opioid innovation in chronic pain

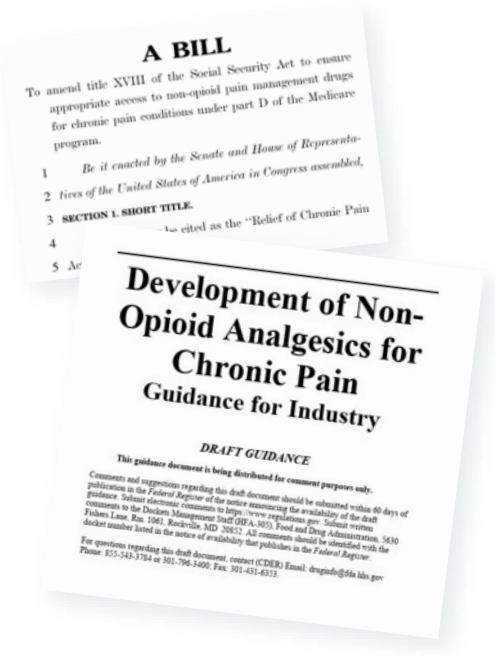
CHRONIC PAIN ROUNDTABLE
October 7, 2025

- Representatives across clinical, patient advocacy, and other experts actively advocating for recognition of chronic pain
- Focused on including people suffering from chronic pain in important pieces of legislation

CATALYSTS IN CHRONIC PAIN MANAGEMENT

Legislation introduced to expand access to non-opioid treatments for Medicare Part D patients

FDA Draft Guidance contemplates indication strategies and clinical trial design



What's next for pilavapadin?

Successful End-of-Phase 2 meeting with FDA

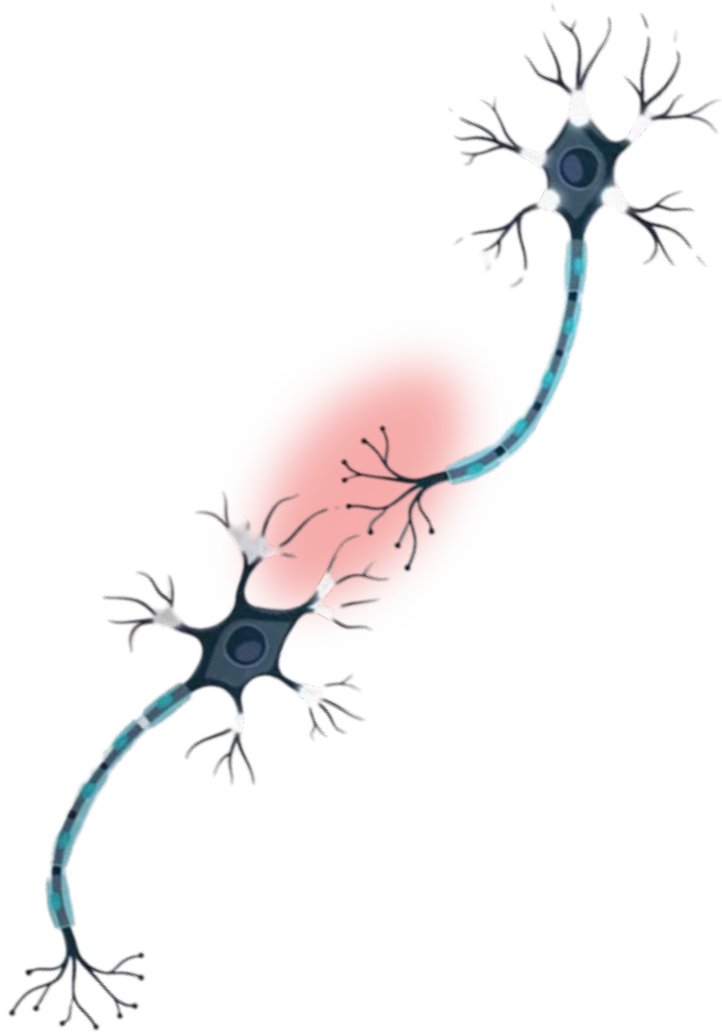
No objections raised to advancement into **Phase 3 development**

Optimized Phase 3 protocol

to reduce variability, including placebo effect; validated by **scientific advisory board**

Evaluating strategic options

Data support broad and significant potential



Financial Overview

Q1 2026 Financial Summary

$ (in millions except per share amounts)

	Q1 2026	Q1 2025
Total revenues	$21.1	$1.3
R&D	($12.8)	($15.3)
SG&A	($9.2)	($11.6)
Total operating expenses	($22.1)	($26.9)
Net loss	($1.0)	($25.3)
Net loss per common share	($ -)	($0.07)

	As of March 31, 2026	As of December 31, 2025
Cash, cash equivalents, short-term investments and restricted cash	$199.7*	$125.2
Total assets	$268.8	$185.0
Total debt	$49.7	$54.0

*Cash balance does not include a $10 million milestone payment received from Novo Nordisk in April 2026

Q1 2026 Financial Highlights and FY 2026 Guidance

Q1 2026 Key
Financial Highlights

- Recognized $21.1 million in total revenue
  - Reflects two $10 million milestone payments from Novo Nordisk
  - $1.1 million in net sales of INPEFA
- Operating expenses continue to decrease reflecting further efficiencies

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

*As of May 7, 2026

Lexicon enters into $100 million loan facility with Hercules Capital

Strengthens balance sheet and expands access to non-dilutive capital

- $55 million funded at close to repay existing loan facility with Oxford Finance
- Floating interest rate equal to the prime rate plus 3.1%, with a floor not less than 9.85%. Expected decrease in interest expense based on current rates
- Initial interest-only payment period of 18 months, subject to extension
- Extended principal payback period (30 months vs. previous 12 months)
- Two additional tranches totaling $45 million available under certain conditions

2026 is a pivotal year for Lexicon

Cardiometabolic

SOTAGLIFLOZIN

HCM

SONATA **enrollment completion** on target for mid-2026

Heart Failure

Viatris **ex-U.S. / ex-Europe efforts ongoing** with launch in UAE and several approvals anticipated, including Canada and Australia

T1D

On track for **NDA resubmission** mid-year, with potential for approval in 2026

LX9851

Obesity

Phase 1 study ongoing

$20 million in milestones received; potential **for additional $10 million near-term**

Chronic Pain

PILAVAPADIN

Neuropathic Pain

Ongoing evaluation of **strategic options**

IND-enabling work for **additional indications continues**

Appendix

Lexicon pharmaceuticals

Hyperlinked Reference List – Sotagliflozin MOA and HCM

- Sotagliflozin MOA
  - 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
  - Sotagliflozin, a Dual SGLT 1 and 2 Inhibitor, Modulated Expression of Glucose Transport and Inflammatory Proteins in Endothelial Cells Following Angiotensin II Stimulation
  - Sotagliflozin Reduces Stroke Outcomes in Patients with Diabetes and Chronic Kidney Disease

- Landmark Studies
  - 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

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

Effects of SGLT1 Inhibition Demonstrated in Animal Models

Disease	Disease Model	*Knockout/Knockdown Model* or SGLT Inhibitor	Target Organ/System		
			Heart	Kidney	Metabolic
Type 1 diabetes	Akita/+ mouse[1]	*Sglt1*$^{-/-}$		↓ GFR ↓ Albuminuria	↓ Blood glucose ↑ Body weight
	STZ mouse[2]	*shSGLT1* (siRNA)	↓ LVEDV/LVESV ↑ Ejection fraction ↑ Fractional shortening ↓ ROS/mitochondrial dysfunction		
Diabetic Kidney Disease	Adenine-induced RF mouse[3]	SGL5213		↓ BUN/Cr Levels ↓Gut-derived uremic toxins	↓ Body weight ↓TMAO
Cardiomyopathy	*PRKAG2* (TG^{T400N})[4]	*TG*^{T400N}/*TG*$^{SGLT1\text{-}DOWN}$ (siRNA)	↓ Heart : body weight ↓ LVEDV		
	Chronic pressure overload[5]	*Sglt1*$^{-/-}$	↓ LVEDV ↑ Fractional shortening ↓ Heart : body weight		
	STZ mouse[6] Failing Human Heart Tissue	phlorizin	↑ Cardiac SGLT1 Expression ↑ Functional changes in SGLT1 in Dz ↑ SGLT1 modulated cardiac glucose uptake		
	STZ mouse[7] DCM Human Serum Samples	mizagliflozin	↑ LVEF, LVSF, FVEDD, & LVESD ↓ Myocardial fibrosis ↓ Myocardial apoposis		↓ Blood glucose

GFR = glomerular filtration rate; LVEDV = left ventricular end diastolic volume; LVESV = left ventricular end systolic volume; LVEF = left ventricular ejection fraction; LVSF = left ventricular systolic function; FVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; TMAO = trimethylaminc N oxide; siRNA = small interfering RNA; STZ = streptozotocin.

1. Song P et al. *Am J Physiol Renal Physiol*. 2019;317: F207–F217. doi:10.1152/ajprenal.00120.2019 2. Wu W et al. *Arch Biochem Biophys*. 2021;709:108968. doi:10.1016/j.abb.2021.108968 3. Ho H et al. *Physiological Reports* 2021; 9: 1-17 doi/10.14814/phy2.15092 4. Ramratnam M et al. *J Am Heart Assoc*. 2014;3:e000899 doi: 10.1161/JAHA.114.000899 5. Matsushita N et al. *Int Heart J*. 2018;59:1123-1133. doi:10.1536/ihj.17-565 6. Banergee S et al. *Cardiovascular Research.* 2009; 84: 111-118 doi:10.1093/cvr/cvp190 7. Lin N et al. *Frontiers in Pharmacology* 2021; 11: 598353 doi.org/10.3389/fphar.2020.598353