September 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
- Strategic options for pilavapadin in Neuropathic Pain and other indications

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

Cardiometabolic

SOTAGLIFLOZIN

HCM
Phase 3 SONATA-HCM enrollment now complete

Topline data expected Q1 2027

T1D
STENO1 (third-party IIS) achieved patient exposure years discussed with FDA

Data reflects DKA rates similar 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 underway by Novo Nordisk

Three $10M milestone payments received in 2026

AAK1

PILAVAPADIN

Neuropathic Pain
DPNP regulatory path to Phase 3 pivotal studies clear

Other Indications
IND-enabling work ongoing across multiple indications

CONTINUED COMMITMENT TO OPERATIONAL EXCELLENCE

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

Pivoting toward pre-commercial planning to maximize asset value

Named Rachel Martens Chief Commercial Officer

- Pivot responsibilities to focus on market access, market research and pre-commercial planning activities
- Marketing and Market access roles added to focus on market positioning – named new head of marketing for sotagliflozin

Enhanced Capabilities within Medical Organization

- Medical science liaisons added
- Focused on driving education of novel SGLT 1 and 2 mechanism

CONTINUED COMMITMENT TO OPERATIONAL EXCELLENCE

Cardiometabolic

SOTAGLIFLOZIN

Late-stage development programs in HCM and type 1 diabetes

Hypertrophic cardiomyopathy (HCM) is characterized by adverse cardiac remodeling associated with myocardial hypertrophy, diastolic dysfunction and fibrosis

Qin, Fuzhong & Pimentel, David & Baka, Tomas & Zhang, Aifeng & Croteau, Dominique & Luptak, Ivan & Colucci, Wilson. (2025). Abstract 4343284: Dual SGLT1 and 2 Inhibition with Sotagliflozin Ameliorates Adverse Cardiac Remodeling and Diastolic Dysfunction in Mice with HCM Due to Tropomyosin E180G Mutation. *Circulation*. 152. 10.1161/circ.152.suppl_3.4343284.

Diastolic Dysfunction is the Underlying Fundamental Issue of Both oHCM and nHCM

nHCM

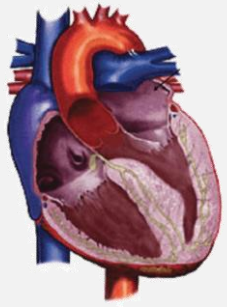
Characterized by global or localized thickening without a significant outflow tract pressure gradient.

LVOT Gradient
< 30 mmHg

Many presentations… one disease

HYPERTROPHIC CARDIOMYOPATHY

Without Obstruction



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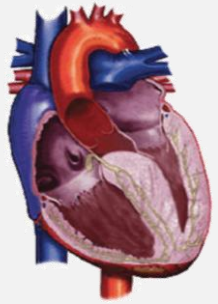


oHCM

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

LVOT Gradient
≥ 30 mmHg

DIASTOLIC DYSFUNCTION
The heart is too stiff to fill properly during relaxation

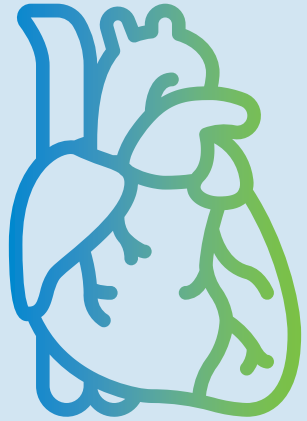
Source: HCMAi, Hypertrophic Cardiomyopathy Association

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.

SONATA-HCM Enrollment Complete

Pivotal study of sotagliflozin fully randomized; topline data anticipated Q1 2027

>500
Patients randomized, substantially exceeding enrollment target

130+
Clinical sites across 20 countries

nHCM + oHCM
Only ongoing Phase 3 study in both HCM subtypes

Q1 2027
Topline results anticipated

Study highlights

- Largest Phase 3 study to date including both non-obstructive (nHCM) and obstructive (oHCM) hypertrophic cardiomyopathy
- Substantial majority of patients have nHCM, a group with limited effective treatment options
- Randomized, double-blind, placebo-controlled trial; primary endpoint is change from baseline to week 26 in KCCQ Clinical Summary Score
- Sotagliflozin is a dual SGLT1 + SGLT2 inhibitor with a differentiated mechanism vs available HCM treatments

> *"Having a well-tolerated medication with a distinct mechanism of action that can complement other therapies would be an important advance for physicians and patients"*

Sharlene M. Day, M.D.,
co-principal investigator for SONATA-HCM, Presidential Professor, Director of Translational Research of the Penn Cardiovascular Institute, University of Pennsylvania

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

Early Market Insights Indicate Significant Opportunity for Sotagliflozin in HCM

CARDIAC MYOSIN INHIBITORS

oHCM efficacy—with mechanism tradeoffs

- Approved for symptomatic obstructive HCM
- Reduce force-producing myosin interactions
- Can cause heart failure from systolic dysfunction
- Multiple nHCM tests did not establish sufficient clinical benefit

REMS — restricted prescribing + scheduled LVEF echocardiograms

$$$$ — Specialty tier pricing with associated access restrictions

SOTAGLIFLOZIN | PHASE 3

A different mechanism — and a broader strategic role[2]

- Dual SGLT1/SGLT2 inhibition targets underlying cause of HCM
- Broad proposed indication for both obstructive + non-obstructive HCM
- Established safety profile in heart failure with limited observed side effects
- Potential for use as a standalone or combination therapy

INITIAL RESEARCH INSIGHTS (IF APPROVED)[1]

nHCM — High unmet need + HCP willingness to adopt as 1L / 2L

oHCM — Flexibility to address individual patient needs (clinical and cost)

$$ — A thoughtful pricing strategy could support unencumbered access and unlock sequencing headroom

Sources: FDA CAMZYOS PI (2025); FDA MYQORZO PI (2025); Ho et al., JACC 2020 (MAVERICK-HCM); Desai et al., NEJM 2025 (ODYSSEY-HCM); ClinicalTrials.gov NCT06481891. [1]Company market assessment. [2]Sotagliflozin is not approved for HCM; any future indication, prescriber access, monitoring, or REMS requirements would be determined by FDA.

Data Received to Date from STENO1 Supports ZYNQUISTA NDA Resubmission

- Achieved years of patient exposure discussed with FDA
- Diabetic ketoacidosis (DKA) rates in the exposed population similar to standard of care in STENO1 and well below rates in treated patients in InTandem studies
- STENO1 providing patient-level data; NDA resubmission anticipated in Q4 2026

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
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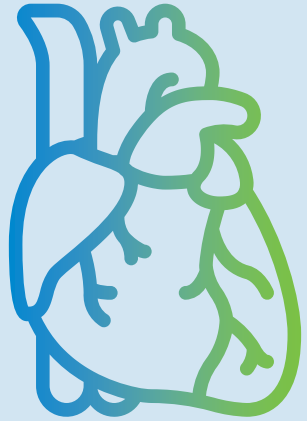

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SONATA-HCM Phase 3 Study for oHCM and nHCM

Enrollment complete; 26-week study with topline data anticipated Q1 2027

SONATA-HCM Enrollment Complete

>500 patients randomized, including both nHCM and oHCM

Topline results anticipated Q1 2027

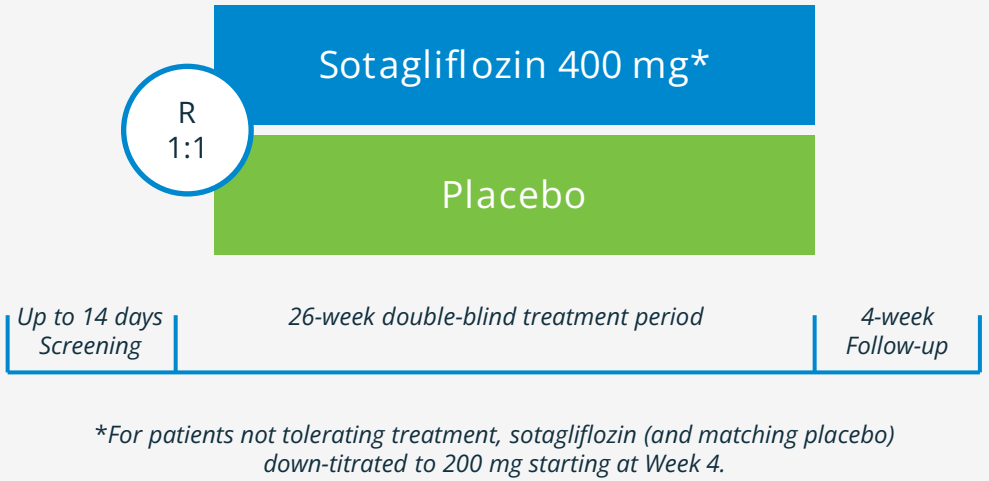
Largest Phase 3 study to date of both nHCM and oHCM

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.

Potential to be a first-line therapy in symptomatic HCM

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Sotagliflozin is both a Hemodynamic and Metabolic Agent in 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

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- STENO1 providing patient-level data; NDA resubmission anticipated in Q4 2026

Phase 1 Trial of LX9851 Ongoing by Novo Nordisk

- First-in-class, non-incretin, oral, small molecule inhibitor of ACSL5 in development for obesity and associated metabolic disorders
- Phase 1 study of LX9851 initiated in March
- Eligible to receive up to $1 billion in total upfront and milestone payments, plus royalties on net sales

Three $10 million milestones achieved in 2026

ACSL5: Acyl-CoA Synthetase 5

AAK1

PILAVAPADIN

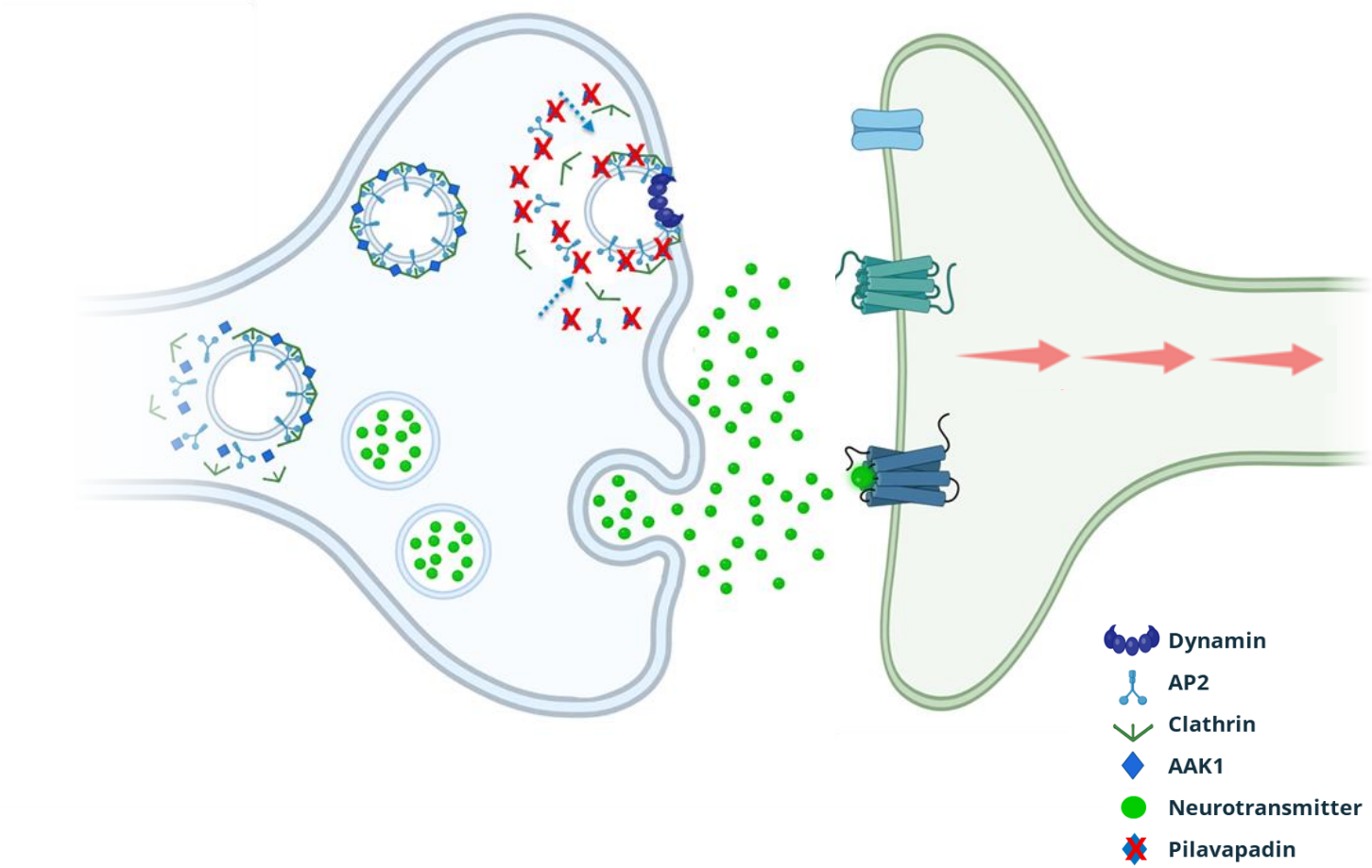
novel, investigational therapy for chronic pain and other high-value indications

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

What's next for pilavapadin?

Successful End-of-Phase 2 meeting with FDA

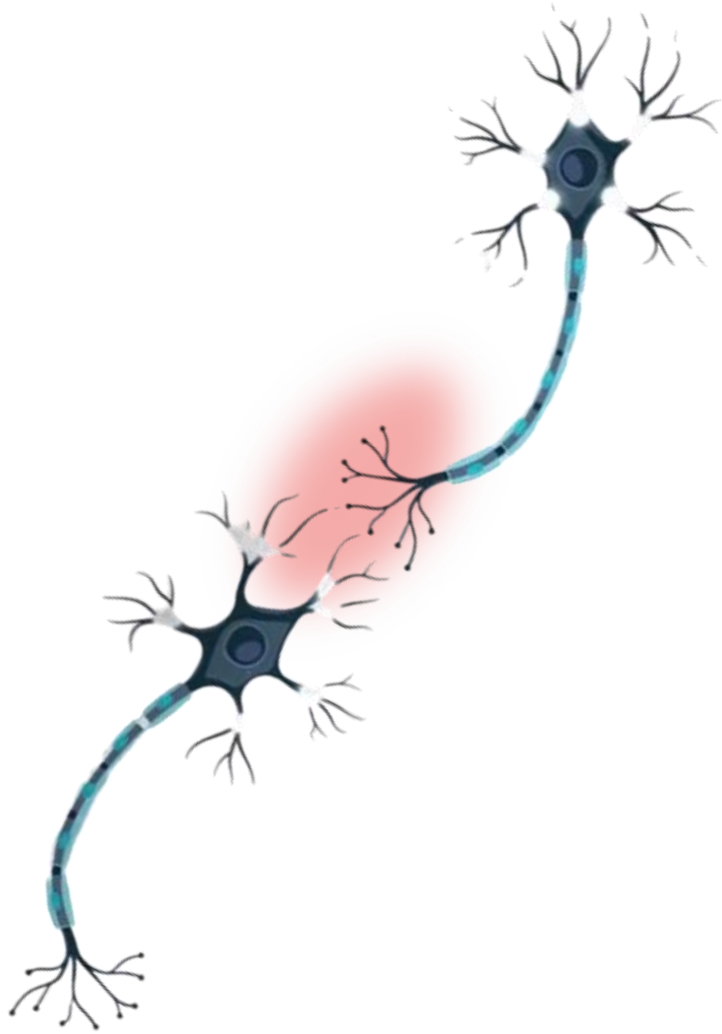
No objections raised to advancement into Phase 3 development

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

Q2 2026 Financial Summary

$ (in millions except per share amounts)

	Q2 2026	Q2 2025
Total revenues	$0.7	$28.9
R&D	($17.4)	($15.7)
SG&A	($9.8)	($9.4)
Total operating expenses	($27.2)	($25.1)
Net income (loss)	($31.8)	$3.3
Net income (loss) per common share	($0.07)	$0.01

	As of June 30, 2026	As of December 31, 2025
Cash, cash equivalents, short-term investments and restricted cash	$190.6	$125.2
Total assets	$250.1	$185.0
Total debt	$51.4	$54.0

Q2 2026 Financial Highlights and FY 2026 Guidance

Q2 2026 Key
Financial Highlights

- Entered into $100 million loan facility with Hercules Capital
  - Strengthened balance sheet and expanded access to non-dilutive capital
  - $55 million funded at close to repay existing loan facility with Oxford Finance
  - Two additional tranches totaling $45 million available under certain conditions

Full Year 2026 Guidance
Operating Expenses*

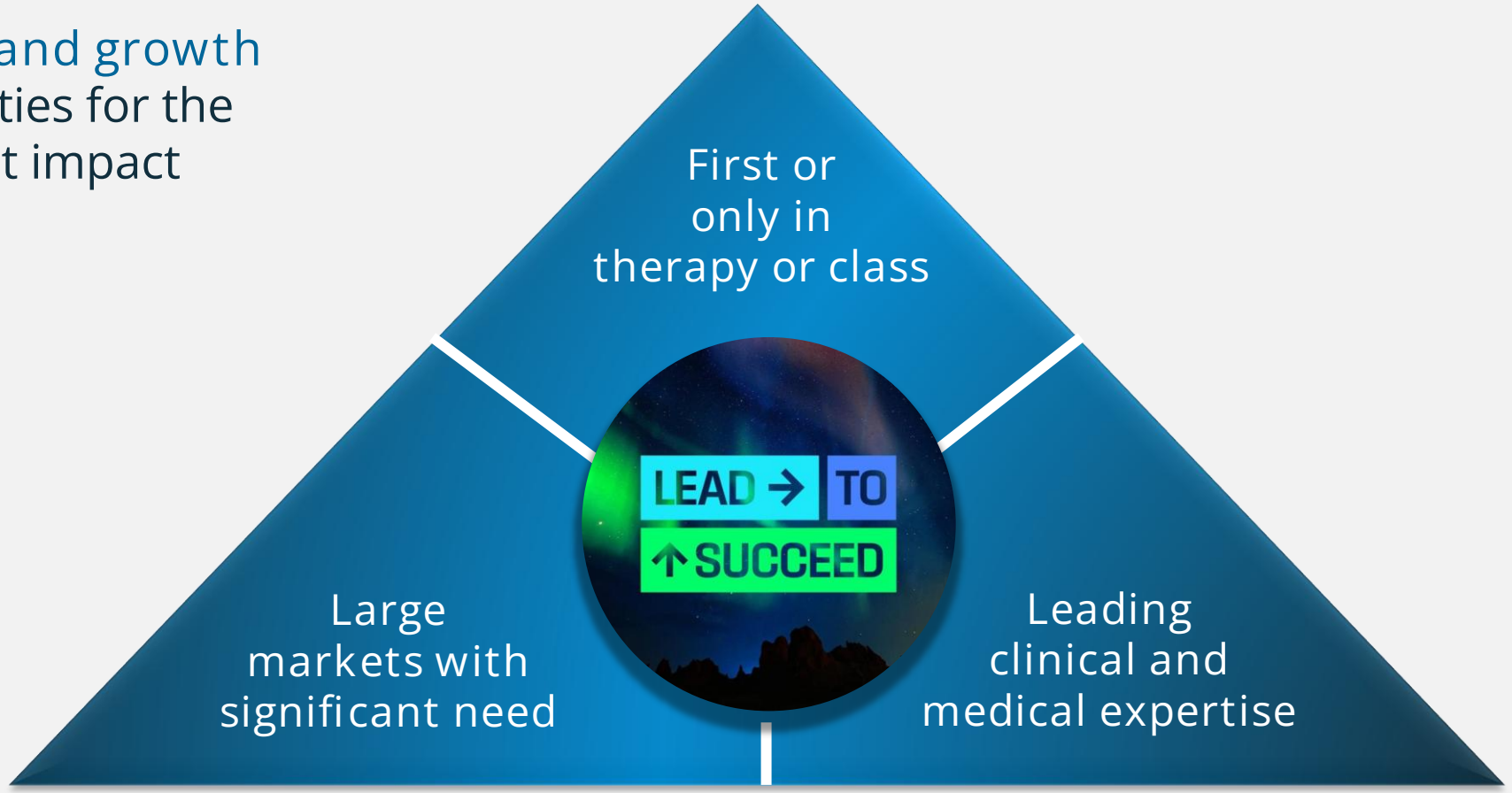
- Total 2026 operating expenses expected to be between $100 - $110 million
  - R&D expected between $63 - $68 million
    - Excludes expenses related to Phase 3 pilavapadin trials
  - SG&A expected between $37 - $42 million
    - Includes targeted investment in pre-commercialization activities

*As of August 6, 2026

Summary

Lexicon's ***Lead to Succeed*** strategy in action

Driving value and growth
with opportunities for the
greatest patient impact



Reshaping Lexicon Over the Next 12 Months

Cardiometabolic

SOTAGLIFLOZIN

HCM

SONATA on target for topline data Q1 2027

Heart Failure

Viatris ex-U.S./ex-Europe efforts progressing well

Approved: UAE and Bahrain
Pending: Canada and Australia (expected 2026)
Ongoing: submissions in other markets

T1D

Data from STENO1 supports potential approval

Finalizing patient-level data collection; anticipated NDA resubmission Q4 2026

LX9851

Obesity

Phase 1 study ongoing

$30 million in milestones received in 2026

AAK1

PILAVAPADIN

Neuropathic Pain and other high-value indications

Ongoing evaluation of strategic options

IND-enabling work for additional indications continues

MAINTAINING OPERATIONAL EXCELLENCE

Financial Discipline

Continued focus on maintaining a strong balance sheet and prudent financial spending

Commercial Pre-Launch Readiness

Measured investments in medical education, marketing preparation and market access in process

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