Building a Fully-Integrated, Commercial-Stage Biopharmaceutical Company with a Deep Pipeline

Jefferies 2019 Healthcare Conference

Jeffrey L. Wade, JD
Executive Vice President, Corporate and Administrative Affairs and Chief Financial Officer
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 level of market acceptance and commercial success of XERMELO®, the expected timing and outcome of review by regulatory authorities of applications for approval of sotagliflozin, the results of and expected timing of the completion of our ongoing and future clinical trials, the expected timing and outcome of discussions with regulatory authorities regarding such trials, the expected timing of initiation of our other planned clinical trials, the expected enrollment in our ongoing and future clinical trials, our other research and development efforts, the status of activities performed under our collaborative agreements 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 Lexicon’s 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 Scientific Platform Has Produced Two Commercial Products and a Pipeline of Innovative Drug Candidates

<table>
<thead>
<tr>
<th>Compound</th>
<th>Partner</th>
<th>Target</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
<th>Marketed</th>
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<tbody>
<tr>
<td>XERMELO®</td>
<td>Wholly owned (US/ Japan)</td>
<td>TPH1</td>
<td>Carcinoid syndrome diarrhea</td>
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<td>XERMELO®</td>
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<td>TPH1</td>
<td>Carcinoid syndrome diarrhea</td>
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<td>Zynquista™</td>
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<td>SGLT1 / SGLT2</td>
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<tr>
<td>Sotagliflozin</td>
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<td>SGLT1 / SGLT2</td>
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<tr>
<td>Telotristat ethyl</td>
<td>Wholly owned (US/ Japan)</td>
<td>TPH1</td>
<td>Biliary tract cancer (BTC)</td>
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<tr>
<td>LX2761</td>
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<td>SGLT1 (GI tract)</td>
<td>Diabetes</td>
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<tr>
<td>LX9211</td>
<td>Wholly owned</td>
<td>AAK1</td>
<td>Neuropathic pain</td>
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*FDA approval Feb 28, 2017; US launch Mar 01, 2017*
*EMA approval Sept 19, 2017; EU launch ongoing*
*EMA approval Apr 26, 2019*
XERMELO® (Telotristat Ethyl)
XERMELO® (telotristat ethyl) – First and Only Oral Treatment Approved for Carcinoid Syndrome Syndrome Diarrhea (CSD)

**Novel, oral tryptophan hydroxylase (TPH) inhibitor**

- Meaningful market opportunity in CSD and additional follow-on indication currently in clinical development

- Reduces frequency of carcinoid syndrome diarrhea through reduction of serotonin overproduction

- US approval on Feb 28, 2017
- US launch on Mar 1, 2017
- EU approval on Sept 19, 2017; launch progressing

- Q1 2019 net U.S. sales – $6.7M
  - +23% YOY growth
  - 104 new paid patient starts
  - 1,269 total paid prescriptions (TRx)
  - ~80% compliance
Bridging the Gap – Potential Applications for Serotonin Synthesis and TPH Inhibition

TPH1

Elevated Levels of Peripheral Serotonin

- GI Effects
  - Pro-Tumorigenic Effect
  - Pro-Fibrotic Effect
- Increased Cell Growth and Proliferation
- Increased Fibrosis

- Carcinoid Syndrome Diarrhea (CSD)
- Carcinoid Syndrome (CS)
- Other GI Disorders
- Neuroendocrine Tumors (NETs)
- Biliary Tract Cancer (BTC)
- Other Tumor Types
- Carcinoid Heart Disease
- Non-Alcoholic Steato-Hepatitis (NASH)
- Idiopathic Pulmonary Fibrosis (IPF)

TE

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Sotagliflozin
Type 1 Diabetes Mellitus (T1D) – High Unmet Medical Need

**DESCRIPTION**

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.

**TYPE 1 DIABETES**

Complete insulin deficiency due to destruction of beta cells in the pancreas

- Hypoglycemia common (severe hypoglycemia annual rate of 7–12%\(^1\))
- DKA common (annual rate 5–8%\(^2\))

<table>
<thead>
<tr>
<th>People with T1D in US</th>
<th>~1.66M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults with T1D in US</td>
<td>~1.55M</td>
</tr>
<tr>
<td>A1C &gt;7%</td>
<td>75%</td>
</tr>
<tr>
<td>A1C &gt;8%</td>
<td>50%</td>
</tr>
<tr>
<td>Over 25 years old are obese</td>
<td>25%</td>
</tr>
</tbody>
</table>

\(^1\) Beck et al, The T1D Exchange Clinic Registry, J Clin Endocrinol Metab 97: 4383–4389, 2012

\(^2\) Weinstock et al, Severe Hypoglycemia and Diabetic Ketoacidosis in Adults with Type 1 Diabetes: Results from the T1D Exchange Clinic Registry, J Clin Endocrinol Metab 98: 3411–3419, 2013 (in each case, proportion of patients reporting at least one severe hypoglycemia or DKA event in the previous 12 months).

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FOR IMMEDIATE RELEASE

ZYNQUISTA™ NOW APPROVED IN THE EUROPEAN UNION FOR TREATMENT OF ADULTS WITH TYPE 1 DIABETES

PARIS and THE WOODLANDS, TX, April 26, 2019 – The European Commission has granted marketing authorization for Zynquista™ (sotagliflozin)*, developed by Sanofi and Lexicon (Nasdaq:LXRX). Zynquista is now approved in the European Union, at once-daily doses of 200 mg and 400 mg, for use as an adjunct to insulin therapy to improve blood sugar (glycemic) control in adults with type 1 diabetes (T1D) mellitus and a body mass index ≥ 27 kg/m², who could not achieve adequate glycemic control despite optimal insulin therapy.
FDA Issued a Complete Response Letter for Sotagliflozin in T1D

Outcome for New Drug Application (NDA) for sotagliflozin
- FDA unable to approve the NDA in its present form

Next steps
- We and Sanofi are following up with the FDA to discuss the contents of the CRL and potential next steps for sotagliflozin in type 1 diabetes

We continue to believe in the benefit–risk profile of sotagliflozin and its clinical importance to patients
Type 2 Diabetes Mellitus (T2D) – A Leading Global Public Health Problem

**DESCRIPTION**

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.

**TYPE 2 DIABETES**

Body does not make or use insulin well;
- Insulin resistance
  - Hypoglycemia uncommon unless person is taking insulin/certain diabetes drugs
  - DKA very rare

**A SNAPSHOT**

- 2 out of 5 Americans will develop T2D in their lifetime\(^1\)
- 40% T2D patients have chronic kidney disease (CKD)\(^2\)
- 15–18% Stage 3/4 CKD Contraindication for many T2D therapies
- 1–2% Stage 3 CKD\(^2,3\)
- 27% Increase in probability of CKD mortality among population aged 20 to 54 years due mainly to diabetes\(^4\)

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1. Center for Disease Control and Prevention.
Phase 3 Program in Type 2 Diabetes – Thirteen Ongoing Studies Targeting Over 20,000 Patients

- Moderate renal impairment (SOTA-CKD3) Study
  - 780 patients
  - (NCT03242252)

- Severe renal impairment (SOTA-CKD4) Study
  - 276 patients
  - (NCT03242018)

- Empagliflozin (SOTA-EMPA) on DPP4 background
  - 700 patients
  - (NCT03351478)

- Uncontrolled on basal insulin or OADs (SOTA-INS) Study
  - 560 patients
  - (NCT03285594)

- Glimepiride (SOTA-GLIM) Study
  - 930 patients
  - (NCT03332771)

- CV and Renal Events (SCORED) Study
  - 10,500 patients
  - (NCT03315143)

- Worsening Heart Failure (SOLOIST-WHF) Study
  - 4,000 patients
  - (NCT03521934)

- Efficacy and Bone Safety (SOTA-BONE) Study
  - 360 patients
  - (NCT03386344)

- Monotherapy Study
  - 400 patients
  - (NCT02926937)

- Combo Study with sulfonylurea or metformin in Chinese pts
  - 369 patients
  - (NCT03761134)

- Uncontrolled on diet & exercise in Chinese pts
  - 369 patients
  - (NCT03760965)

- Metformin Study
  - 500 patients
  - (NCT02926950)

- Worsening Heart Failure Study
  - 4,000 patients
  - (NCT03066830)

- Denotes completion of patient enrollment
Significant Opportunity in a Growing SGLT Class

- Evidence continues to build that SGLT inhibitors should become treatment of choice for T2D
  - Strong A1C benefits
  - Benefits beyond A1C in weight loss and blood pressure
  - Improvements in cardiovascular outcomes, demonstrated only by SGLT inhibitors and select GLP-1 receptor agonists among T2D therapeutics
  - Building evidence for renal protection, slowing progression of chronic kidney disease (CKD)

- Sotagliflozin’s dual SGLT1/SGLT2 inhibitory mechanism offers opportunity for potential best-in-class profile
  - SGLT1 mechanism reduces post-prandial glucose, elevates GLP-1 release, with lower SGLT2-associated urinary glucose excretion
  - 20,000-patient Phase 3 program designed to demonstrate differentiation and broad benefits in T2D population

- Core Phase 3 studies are fully enrolled; data expected throughout 2019
An Opportunity to Earn Meaningful Sotagliflozin Regulatory and Development Milestones

Regulatory Milestones
- **$220M** – Milestones linked to first commercial sale after regulatory approval for T1D and T2D in U.S. and Europe

Development Milestones
- **$110M** – Milestones linked to Phase 3 study results in T2D
- **$100M** – Milestone linked to success in either of two T2D outcomes studies

Sales Milestones and Royalties
- **$990M** – Sales milestones
- **Royalties** on net sales

Total: **$430M**
LX9211 – An Innovative Approach to Treat Neuropathic Pain via AAK1 Kinase Inhibition

- Discovered in Lexicon’s neuroscience drug discovery alliance with Bristol-Myers Squibb
- Lexicon acquired exclusive development and commercialization rights
- Potent, highly-selective, oral small molecule inhibitor of AAK1, a target discovered and extensively characterized in alliance
- Preclinical data demonstrate:
  - Excellent CNS penetration
  - Reduction in pain behavior in preclinical models of neuropathic pain
- Phase 1a data:
  - Support preclinical profile
  - Favorable PK profile supports once-daily dosing
  - Well tolerated with headache/dizziness as most common adverse event at higher than expected therapeutic doses
  - Maximum tolerated dose reached
- Initiated Phase 1b multiple ascending dose study and plans for proof-of-concept studies underway

Substantial need for new therapies for neuropathic pain without addictive potential
Neuropathic Pain – High Level of Unmet Need Despite Presence of Marketed Therapeutics

**DESCRIPTION**

Neuropathic pain is a lesion or disease of the somatosensory nervous system, which can lead to numerous chronic painful conditions such as: diabetic peripheral neuropathy, postherpetic neuralgia, trigeminal neuralgia, radiculopathy.

**DISEASE BURDEN**

Includes:
- Severe pain associated with worsening health
- Impaired quality of life
- Meaningful socio/economic burden

![Graph](image.png)

**Expansion of Neuropathic Pain Population**

- **2016**: 360 million
- **2025**: 420 million
- **1.1% CAGR**

**People with neuropathic pain achieve over 50% pain relief**

- 1 in 4

**General population with chronic neuropathic pain**

- 3-17%

**Global neuropathic pain market in 2017**

- $8.5B

**Opioid sales as a percentage of neuropathic pain market**

- 33%

**CAGR for opioid sales (2017-2026)**

- 2.5%

1International Association for the Study of Pain 2014–2015.
3DataMonitor, “Neuropathic Pain Market and Forecast Analysis to 2026”. Global market represents US, SEU and Japan.
Financial Highlights
# Q1 2019 Financial Highlights

## Selected Income Statement Data:

<table>
<thead>
<tr>
<th></th>
<th>First Quarter 2019</th>
<th>First Quarter 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue from Collaborations</td>
<td>$2.4M</td>
<td>$19.8M</td>
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<tr>
<td>Net Product Revenue</td>
<td>$6.7M</td>
<td>$5.5M</td>
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<tr>
<td>Operating Expenses (^1)</td>
<td></td>
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<tr>
<td>R&amp;D</td>
<td>$12.0M</td>
<td>$47.7M</td>
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<tr>
<td>SG&amp;A</td>
<td>$14.1M</td>
<td>$14.9M</td>
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<tr>
<td>Total Operating Expenses</td>
<td>$26.7M</td>
<td>$63.1M</td>
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<tr>
<td>Net Loss</td>
<td>$(21.8)M</td>
<td>$(41.8)M</td>
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<tr>
<td>Net Loss Per Common Share</td>
<td>$(0.21)</td>
<td>$(0.40)</td>
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\(^1\)Includes stock-based compensation expenses

## Selected Balance Sheet Data:

<table>
<thead>
<tr>
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<th>As of March 31, 2019</th>
</tr>
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<tbody>
<tr>
<td>Cash &amp; Investments</td>
<td>$133.1 million</td>
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<tr>
<td>Total Assets</td>
<td>$258.5 million</td>
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<tr>
<td>Total Debt</td>
<td>$245.0 million</td>
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<td>Common Shares Outstanding</td>
<td>106.3 million</td>
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## Anticipated Milestones

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<th>Drug/Condition</th>
<th>Est. Timing</th>
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<tbody>
<tr>
<td><strong>Sotagliflozin</strong> – Type 1 Diabetes</td>
<td><strong>Timing</strong></td>
</tr>
<tr>
<td>Endocrinologic and Metabolic Drugs Advisory Committee meeting</td>
<td>Jan 17, 2019 ✓</td>
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<tr>
<td>CHMP opinion</td>
<td>Feb 28, 2019 ✓</td>
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<tr>
<td>U.S. regulatory decision</td>
<td>CRL Mar 22, 2019 (Ongoing)</td>
</tr>
<tr>
<td>European Commission approval</td>
<td>April 26, 2019 ✓</td>
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<tr>
<td>Presentation of new analyses at ADA and EASD</td>
<td>Jun, Sept 2019</td>
</tr>
<tr>
<td><strong>Sotagliflozin</strong> – Type 2 Diabetes</td>
<td><strong>Timing</strong></td>
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<tr>
<td>Patient enrollment in two outcome studies</td>
<td>Ongoing</td>
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<tr>
<td>Topline results from core Phase 3 studies</td>
<td>Starting H1 2019</td>
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<tr>
<td><strong>LX9211</strong> – Neuropathic Pain</td>
<td><strong>Timing</strong></td>
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<tr>
<td>Patient enrollment in Phase 1b study</td>
<td>Ongoing</td>
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<tr>
<td><strong>XERMELO</strong> – Carcinoid Syndrome Diarrhea</td>
<td><strong>Est. Timing</strong></td>
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<tr>
<td>Launches in additional EU countries, Canada</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Manuscript publications</td>
<td>Q1 2019 ✓</td>
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<tr>
<td><strong>Telotristat Ethyl</strong> – Oncology</td>
<td><strong>Timing</strong></td>
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<tr>
<td>Patient enrollment in Phase 2 study in biliary tract cancer</td>
<td>Ongoing</td>
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✓ Denotes completed milestone