Fourth Quarter and Full Year 2025 Earnings

March 5, 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.

Business Highlights

Mike Exton Ph.D.
Director and Chief Executive Officer

2025 Accomplishments

Advancing our pipeline of novel targeted therapies in cardiometabolic and pain

Cardiometabolic

SOTAGLIFLOZIN

HCM
All sites initiated

Accelerated enrollment

T1D
Identified path forward for NDA resubmission with FDA using STENO1 IIS data

Global Expansion
Viatris submitted applications for regulatory approval for Heart Failure in six ex-US and ex-Europe markets, with approval in UAE

LX9851

Obesity
Worldwide license with Novo Nordisk

IND-enabling studies completed

Chronic Pain

PILAVAPADIN

Neuropathic Pain
PROGRESS readout + post hoc Phase 2 analyses

EOP2 meeting completed

Engaged 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)

Ambitions for 2026

Advance our late-stage regulatory programs

- SONATA-HCM
- ZYNQUISTA®

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

2026 is off to a strong start

- Confirmation of successful FDA End-of-Phase 2 meeting for pilavapadin in DPNP
- Strengthened financial position with more than $100 million in additional cash from capital raise and Novo Nordisk milestone payment
- Phase 3 SONATA-HCM study on track for mid-year completion of enrollment
- Progressed regulatory path for potential NDA resubmission for Zynquista in T1D

Pipeline Updates

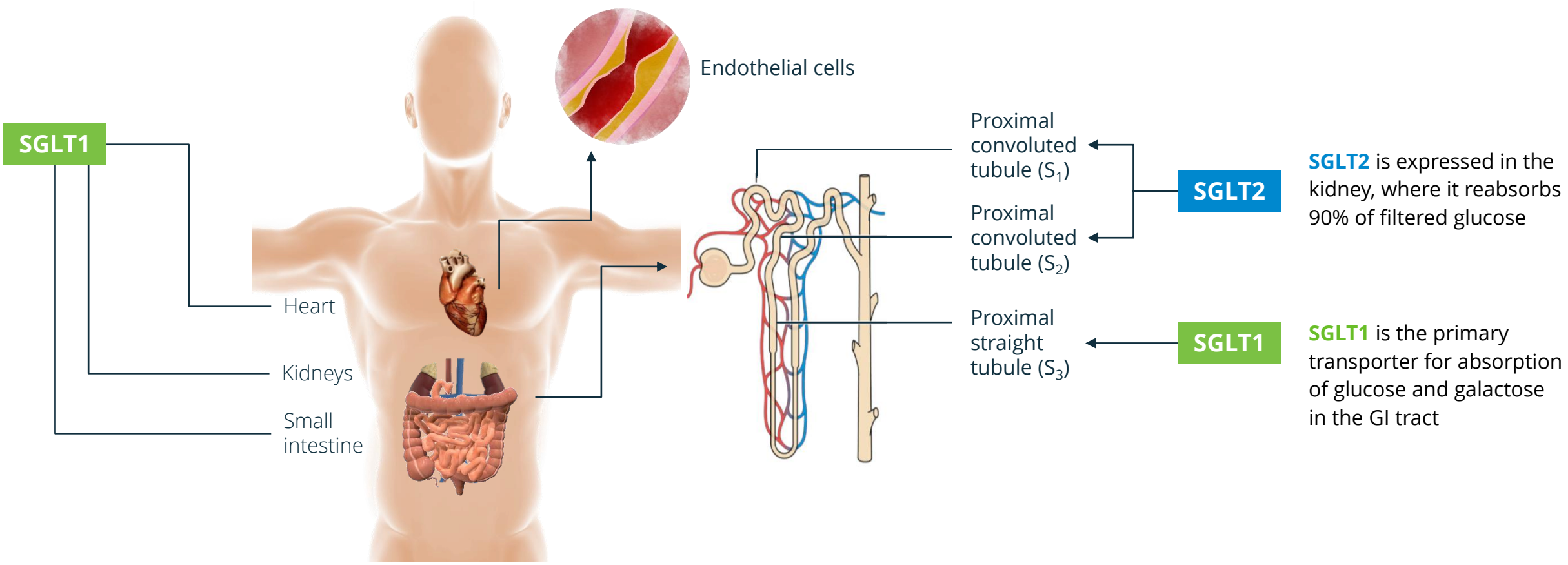
Craig Granowitz, M.D. Ph.D.
Senior Vice President and Chief Medical Officer

Cardiometabolic

SOTAGLIFLOZIN

Late-stage development programs in HCM and type 1 diabetes

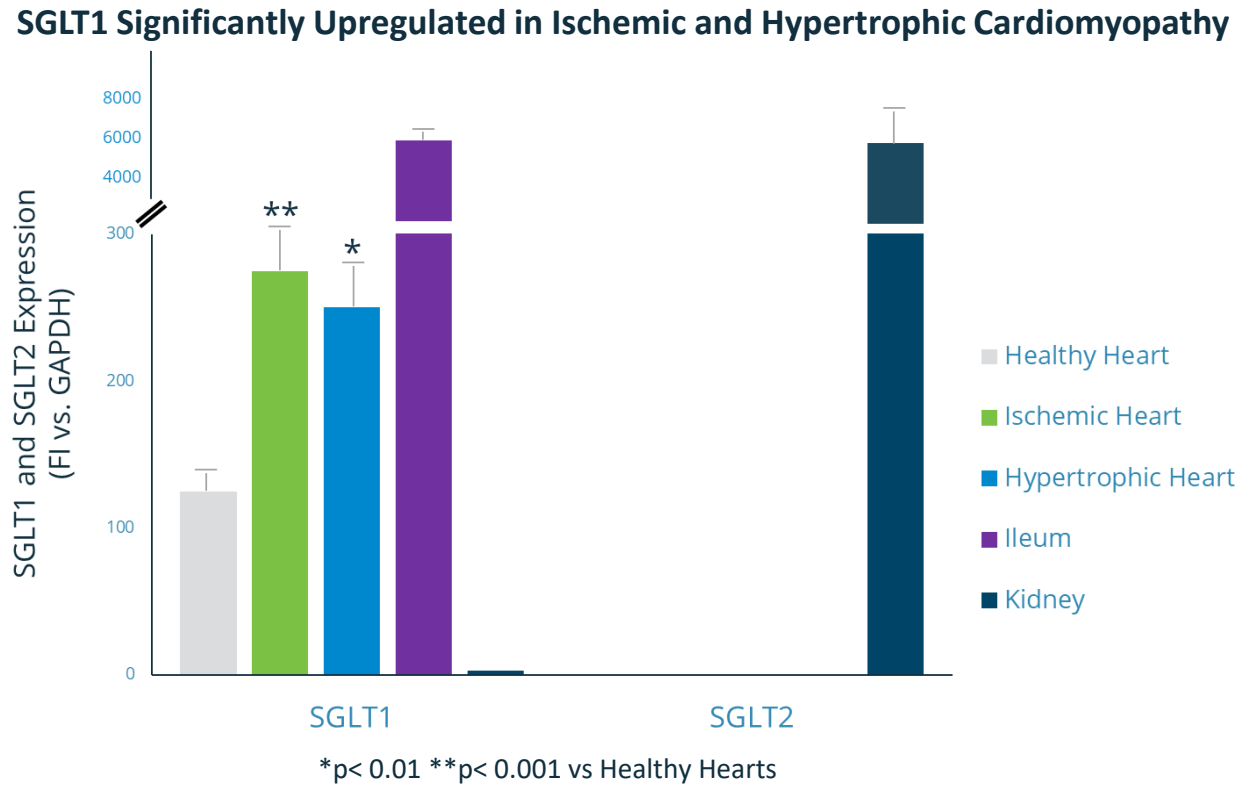
Sotagliflozin Inhibits Two Targets With Important Cardiometabolic Profiles



SGLT2 is expressed in the kidney, where it reabsorbs 90% of filtered glucose

SGLT1 is the primary transporter for absorption of glucose and galactose in the GI tract

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

Cardiometabolic program highlights

HCM

- SONATA-HCM Phase 3 study, evaluating approximately 500 patients with **obstructive or non-obstructive HCM**, anticipate mid - 2026 enrollment completion
- Patients now randomized across 130 active sites in 20 countries
- Topline data anticipated in Q1 2027

Type 1 Diabetes

- On track for 2026 resubmission and potential approval of the NDA for ZYNQUISTA as an adjunct to insulin for **glycemic control in adults with type 1 diabetes** based on clinical data from the STENO1 investigator-initiated study

SONATA-HCM Phase 3 study for oHCM and nHCM

Target achieved — all 130+ sites initiated with **enrollment on track**

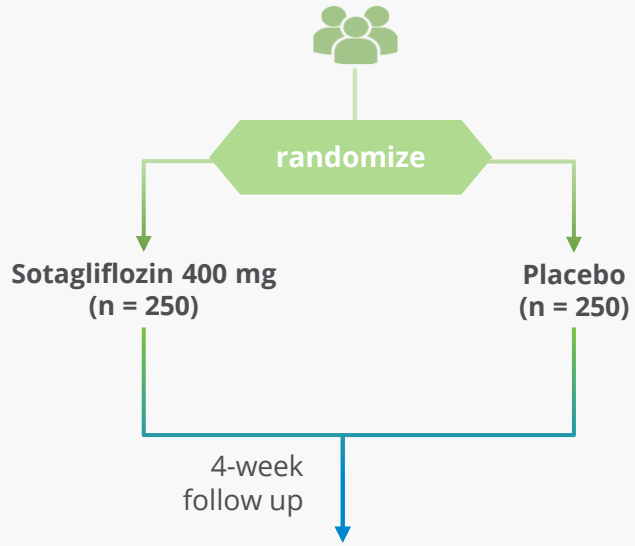
Global footprint — Sites active in **US, EU, UK, Israel, and LATAM**

Broad potential — Only ongoing trial in both **obstructive and non-obstructive HCM**

SONATA-HCM Study Schema

Patient Population

- Adults with HCM
- LVEF ≥50% or ≥55% for those on a CMI
- KCCQ23 CSS <85
- NYHA Class II or III



Double-Blind Treatment
26 weeks

Primary Endpoint

- Change from baseline in KCCQ Clinical Summary Scale score

CMI: cardiac myosin inhibitor

Potential competitive advantages of sotagliflozin in oHCM and nHCM

- The only HCM agent that **works inside and outside the heart** to reduce symptoms of HCM, as well as reduce HF and MACE events
- SGLT1 inhibition acts 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
- Approved for heart failure with **no observed increased risk of Afib to date**

Proposed indication for both nHCM and oHCM, with potential for use alone or in combination

Investigator-initiated studies complement ongoing registrational study

SOTA-P-CARDIA

- Investigated cardiorenal mechanistic benefits of sotagliflozin in **HFpEF without diabetes**
- 88 patients, 6-month treatment period
- Only SGLTi to demonstrate improvements in symptoms and cardiac function (KCCQ, LVM)

SOTA-CROSS

- Estimated completion in 2027
- Evaluating sotagliflozin on physical function in **symptomatic nHCM**
- 12-week crossover study
- 26 patients

SONATA-HCM

- Evaluating sotagliflozin in patients with **both subtypes of symptomatic HCM**
- 26-week study
- Approximately 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)

SOTA-P-CARDIA: A Randomized Trial of Sotagliflozin in HFpEF Patients Without Diabetes, Icahn School of Medicine at Mount Sinai (https://clinicaltrials.gov/study/NCT05562063);
SOTA-CROSS: Sodium Glucose Co-transporter (SGLT) Inhibitors in Nonobstructive Hypertrophic Cardiomyopathy, University of Pennsylvania (https://clinicaltrials.gov/study/NCT06433050)

Unique benefits of sotagliflozin and SGLT1 inhibition in HFpEF provide possible readthrough to HCM

HCM SOCIETY

Oral Presentation

Dual SGLT1 and 2 Inhibition with Sotagliflozin Ameliorates Adverse Cardiac Remodeling and Diastolic Dysfunction in Mice with HCM Due to Tropomyosin E180G Mutation

Dr. Fuzhong Qin, BU Medical Center, Boston, MA

November 2025

American Heart Association.

Late-breaker Oral Presentation

SOTA-P-CARDIA Trial: a Randomized Trial of Sotagliflozin in HFpEF Patients Without Diabetes

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

Poster Presentation

Effects on Major Adverse Cardiovascular Events in Persons Treated with Sotagliflozin: Prespecified Pooled Analyses of the Phase 3 Type 2 Diabetes Program

Dr. Darren McGuire, UT Southwestern, Dallas, TX

November 2025

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

March 2026

ZYNQUISTA resubmission in T1D planned based on new clinical data

- Type D meeting with FDA confirmed **IIS study (STENO1) adequate** to support resubmission of NDA if patient exposure and safety data requirements are achieved
- Current exposure trajectory and safety data support potential **NDA resubmission** and **regulatory 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

Global development of LX9851 on track with licensee Novo Nordisk

- IND-enabling studies fully completed and delivered to Novo Nordisk
- Initial $10 million milestone achieved, with potential to achieve $20 million in additional development milestones in 2026
- Ongoing support for ACSL5-targeted mechanism; recently featured paper in the *Journal of the Endocrine Society*

Featured paper – March edition

Acyl-CoA Synthetase 5 Knockout and Inhibitors Protect Against Diet-Induced Obesity in Mice by Activating the Ileal Brake

David R Powell and others

Genes regulating body fat are shared by mice and humans, and mouse knockout phenotypes for known drug targets correlate well with drug efficacy, suggesting that mouse knockout phenotyping can identify anti-obesity drug targets. Mice with an intestine-specific *Acsl5* knockout are protected from high-fat diet (HFD)-induced obesity, insulin resistance, glucose intolerance and hepatic steatosis, and show increased GLP-1 levels, delayed gastric emptying (GE), and decreased food consumption (FC).

ACSL5: Acyl-CoA Synthetase 5

Powell DR et al. J Endocr Soc. 2025;10(2):bvaf196. doi:10.1210/jendso/bvaf196

Chronic Pain

PILAVAPADIN

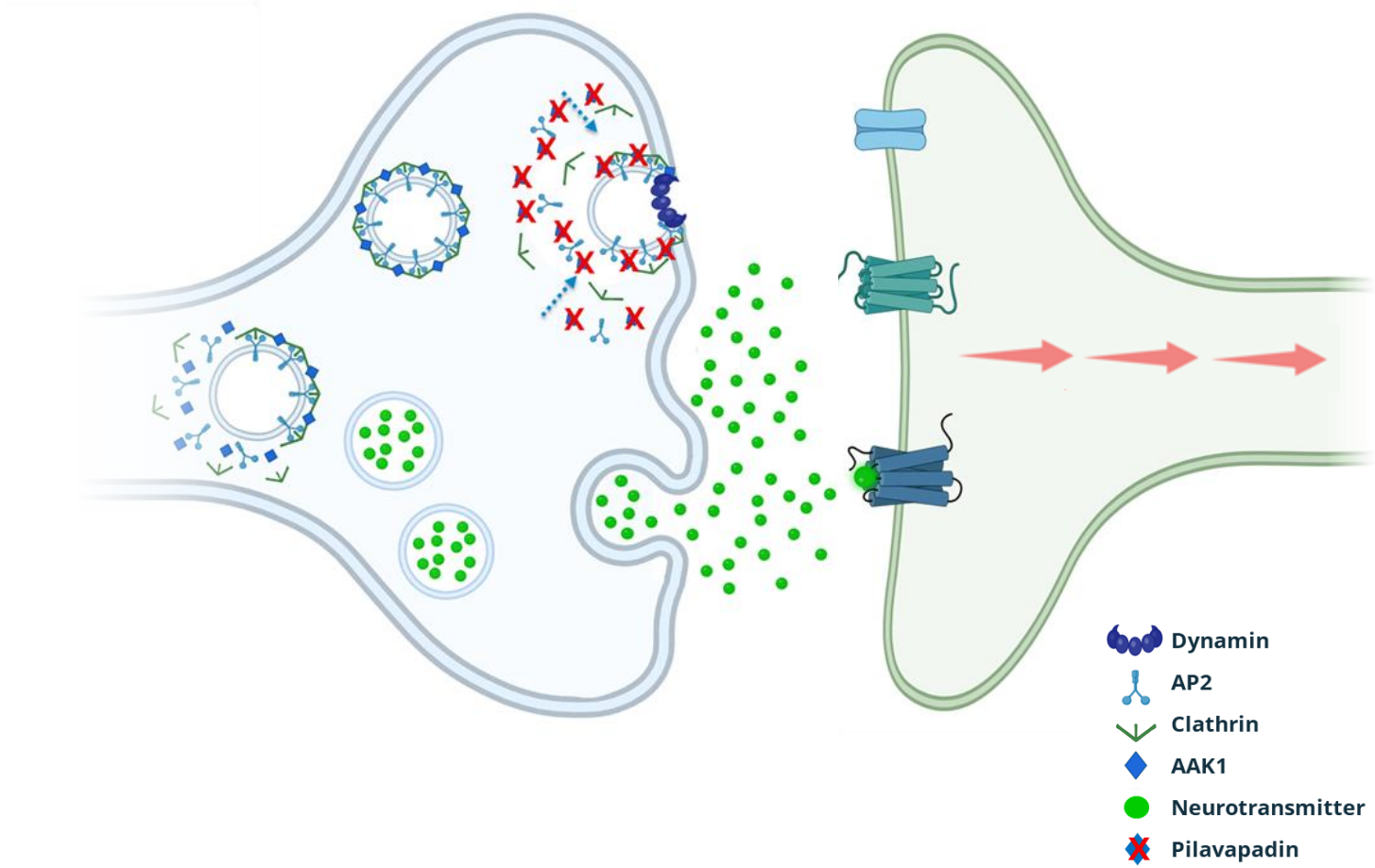
non-opioid neuropathic pain investigational therapy

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**



What's next for pilavapadin?

Successful End-of-Phase 2 meeting with FDA

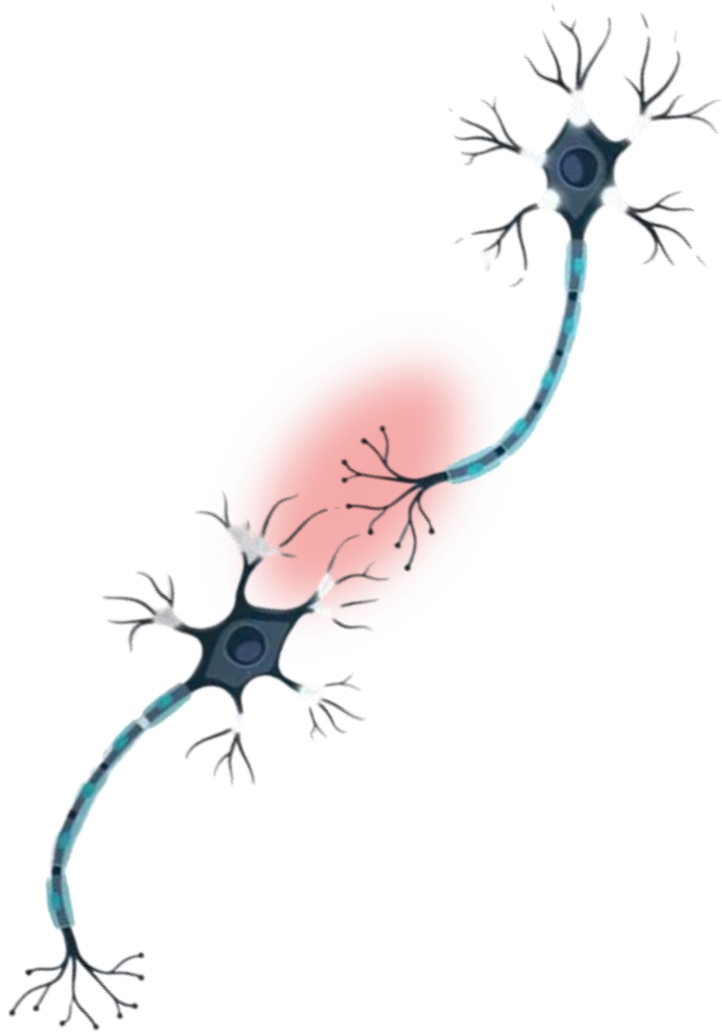
No objections raised to advancement into **Phase 3 development**

Optimized Phase 3 protocol

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

Partnership discussions progressing

Following **completion of EOP2 process**



Financial Overview

Scott Coiante
Chief Financial Officer

Q4 and Full Year 2025 Financial Summary

$ (in millions except per share amounts)

	Q4 2025	Q4 2024	FY 2025	FY 2024
Total revenues	$5.5	$26.6	$49.8	$31.1
R&D	$11.3	$26.7	$61.1	$84.5
SG&A	$8.8	$32.3	$37.3	$143.1
Total operating expenses	$20.3	$59.3	$98.7	$228.2
Net loss	($15.5)	($33.8)	($50.3)	($200.4)
Net loss per common share	($0.04)	($0.09)	($0.14)	($0.63)

	As of December 31, 2025	As of December 31, 2024
Cash, cash equivalents, short-term investments and restricted cash	$125.2	$238.0
Total assets	$185.0	$298.4
Total debt	$54.0	$100.3

Q4 and Full Year 2025 Financial Highlights

Q4 2025 Key
Financial Highlights

- Recognized $5.5 million in total revenue
  - $4.3 million of licensing revenue under Novo Nordisk license agreement
  - $1.1 million in net sales of INPEFA
- Quarter over quarter operating expenses decreased by $39 million

Full Year 2025
Financial Highlights

- Recognized $49.8 million in total revenue for 2025
  - Driven by upfront payment of $45 million in April 2025 under Novo Nordisk license agreement
  - $4.6 million in net sales of INPEFA
- Total year over year operating expenses decreased by $129.5 million
  - Driven primarily by strategic repositioning in late 2024 and significantly reduced marketing and promotional efforts for INPEFA in 2025
- Reduced long-term debt
  - Debt reduction of $46.3 million in 2025, primarily leveraging the Novo Nordisk upfront payment

Full Year 2026 Financial Guidance

Full Year 2026
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 March 5, 2026

Summary

Mike Exton Ph.D.
Director and Chief Executive Officer

2026 a pivotal year with significant potential catalysts

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** with potential for approval in 2026

LX9851

Obesity

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

Chronic Pain

PILAVAPADIN

Neuropathic Pain

Ongoing partnership discussions

IND-enabling work for **additional indications**

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

Lexicon pharmaceuticals

THANK YOU

Lexicon pharmaceuticals

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