January 2025 Investor Presentation

Lexicon pharmaceuticals

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, LX9211, LX9851 and our other drug programs, 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.

2024 progress has fueled optionality for the future

- **Restructured and refocused resources where Lexicon has potential to Lead to Succeed**
- **Accelerated top-line data readout of PROGRESS, Phase 2b dose optimization study of LX9211**
- **Initiated enrollment in pivotal Phase 3 study of sotagliflozin in SONATA-HCM**
- **Advanced IND-enabling studies of LX9851 in obesity and related cardiovascular disorders**
- **Reinvigorated business development efforts, beginning with Viatris licensing agreement**

Multiple potential catalysts for value creation in 2025

ATTRACTIVE ASSETS

- Diversified pipeline platform potential
- Partnership potential
- Earlier-stage opportunities in add'l indications

DEVELOPMENT EXPERTISE

- Clinical drug development expertise
- Adaptive, efficient trial designs
- Multiple late-stage candidates

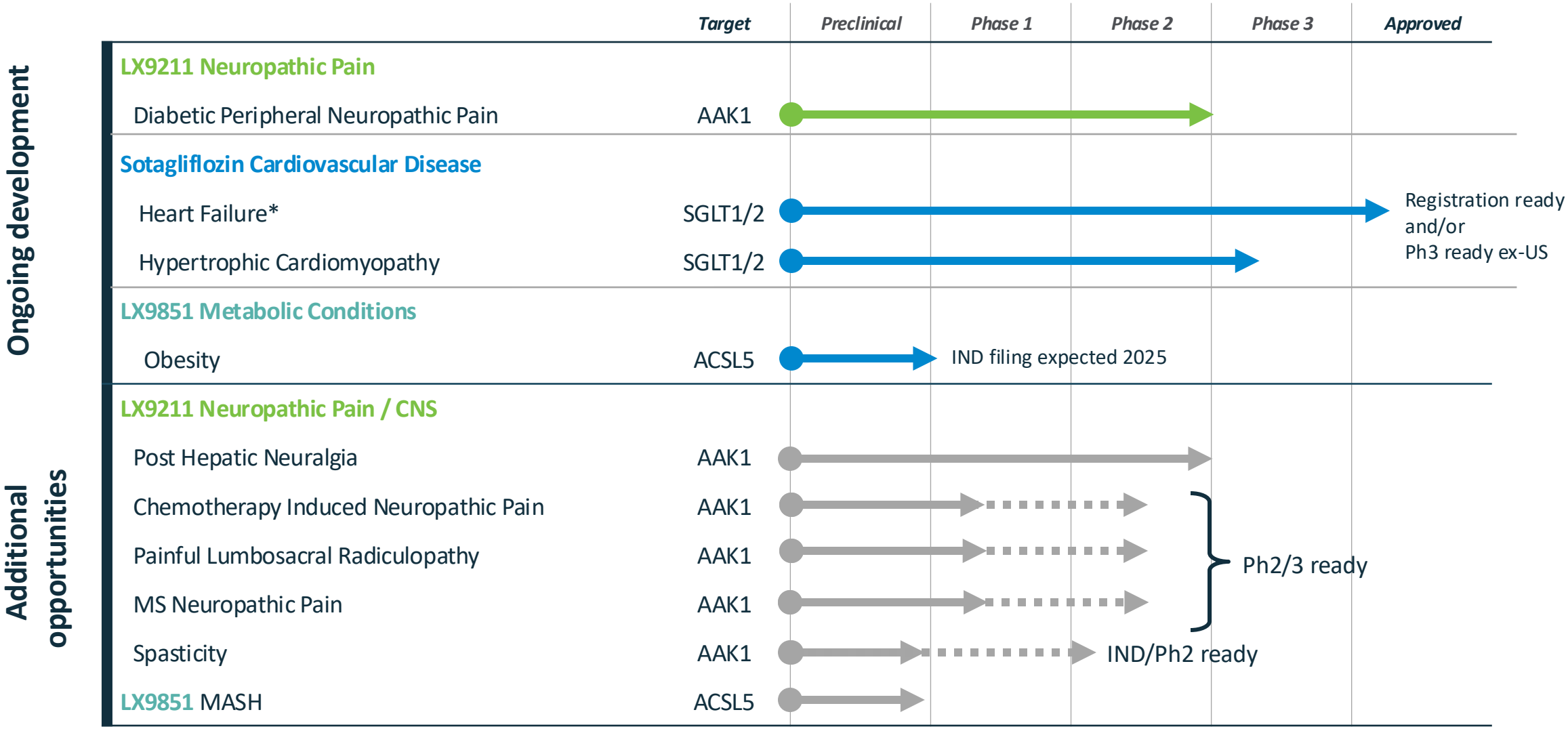
LEAN, AGILE ORGANIZATION

- Full focus as a development company
- Minimum viable sotagliflozin support for patient access
- Strong cash runway

NEAR-TERM CATALYSTS

- LX9211 Ph. 2 topline expected in 1Q
- SONATA HCM Ph. 3 enrollment underway
- Expected 2025 IND filing for LX9851

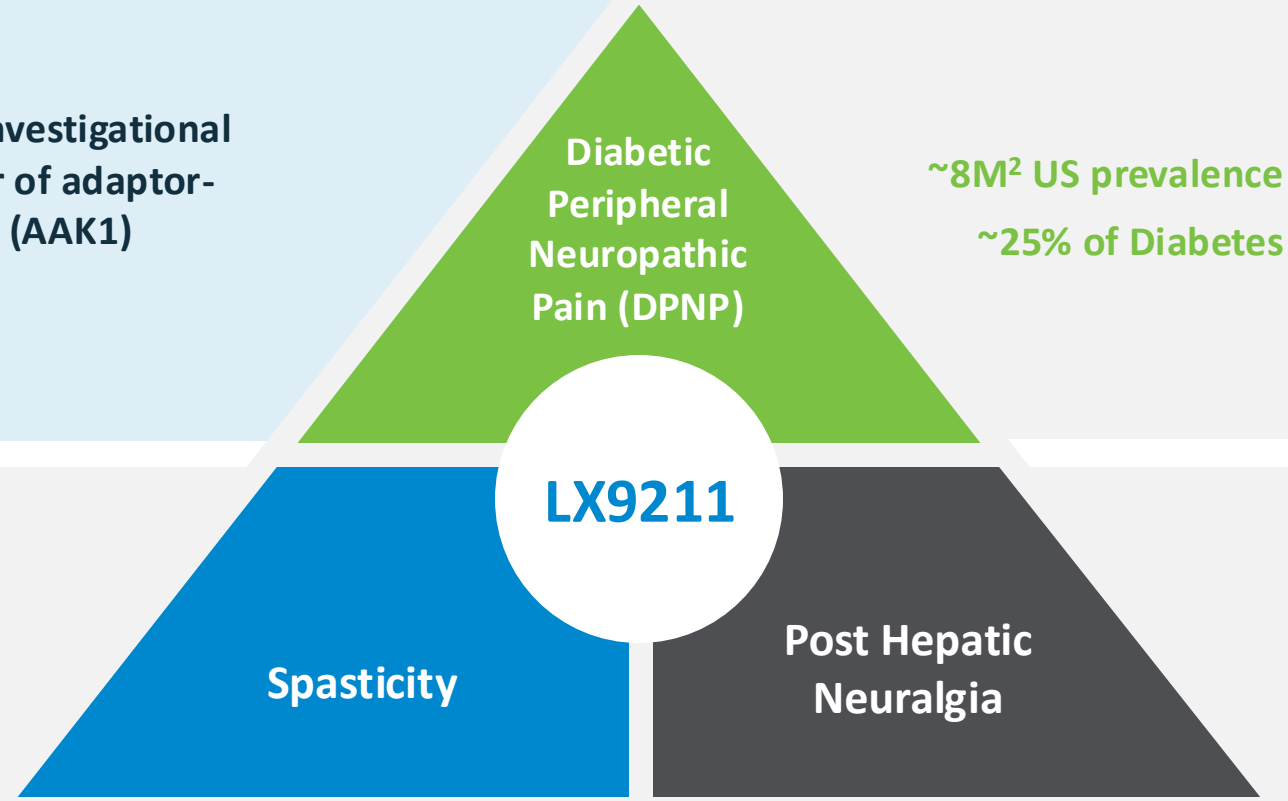
Pipeline assets position Lexicon for near-term and future growth



*approved in U.S.

LX9211: a neuroscience program with multiple possible therapeutic applications

Oral, potent, selective, investigational small molecule inhibitor of adaptor-associated kinase 1 (AAK1)



~8M[2] US prevalence

~25% of Diabetes

One of the most prevalent chronic complications of diabetes

Chronic condition affecting large patient population

~1M[3] US prevalence

~1.5M[1] US prevalence

Significant annual incidence and high unmet

Potential to launch in multiple markets with significant unmet need

[1] Thompson et. Al. 2020. Clin Infect Dis [2] ACS Cancer Treatment and Survivorship Report (2019– 2021); Islami et. Al. 2021. Nature; Selvy et. Al. 2021 Front Pharmacol; Seretny et. Al. Pain 2014 [3] 2030 U.S. prevalent patient population with spasticity; PSS and ALS spasticity segmentation at diagnosis [4] Andrews et. Al. BMC J Open. 2020. DPNP: Diabetic Peripheral Neuropathic Pain; HZ: Herpes Zoster; PHN: Post-Herpetic Peripheral Neuralgia. Source: Physician Interviews; ClearView Analysis.

Unique potential advantages of LX9211

New and Novel

no approved options for neuropathic pain in over 2 decades

Proof of Concept

clinically and statistically significant reductions compared to placebo

Oral Once Daily

monotherapy or in combination with standard of care

Non-Opioid

MOA distinct from current standard of care

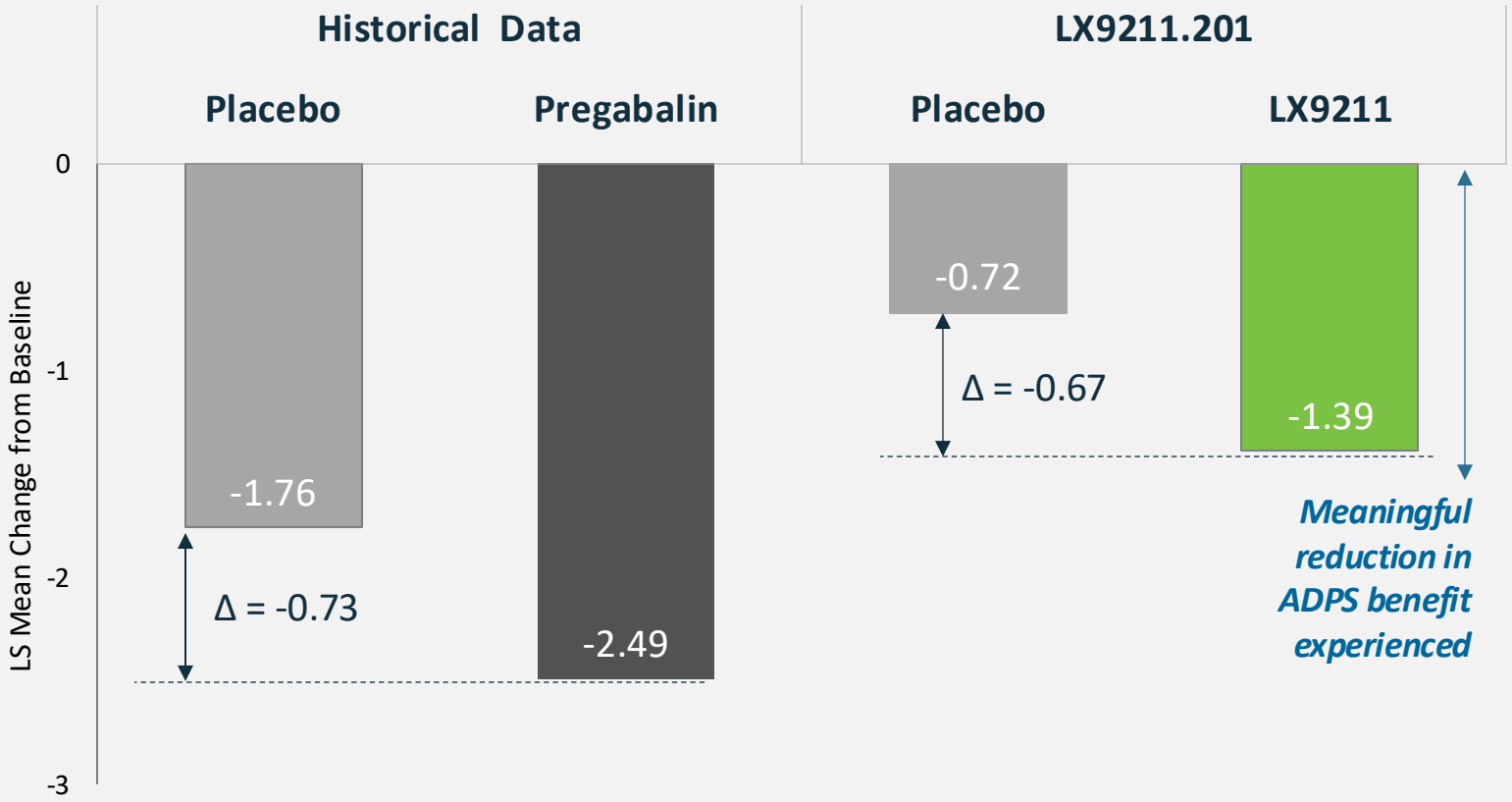
Broad Potential

including peripheral and central neuropathic pain, and spasticity

Pragmatic Trial Design

aligned to real-life pain management in patients

LX9211 meaningfully reduced ADPS in placebo-controlled RELIEF-DPN1 Phase 2 study while DPNP patients remained on SOC



Patients allowed to continue background SOC

2-week run-in period to establish DPNP

Reduced placebo effect (and impacted change from Baseline)

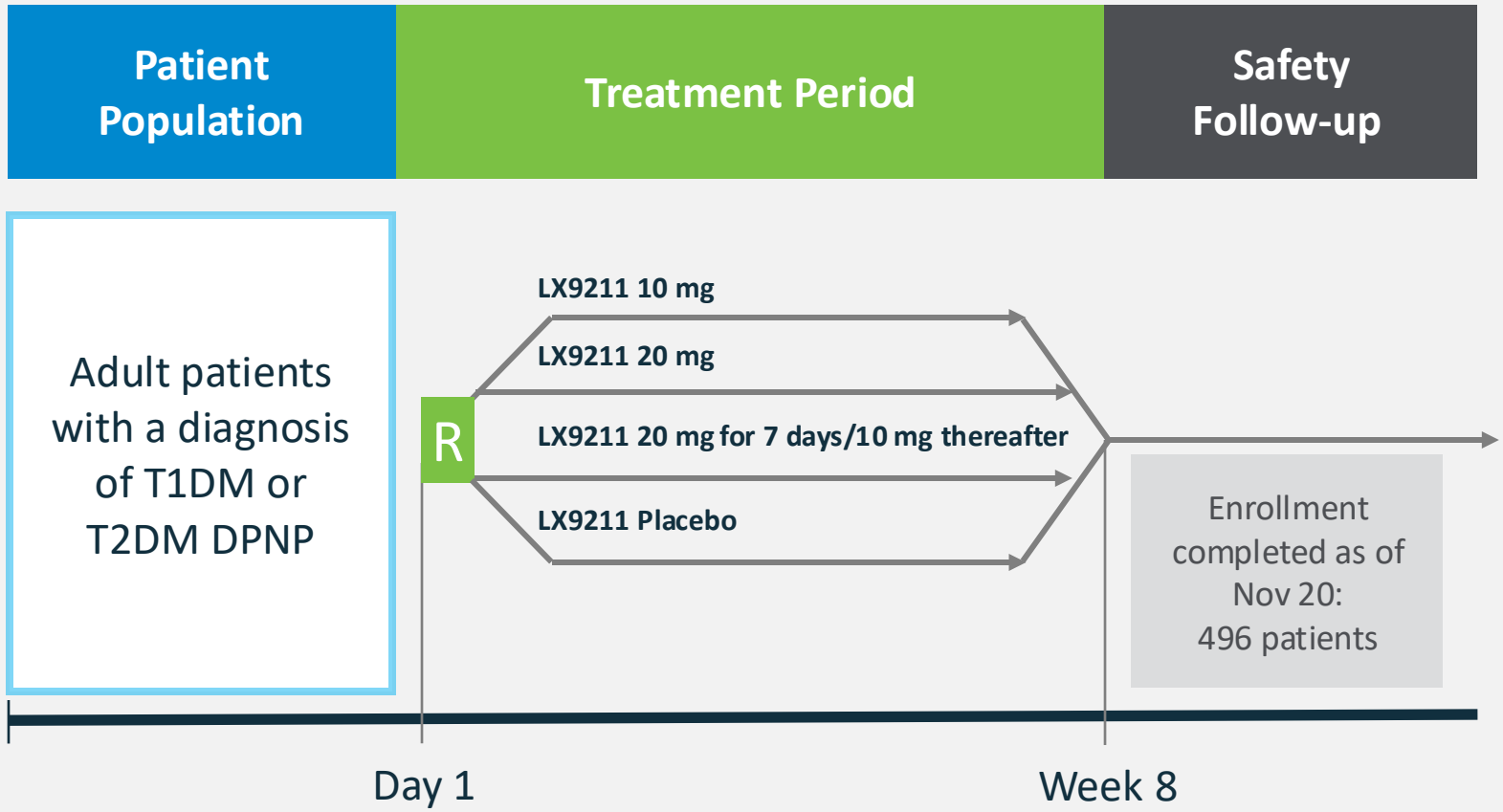
Improvement vs. Placebo was maintained for study duration

LX9211 = LX9211, 100 mg/10 mg; ADPS: average daily pain score

Source: Vinik, A., Emir, B., Parsons, B., & Cheung, R. (2014). Prediction of pregabalin-mediated pain response by severity of sleep disturbance in patients with painful diabetic neuropathy and post-herpetic neuralgia. *Pain medicine (Malden, Mass.), 15*(4), 661–670. https://doi.org/10.1111/pme.12310

PROGRESS Phase 2b study enrollment complete

Topline data read-out now anticipated for Q1 2025



- **Aligns with how DPNP drugs are used in clinical practice**
- **Placebo controlled study**
- **Study designed to identify optimal dose for phase 3**
- **Enrollment exceeded target by 20% and ahead of schedule**

Sotagliflozin: taking steps now to further differentiate among SGLT class

Next 18 months

Strategic scientific presence in HF; Completion of Ph. 3 study in HCM

- 6 ongoing trials designed to generate more evidence on unique CV and dual-inhibition benefits (SOTA-P-CARDIA, SOTA THROMBUS)
- Completion of SONATA Phase 3 study in HCM
- Ex-US, ex-EU registration and regional development through Viatris

Next 24 months

Establish clinical differentiation; Complete sNDA submission for HCM indication

- Data available to further establish clinical benefits and differentiation
- sNDA submission for label expansion of sotagliflozin in HCM
- Geographic expansion through Viatris licensing arrangement

2027 - 2028

Re-emerge with compelling clinical story, new HCM indication

- Demonstrate clinical benefit of dual-inhibition
- Evolution of competitive landscape including existing market access barriers
- Greater awareness of HFpEF as the predominant form of HF

Sotagliflozin has potential to occupy a unique position in symptomatic HCM (oHCM and nHCM)

HCM Disease Progression and Treatment Journey

Beta Blocker (BB) +/- Calcium Channel Blocker (CCB)

- ✓ Common tolerability/ side-effect issues

Sotaglifozin Opportunity

Gap in treatment for people who are intolerant / do not respond to BB/CCB

- ✓ Safe & easy to use
- ✓ Limited side effects
- ✓ Reduced cost burden to patients and broader healthcare system
- ✓ Strong scientific rationale
- ✓ Broad proposed indication for both nHCM and oHCM
- ✓ Potential for use as standalone or combination therapy

Cardiac Myosin Inhibitor (CMI)

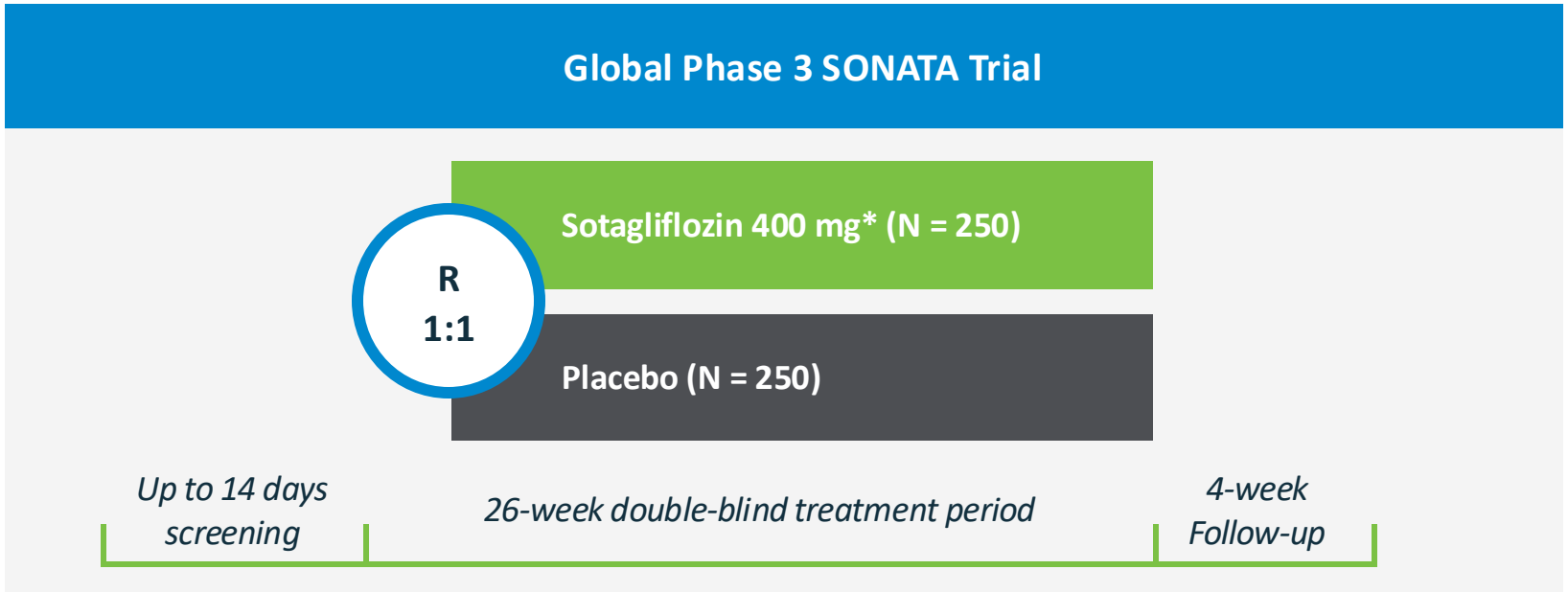
- ✓ High cost burden

Surgical Intervention / Myectomy

~1.1M	U.S. Prevalence of HCM[1]	**~30%**	Diagnosed with nHCM	**~70%**	Diagnosed with oHCM	**~43%**	Have Progressive Heart Failure

Source: 1. CVrg Market Strategies. Cardiovascular Resource Group, Oct. 2023.

SONATA Phase 3 study for oHCM and nHCM



Inclusion Criteria	• Adults with HCM (obstructive/non-obstructive) • LVEF ≥50%	• KCCQ23 CSS <85 • NYHA Class II or III
Primary Endpoints	• Change from baseline in KCCQ Clinical Summary Scale (CSS) score	

Enrollment underway

Only ongoing trial to evaluate both obstructive and non-obstructive HCM

Potential for supplemental new drug application (sNDA) with broad label

Viatris license expands reach of sotagliflozin while preserving partnership opportunities for other assets, territories and indications

VIATRIS™

Exclusive licensing agreement for sotagliflozin in all markets outside of the U.S. and Europe

- $25M upfront payment along with nearly $200M potential milestone payments and tiered double-digit royalties
- Bolstered evidence generation resources to support and expand sotagliflozin's clinical differentiation
- Viatris responsible for all regulatory and commercialization activities in licensed territories

LX9851 offers the potential to address unmet needs in obesity & related cardiometabolic disorders

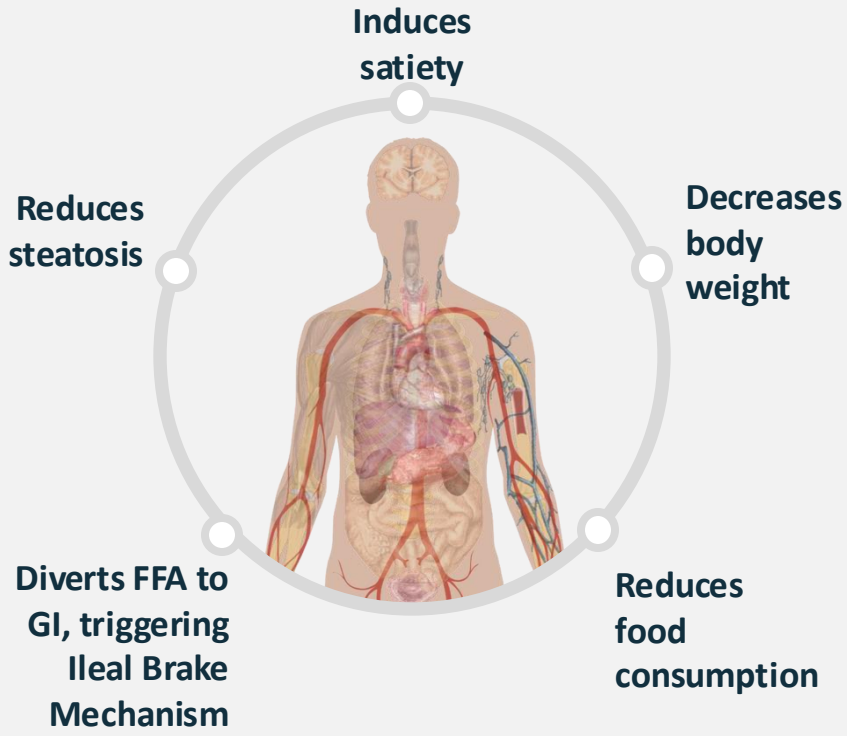
GLP-1 Treatment Challenges

- Muscle wasting
- Patient tolerability
- Injectable
- Adverse side effects
- Regain of weight
- Cost and Access

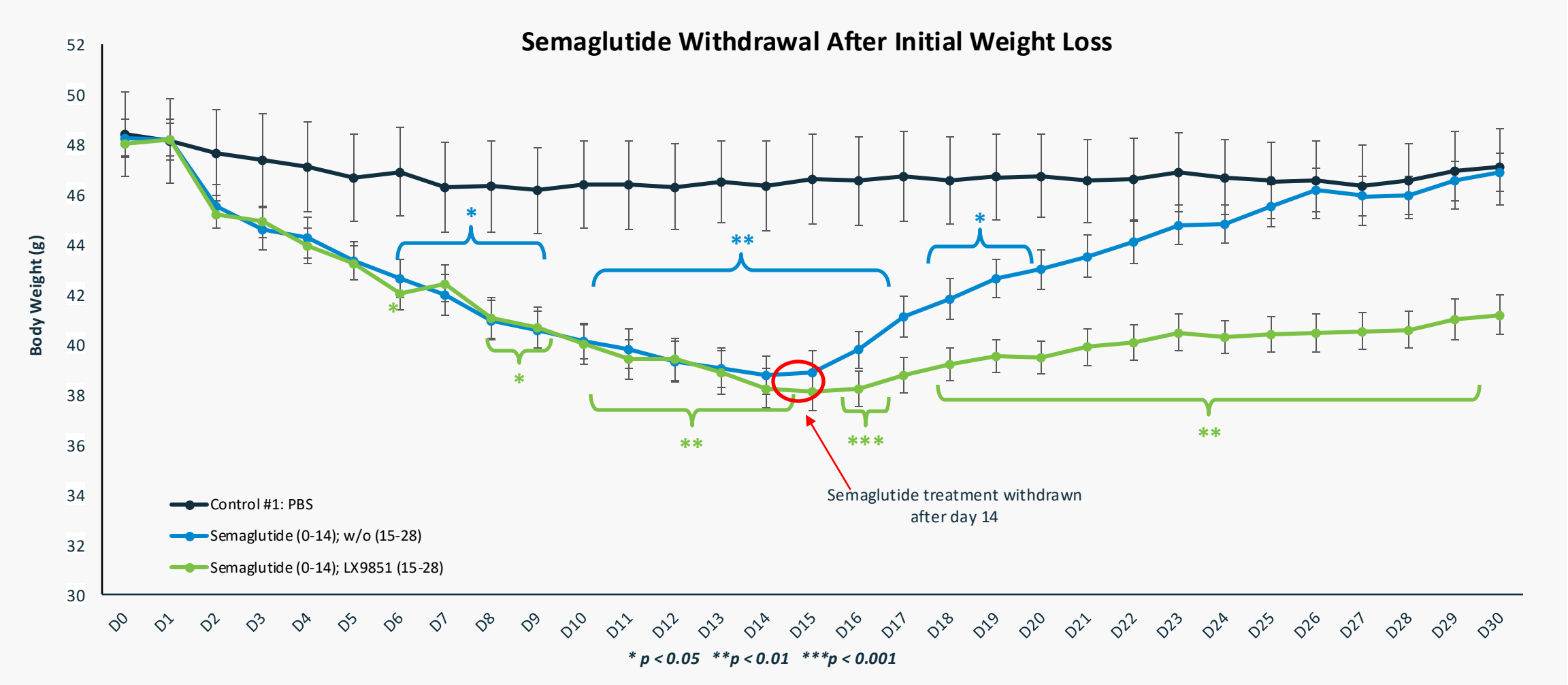
Potential Advantages of LX9851

- Oral agent/chronic use
- Reduction in body fat
- Improved metabolic profile
- Use alone or on top of GLPs
- Potential additional, related indications/benefits

Biology-based Mechanism to Address Obesity



LX9851: Weight loss maintained after semaglutide discontinuation in HFD-fed DIO mice



Efficient and effective approach to drug development

Research and development capabilities and approach have successfully resulted in multiple late-stage assets and product approvals

Deep Industry Relationships

- Strong relationships with industry experts in cardiometabolic, pain and neurology
- Studies externally supported and validated
- Relevant and clinically meaningful endpoints

Pragmatic Trial Design

- Adaptive approach with efficient, quick and cost-effective studies
- Trials powered for success
- Leverage clinical and real-world data

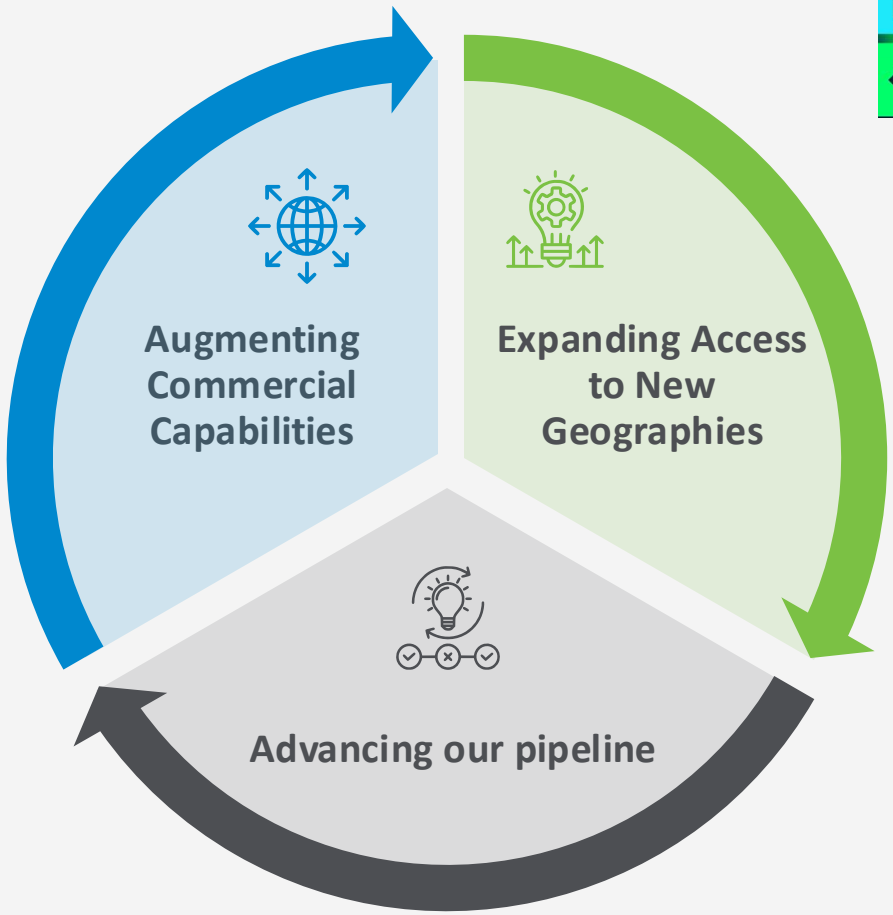
Track Record of Success

- Have advanced several indications into Phase 3 and beyond
- Total of over 25 Phase 2 and 3 studies successfully completed
- Proprietary datasets enable early validation and higher probability of success

Partnering is an important element of our Lead to Succeed strategy

Pursuing partnerships as a source of non-dilutive capital to maximize the value of our portfolio

Significant opportunities for partnering remain ahead



Significant number of planned catalysts through 2025

Pipeline	Indication	Planned Catalyst 2025
Sotagliflozin	• Hypertrophic Cardiomyopathy	• Phase 3 study enrollment underway
LX9211	• Diabetic Peripheral Neuropathic Pain	• Top line data Q1 2025

Virtual LX9211 focused R&D day planned for January 28th ahead of anticipated top line data

LX9851	• Obesity & Weight Management	• IND filing planned in mid-2025

Thank You