



# Lexicon Corporate Presentation September 2024

PRECISION SCIENCE. PIONEERING MEDICINE. PATIENT DRIVEN.

# 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 INPEFA® (sotagliflozin), ZYNQUISTA™ (sotagliflozin), LX9211, LX9851 and our other drug programs, the success of our commercialization efforts with respect to INPEFA 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.
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# 2024 has been transformational for Lexicon

With significant near-term potential catalysts through 2025



Resubmitted NDA for ZYNQUISTA™ (sotagliflozin) for glycemic management in type 1 diabetes (T1D); PDUFA December 20, 2024



Phase 3 study underway of sotagliflozin in hypertrophic cardiomyopathy (HCM) with multiple sites open



Enrollment in Phase 2b study of LX9211 in diabetic peripheral neuropathic pain (DPNP) on target for first half 2025 topline data



LX9851, an oral drug candidate for obesity/weight management addressing novel ACSL5 target, entered IND enabling studies



Strategic realignment of resources across portfolio expected to reduce 2025 operating costs by \$40M

# Lexicon *Lead to Succeed* strategy

Designed to drive value for all stakeholders



Driving value and growth for Lexicon with opportunities that have the most impact for patients

# *Lead to Succeed* is designed to drive value and growth across portfolio

Refocusing resources where Lexicon has potential to lead and succeed

Prioritizing investment in ZYNQUISTA™ ahead of potential launch

Continued targeted promotion of INPEFA® in Heart Failure, focused on growth and market access

Fully investing in R&D programs:

- Pivotal Phase 3 study of sotagliflozin in HCM
- Phase 2b dose optimization study of LX9211 in DPNP
- IND-enabling studies of LX9851 for obesity and weight management

# Sotagliflozin has three potential indications which position it as a “pipeline in a pill”

## Sotagliflozin

INPEFA  
Heart Failure

Approved

Two SGLT alternatives

ZYNQUISTA  
Type 1 Diabetes

PDUFA Dec. 20, 2024

No SGLTs Indicated

Sotagliflozin  
Hypertrophic  
Cardiomyopathy

Future Opportunity

No SGLTs Indicated

Areas of Significant Potential Value  
and Future Growth

\*CKD estimated at 20 -25% of total \$4B T1D market. \*Estimates provided are global and based on internal Lexicon analysis. EvaluatePharma Market size forecasts. Date accessed April 17, 2024.

# Zynquista has potential to address a major treatment gap

with an opportunity to demonstrate benefit:risk at AdCom Oct 31



**Zynquista**<sup>™</sup>  
(sotagliflozin) tablets **200 mg**

1

High unmet need for adjunctive glycemic control in adults with T1D and CKD

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2

Estimated >400k addressable patients in US alone per proposed label

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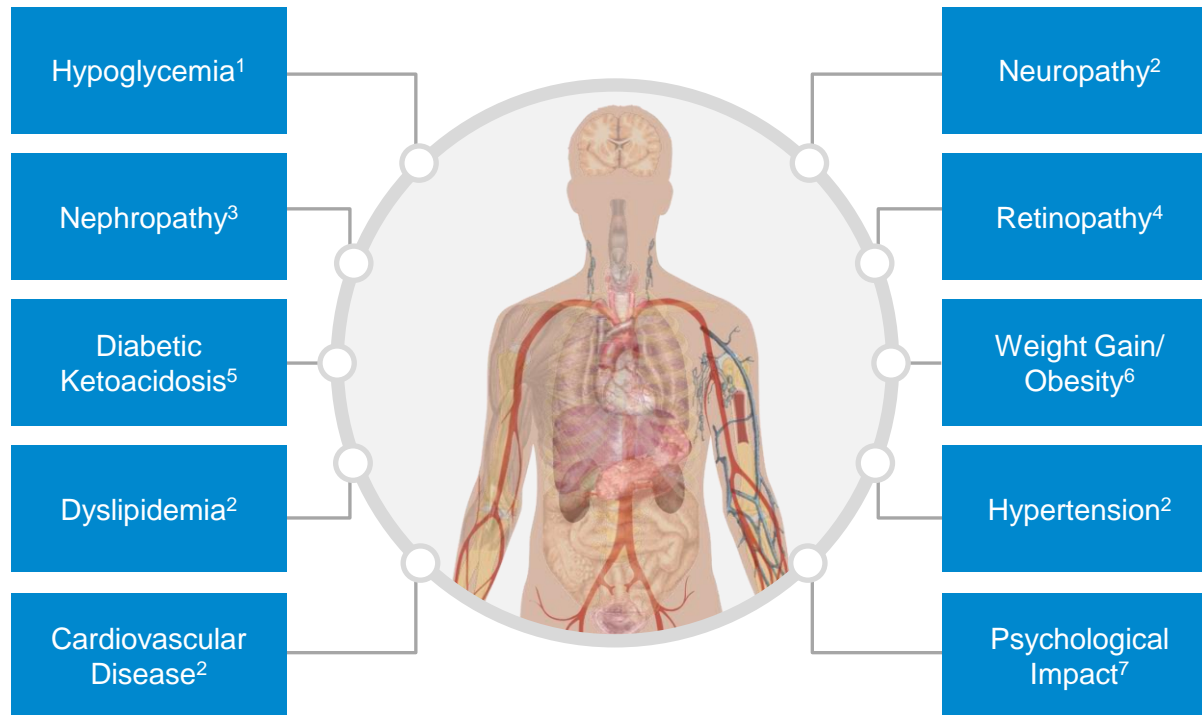
3

Potential to be *only approved SGLT inhibitor therapy* with treatment provided by a concentrated group of endocrinologists

# Glycemic control is critical in T1D + CKD

## yet insulin alone often not sufficient

Type 1 Diabetes Involves Significant Short- and Long-Term Complications



## Clinically Observed Benefits of ZYNQUISTA

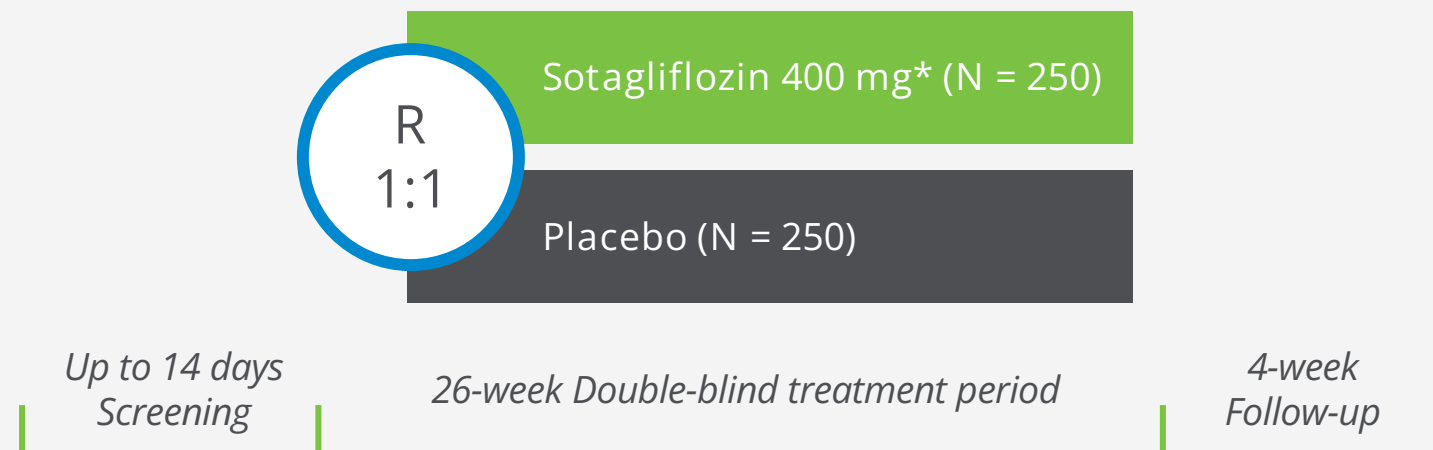
- ✓ Glycemic control on top of optimized insulin
- ✓ Reduction in body weight
- ✓ Reduction in blood pressure
- ✓ Improvement in time-in-range
- ✓ Reduction in risk of hypoglycemia
- ✓ Reduce postprandial glucose peaks

1. Bode BW, Garg SK. *Endocr Pract.* 2016;22(2):220-230. 2. Stadler M, et al. *Diabetes Obes Metab.* 2017;19(8):1171-1178. 3. Costacou T, Orchard TJ. *Diabetes Care.* 2018;41(3):426-433. 4. Katsarou A, et al. *Nat Rev Dis Primers.* 2017;3:17016. 5. Fazeli Farsani S, et al. *BMJ Open.* 2017;7:e016587. 6. Bae JP, et al. *J Diabetes Complications.* 2016;30(2):212-220. 7. Pallayova M, Taheri S. *Diabetes Spectr.* 2014;27:143-149.



# SONATA Phase 3 study has commenced

with pragmatic design designed to enable a broad indication for HCM



- Adults with HCM (obstructive/non-obstructive)
- LVEF  $\geq 50\%$

- KCCQ23 CSS  $< 85$
- NYHA Class II or III

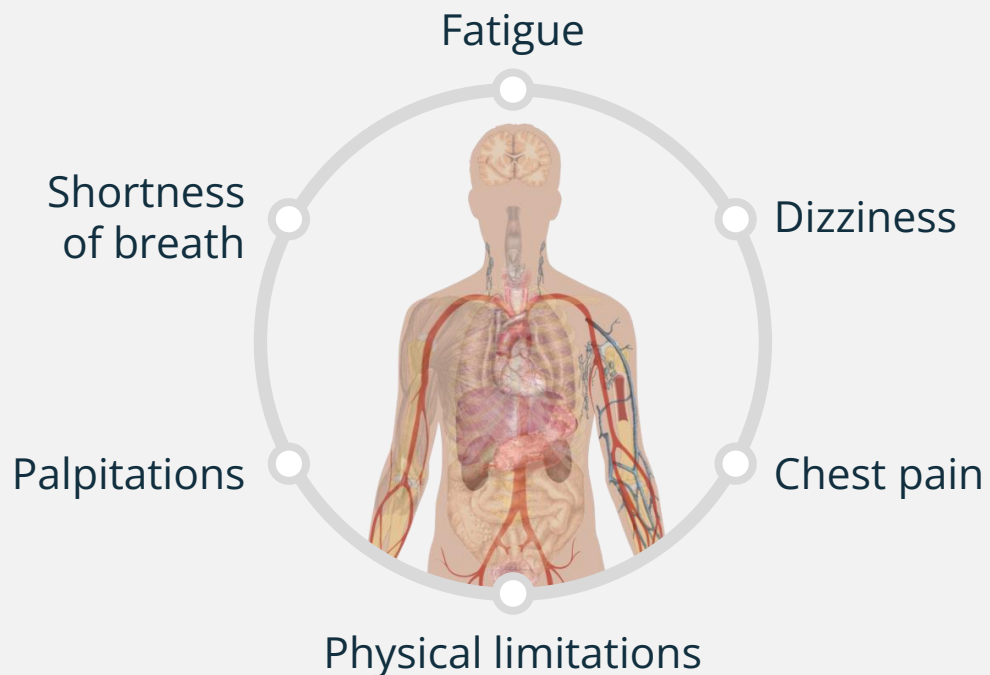
FDA Feedback Supports Potential Broad Label in HCM Based on Single Phase 3 Study

Primary endpoint:  
Change from baseline in KCCQ Clinical Summary Scale (CSS) score

# Potential to address a substantial treatment gap in HCM

positioned between, or on top of, use of basal therapies and CMLs

## HCM



## Limitations of Current Care

- Access to care
- Cost
- Complexity
- Effectiveness
- Invasiveness of surgical interventions
- No approved nHCM options

## Potential Advantages of Sotagliflozin

- ✓ Potential for broad adoption
- ✓ Ease in prescribing
- ✓ Known safety profile
- ✓ Familiarity with heart failure benefits
- ✓ Reduced cost burden
- ✓ Potential to treat across the spectrum of HCM

# LX9211 has potential to redefine standard of care for neuropathic pain with pipeline in a pill potential across NP and spasticity



High unmet medical need



Proof of concept achieved – FDA fast track designation



Late-stage clinical development underway



Potential for significant commercial opportunity across many indications

DPNP: Diabetic peripheral neuropathic pain

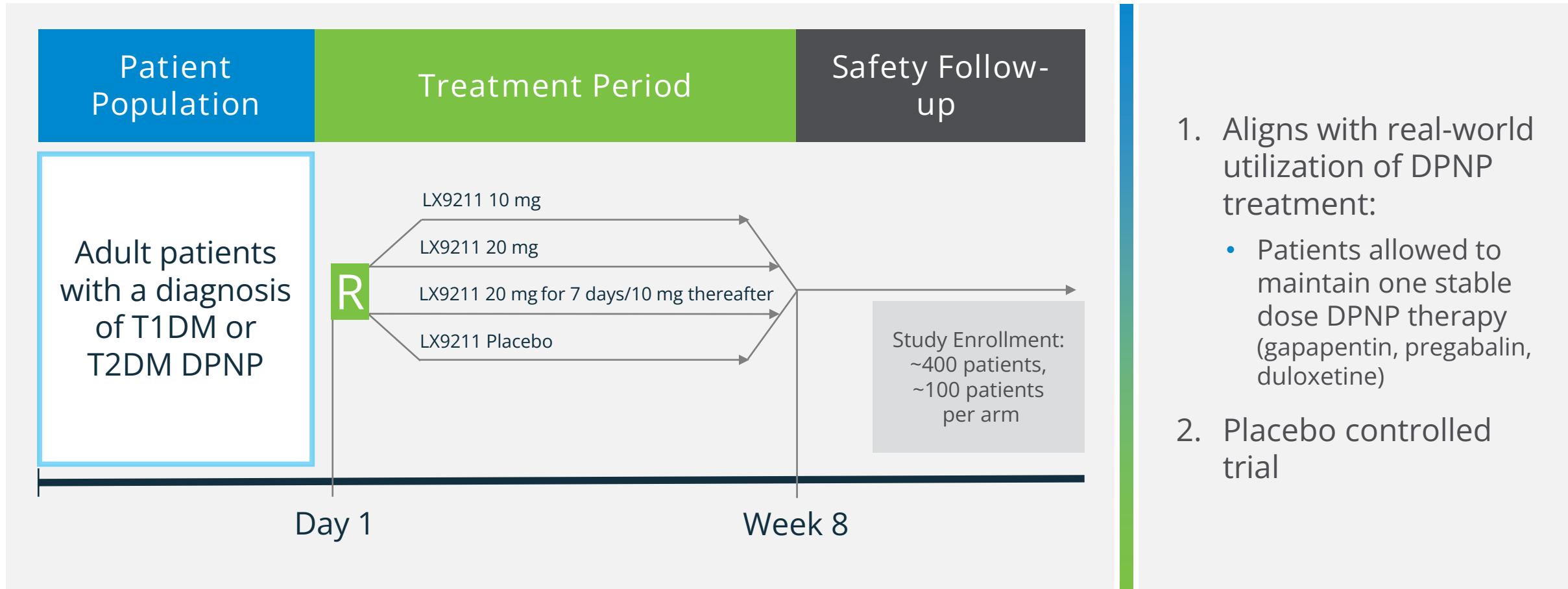
Patient Data: Decision Resources Group, Landscape & Forecast Neuropathic Pain Report, June 2020

Massachusetts General Hospital. Neuropathy Overview. [Internet] 2021

Schembri, E. Are Opioids Effective in Relieving Neuropathic Pain? SN Compr. Clin. Med. 1, 30–46 (2019)

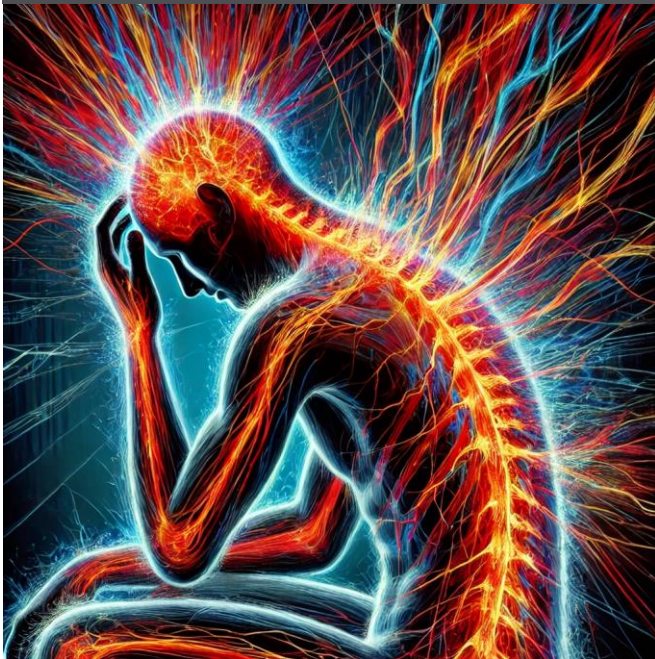
Finnerup et al. Algorithm for neuropathic pain treatment: an evidence-based proposal. Pain 2005; 118(3): 289-305

# PROGRESS Phase 2b study in DPNP is recruiting strongly with pragmatic design for "real world" implementation



LX9211 has the potential for multiple therapeutic applications and is potentially the *first and only* innovation on top of SoC in NP

## Neuropathic Pain



## LX9211

- ✓ First-in-class mechanism
- ✓ AAK1 specifically chosen (*over NaV1.8*)
- ✓ Non-opioid
- ✓ Use alone or on top of existing therapy
- ✓ Statistically significant placebo-controlled studies
- ✓ Paucity of innovation in neuropathic pain (NP)
- ✓ Strong pre-clinical evidence in many forms of NP as well as MS-related spasticity

# LX9851 is the *first and only* investigational medicine to inhibit ACSL5 with mechanism that is complementary and independent to incretins

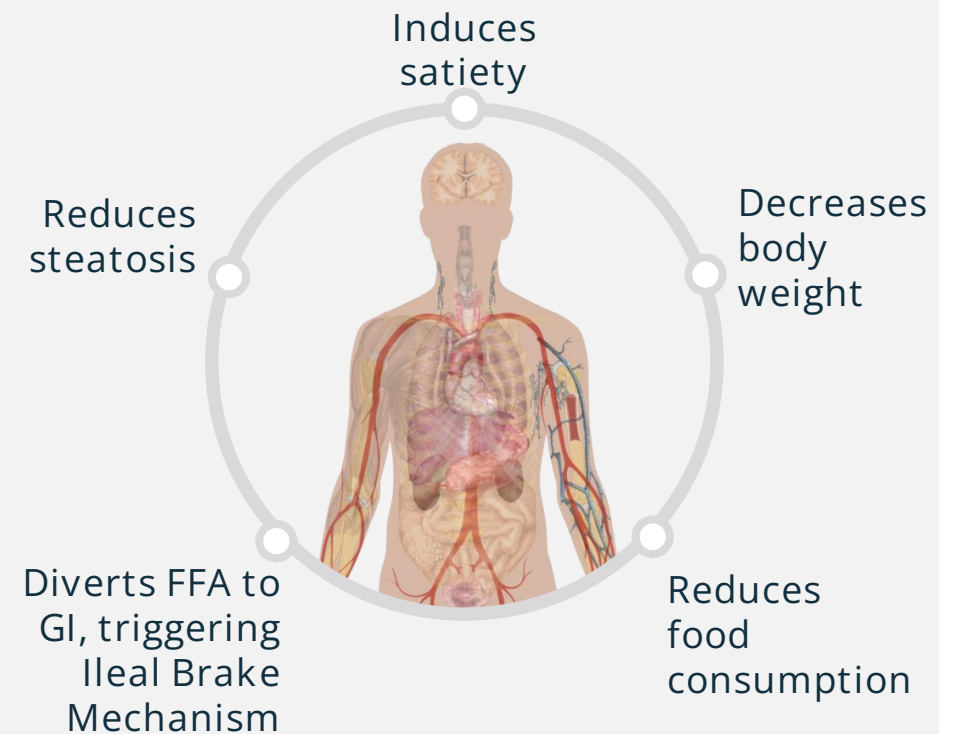
## Challenges Remain in with GLP-1 treatment

- Muscle wasting
- Patient discontinuation/  
tolerability
- Injectable
- Adverse side effects  
(nausea/vomiting)
- Regain of weight  
following  
discontinuation

## Potential Advantages of LX9851

- ✓ Oral agent for chronic  
weight management
- ✓ Reduction in body fat that  
spares lean body mass
- ✓ Improved metabolic profile
  - ✓ Reduced cholesterol and  
triglycerides, improved insulin  
sensitivity
- ✓ Effective both alone and on top  
of GLP-1s
- ✓ Potential additional,  
related indications/benefits:  
metabolic syndrome and MASH

## Biology-based Mechanism to Address Obesity



# Lexicon's pipeline is making significant progress and is positioned for near- and long-term company growth



# Lexicon has a significant number of near-term potential catalysts with potential to further drive the company transformation

Pipeline	Indication	Planned Catalyst 2024 – 2025
ZYNQUISTA™ (sotagliflozin)	<ul style="list-style-type: none"> <li>Type 1 Diabetes with Chronic Kidney Disease</li> </ul>	<ul style="list-style-type: none"> <li>PDUFA Goal Date Dec. 20, 2024; FDA Advisory Committee Meeting Oct. 31</li> <li>Launch Q1 2025</li> </ul>
Sotagliflozin	<ul style="list-style-type: none"> <li>Hypertrophic Cardiomyopathy</li> </ul>	<ul style="list-style-type: none"> <li>Phase 3 study commenced with multiple sites open</li> </ul>
LX9211	<ul style="list-style-type: none"> <li>Diabetic Peripheral Neuropathic Pain</li> </ul>	<ul style="list-style-type: none"> <li>Enrollment completion 2024; Top line data Q2 2025</li> <li>Partnership opportunity</li> </ul>
LX9851	<ul style="list-style-type: none"> <li>Obesity &amp; Weight Management</li> </ul>	<ul style="list-style-type: none"> <li>Commenced IND-enabling studies; file IND in 2025</li> </ul>



# Thank You