Lexicon Pharmaceuticals

JP Morgan Healthcare Conference

JANUARY 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.

Lexicon's evolution to produce novel targeted therapies

Began as a
PIONEER OF GENOMIC DISCOVERY
in the mid-1990s

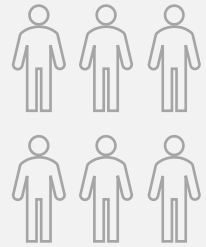
GENETICALLY-INFORMED
drug discovery

Our efforts have yielded
MULTIPLE DRUG CANDIDATES

2
MEDICINES APPROVED
and
BROUGHT TO MARKET

inpefa
sotagliflozin tablets

APPROVED
for the treatment of heart failure



80+
CLINICAL TRIALS
in tens of thousands of patients worldwide

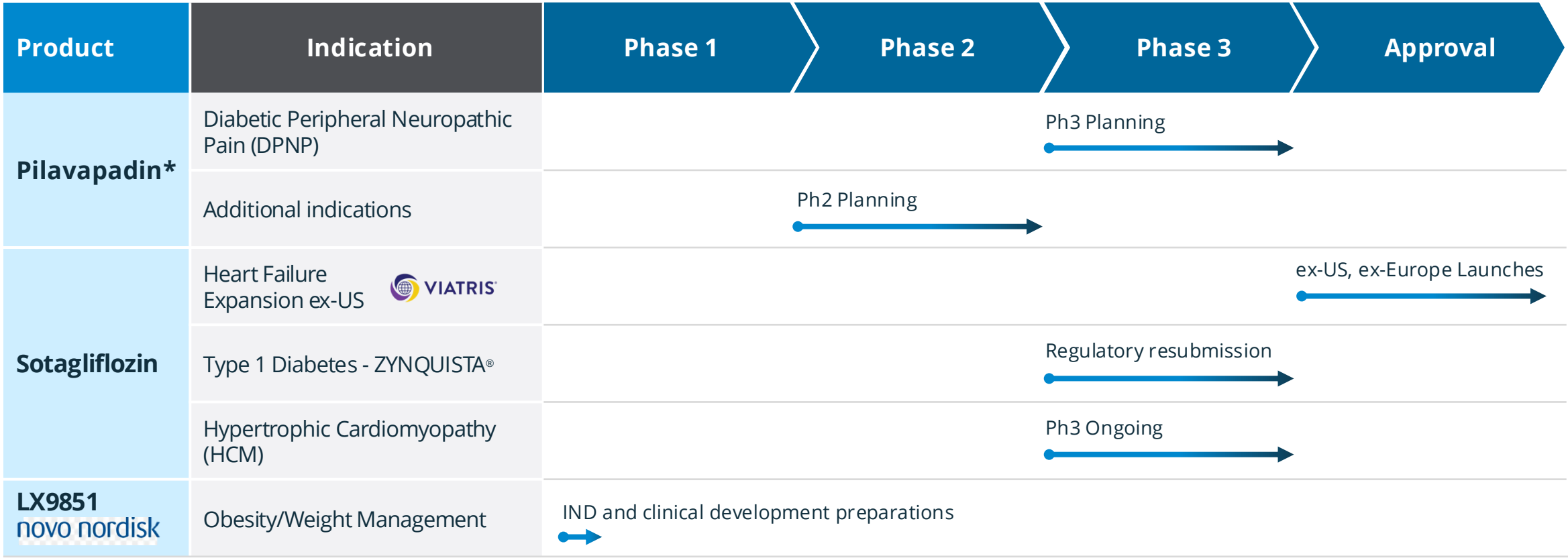
~5,000 **GENES TARGETED**
in the Genome5000™ project

NOVEL NON-OPIOID APPROACH
to neuropathic pain advanced into late-stage development

FIRST-IN-CLASS,
non-incretin obesity investigational therapy

Well-positioned with a portfolio of potential “pipelines in a pill”

Exploring opportunities across multiple therapeutic areas



**Execution of trials and subsequent regulatory support would require partnership or additional funding*

Lexicon development assets in two primary therapeutic areas

CARDIOMETABOLIC

Sotagliflozin – an oral SGLT1/SGLT2 inhibitor

- FDA-approved as **INPEFA** for **heart failure**
- In Phase 3 development for **HCM**
- Subject of regulatory discussions as **Zynquista** for as an adjunct to insulin for glycemic control in adults with **type 1 diabetes**

LX9851 – a first-in-class, oral non-incretin development candidate in **obesity** and associated metabolic disorders

PAIN

Pilavapadin – non-opioid small molecule AAK1 inhibitor

- A novel target for **neuropathic pain** which inhibits reuptake and recycling of neurotransmitters involved in pain signaling without affecting opiate pathways
- A **Phase 3-ready** lead indication in DPNP and additional indications ready for Phase 2

Setting the stage for 2026

SOTAGLIFLOZIN

HCM
All sites initiated

Accelerated enrollment

T1D
STENO-1 data submitted to FDA

Type D process continued

PILAVAPADIN

Neuropathic Pain
PROGRESS readout + Phase 2 analyses

EOP2 meeting completed

Engaged potential partners

LX9851

Obesity
Secured worldwide license with Novo Nordisk

IND-enabling studies completed

Operational Excellence & Partnerships

Reduce operational expenses

INPEFA virtual sales

First ex-US INPEFA approval

INPEFA submissions ex-US, ex-Europe

Key strategic focus as Lexicon enters a pivotal 2026

- Partner **pilavapadin** and progress into Phase 3 registrational trials
- Complete enrollment in **SONATA Phase 3 study for HCM**
- Fully evaluate potential regulatory path forward for **Zynquista**
- Support **international** expansion of sotagliflozin by Viatris
- Sustain **operational discipline** to support long-term growth

Cardiometabolic

SOTAGLIFLOZIN

Late-stage development programs in HCM and type 1 diabetes

Cardiometabolic program highlights

HCM

- SONATA-HCM Phase 3 study, evaluating approximately 500 patients with **both obstructive and non-obstructive HCM**, accelerating towards 2026 enrollment completion
- Study continues to enroll on-schedule, with patients now randomized across 130 active sites in 20 countries
- Topline results anticipated in Q1 2027

Type 1 Diabetes

- On track for 2026 resubmission of the New Drug Application (NDA) for Zynquista (sotagliflozin) as an adjunct to insulin for **glycemic control in adults with type 1 diabetes (T1D)** based on clinical data from the STENO1 study

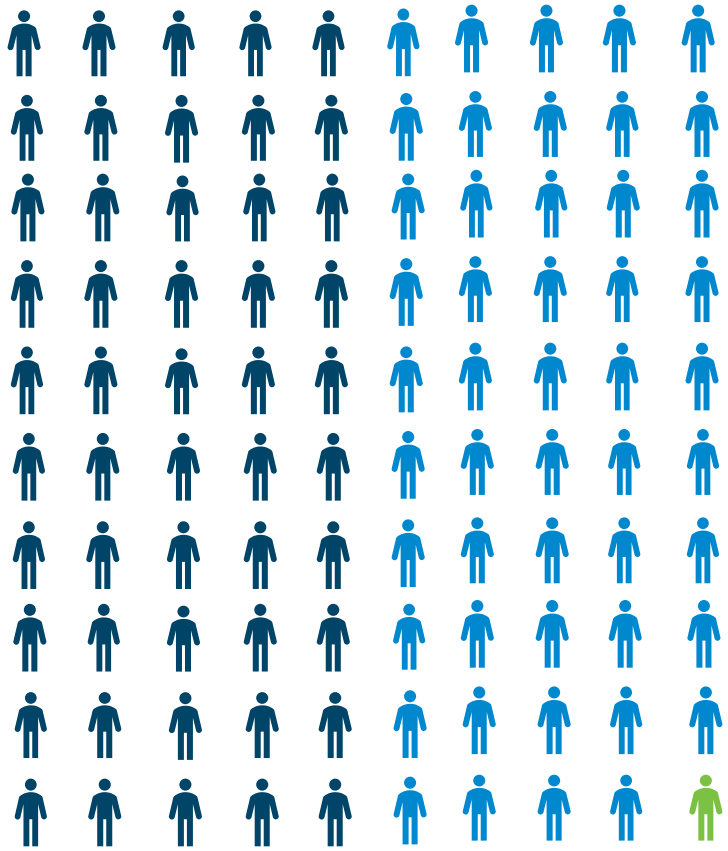
HCM: A significant and underpenetrated market with high disease burden

~1.1M people in the U.S. have either obstructive or non-obstructive HCM*

Common signs include **altered cardiac energetics, fibrosis, and diastolic dysfunction**

Common symptoms include **shortness of breath, fatigue and dizziness****

HCM can lead to **heart failure, atrial fibrillation and stroke**



50% Diagnosed with oHCM

50% Diagnosed with nHCM

~1% CMI total market penetration

43% Progress to heart failure

*CVrg Market Strategies. Cardiovascular Resource Group, Oct. 2023.
** Zaiser, Erica, et al. "Patient Experiences with Hypertrophic Cardiomyopathy: A Conceptual Model of Symptoms and Impacts on Quality of Life." Journal of Patient-Reported Outcomes, vol. 4, no. 1, Dec. 2020

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
- Dual SGLT1/SGLT2 MOA 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 dramatically improve symptoms and function (KCCQ, LVM)

SOTA-CROSS

- Readout mid-to-late 2026
- Evaluating sotagliflozin 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)

*HFpEF: heart failure with preserved ejection fraction; nHCM: non-obstructive hypertrophic cardiomyopathy; *KCCQ: Kansas City Cardiomyopathy questionnaire*

Zynquista resubmission in T1D planned based on new clinical data

- Type D meeting with FDA confirmed **IIS study (STENO1[1]) adequate** to support resubmission of Zynquista NDA
- Current enrollment estimates 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

1) Multifactorial Intervention to Reduce Cardiovascular Disease in Type 1 Diabetes (Steno1). Clinicaltrials.Gov, www.clinicaltrials.gov/study/NCT06082063. Accessed 4 Sept. 2025.

Pain

PILAVAPADIN

non-opioid neuropathic pain investigational therapy

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

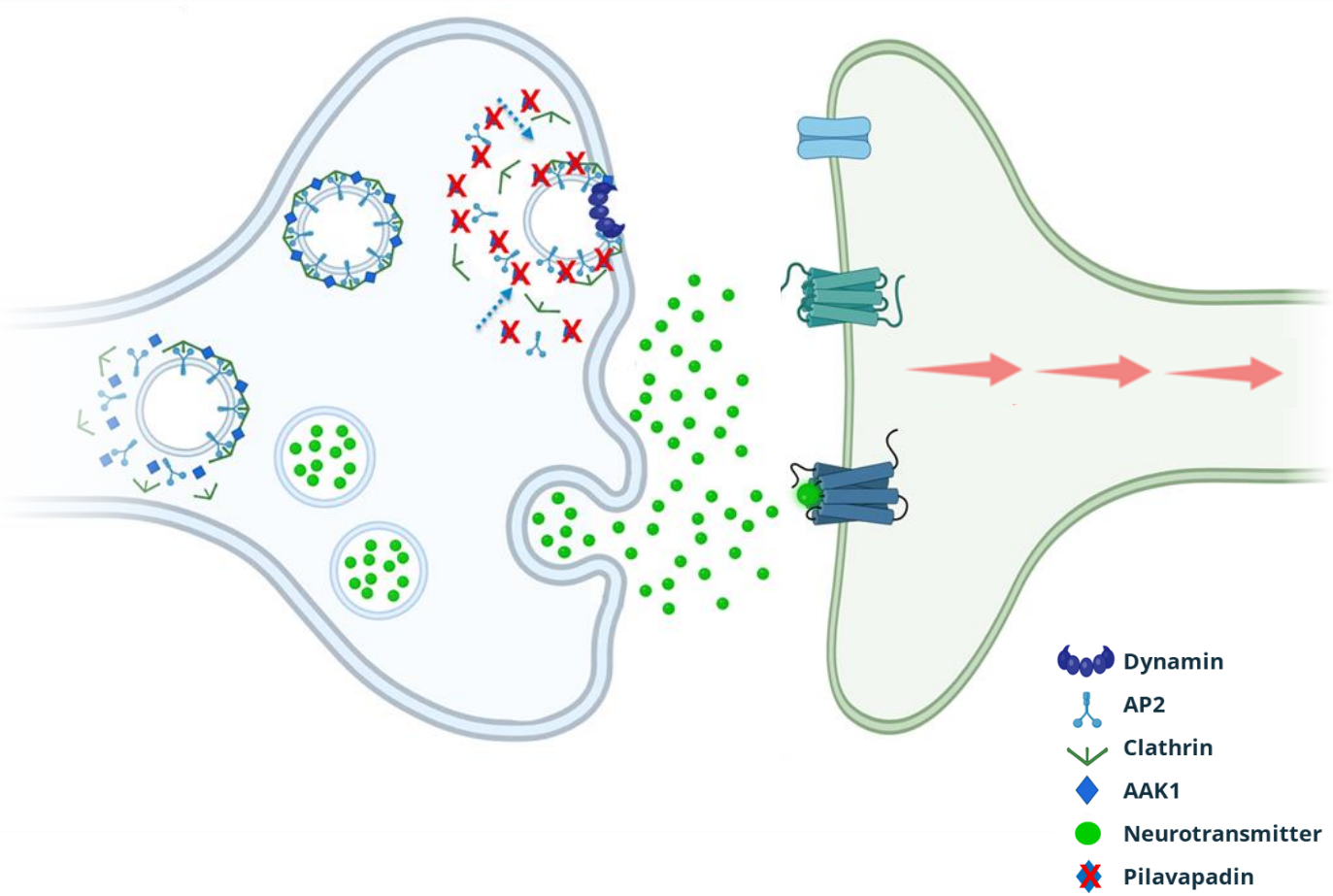
1. Includes diagnosed patients only, CDC National Diabetes Statistics Report 2024. Source: prevalence rate of DPNP in diabetics is based on primary and secondary research; Source: Clearview Analysis. 2. Veeva Compass data; based on internal Lexicon claims analysis.

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**



Conclusions from pooled analyses of Phase 2 studies in DPNP

- **Validated biological activity**, as evidenced by a linear relationship between increased plasma levels of pilavapadin and pain reduction
- **Clinically meaningful efficacy** of the 10mg dose, with a 2-point average daily pain score (ADPS) reduction from baseline at 12 weeks
- **Acceptable tolerability profile** of the 10mg dose, with placebo-like treatment completion rates
- **Acceptable safety profile** in line with standard of care, further bolstered by additional studies

Analyses support advancement of 10mg into Phase 3 development

Environment supportive of non-opioid innovation in chronic pain

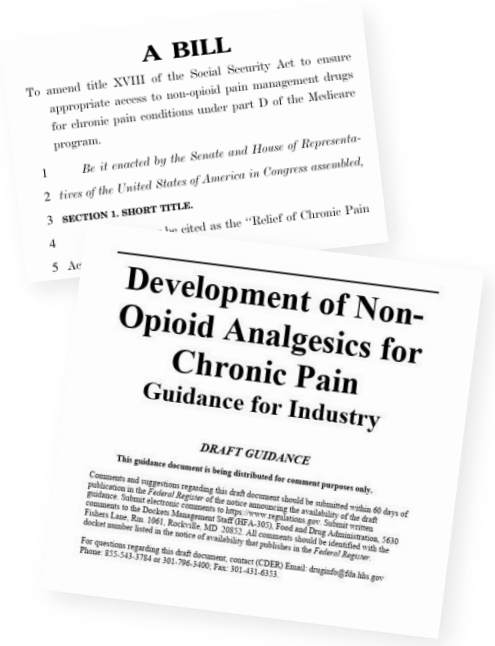
CHRONIC PAIN ROUNDTABLE
October 7, 2025

- 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


A BILL

To amend title XVIII of the Social Security Act to ensure appropriate access to non-opioid pain management drugs for chronic pain conditions under part D of the Medicare program.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

Development of Non-Opioid Analgesics for Chronic Pain

Guidance for Industry

DRAFT GUIDANCE

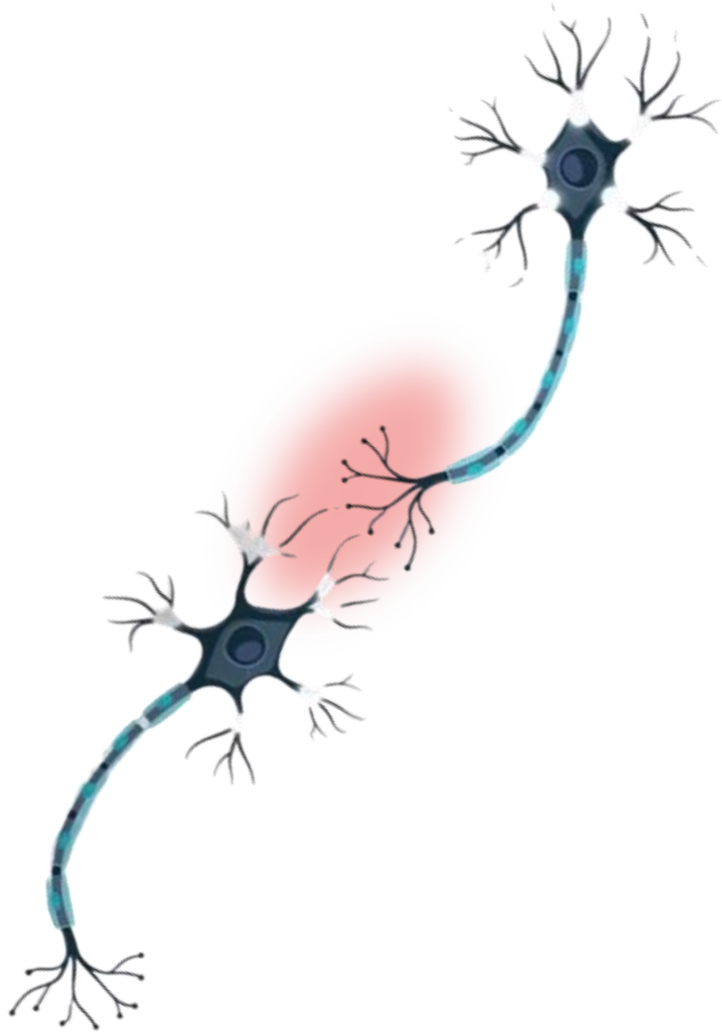
This guidance document is being distributed for comment purposes only.

What's next for pilavapadin?

Productive End-of-Phase 2 meeting with FDA
final feedback anticipated **January 2026**

Optimized Phase 3 protocol
to reduce variability, including placebo effect; validated by **scientific advisory board**

Partnership discussions progressing
with potential for **broad partnership**



Business Highlights

Partnership strategy poised for continued value creation

Innovative and flexible strategy in action to unlock long-term value

Geographic expansion through Viatris' global capabilities

- Sotagliflozin recently approved in UAE for recent and worsening heart failure
- Recent regulatory submissions in Saudi Arabia, Canada, Australia, New Zealand, Mexico and Malaysia
- Regulatory filings ongoing in 2026

VIATRIS

Global development of LX9851 on track

- IND-enabling studies fully completed and delivered to Novo Nordisk
- Initial $10 million milestone achieved, with potential to achieve $20 million in additional milestones in 2026

novo nordisk

Preliminary Full Year 2025 Financials

Full Year 2025 Cash, Investments and Restricted Cash

- Ended 2025 with cash, investments and restricted cash of $125.2 million (unaudited), **sufficient to support planned operations into 2027**
  - Cash runway excludes the impact of milestone payments related to LX9851 and other non-dilutive capital opportunities related to pilavapadin
  - $10 million milestone payment triggered in January, with potential for up to an additional $20 million in milestone payments in 2026
  - $45 million received from Novo Nordisk to date; up to $950 million in remaining potential milestones plus tiered royalties on net sales

Ambitions for 2026

Advance our late-stage regulatory programs: SONATA-HCM and ZYNQUISTA

Expand internationally and through partners with support of ongoing Viatris and Novo partnerships and establishment of a new partner for pilavapadin

Remain operationally disciplined and focused to support long-term growth and value

Lead to Succeed

Thank You