This presentation contains “forward-looking statements,” including statements about Lexicon’s strategy and operating performance, 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 status of any collaborative agreements or clinical trials, the expected timing of the completion of our ongoing and future clinical trials, the expected timing of discussions with our regulators regarding such trials and the results of such trials, including top-line data, expected timing of initiation of our planned clinical trials, expected enrollment in our ongoing and future clinical trials, our research and development efforts, and 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 Focused Strategy for Value Creation

1. Strong scientific foundation in biology and drug discovery
   - Genome-wide discovery of target biology enabled Lexicon to identify high-value targets from 5,000 druggable genes
   - Small molecule drug discovery for multiple targets created pipeline of internally-discovered, proprietary NMEs

2. Translate Lexicon’s science into stakeholder returns from high-value Orphan/Specialty markets: Carcinoid Syndrome and Type 1 Diabetes (T1DM)
   - Telotristat etiprate (LX1032) for carcinoid syndrome: Proceed with Phase 3 completion, NDA submission and commercialization
   - Sotagliflozin (LX4211) for type 1 diabetes: Progress Phase 3 program

3. Each drug candidate on its own offers opportunity to drive significant corporate value for Lexicon
   - Both drug candidates offer opportunity for major advances in patient care in areas of high unmet medical need, few treatment options, and limited recent pharmaceutical innovation

4. Maintain valuable U.S. market opportunity, while adding value through strategic ROW partnerships
   - Commercial collaboration with Ipsen for telotristat etiprate in Europe, Canada and other markets creates near and long term value
   - ROW partnership potential for T1DM as Phase 3 development advances

© 2015 Lexicon Pharmaceuticals, Inc.
Telotristat Etiprate: A Peripherally–Acting Serotonin Synthesis Inhibitor

- **Telotristat etiprate** is a novel, orally-delivered inhibitor of tryptophan hydroxylase (TPH) that reduces serotonin production
  - Absorbed into peripheral circulation
  - Does not cross the blood–brain barrier

- Serotonin is a key mediator of gastrointestinal motility, pain and inflammation

- High serotonin implicated in carcinoid heart disease and cardiac valve damage

- Telotristat etiprate has received fast track and orphan designation from FDA, and orphan designation from EMA

Carcinoid syndrome results from metastatic carcinoid tumor, a life-threatening neuroendocrine tumor that produces large amounts of serotonin; associated with diarrhea, flushing, pain, and valvular disease
12–Week Phase 2 Results Correspond to Duration of Placebo–Controlled Portion of Pivotal Phase 3 Study

Mean BM Frequency

-43.5% change from baseline at weeks 11–12

Change in Mean Bowel–Movement Frequency in 12–week Open–label Phase 2 Study
Patients in Phase 2 Achieved Clinically Meaningful Benefit

Individual Patient Bowel-Movement Frequency in 12-week Open-label Phase 2 Study
Telotristat Etiprate Progressing Toward Market

- Enrollment completed
- Phase 3 program designed to satisfy requirements for approval in U.S. and Europe

**Pivotal Phase 3 study, TELESTAR**

- Phase 3, randomized, placebo-controlled, double-blind study
- 135 patients on somatostatin analog (SSA) therapy
- Double-blind treatment period: 12 weeks
- Open-label extension and follow-up period: 36 weeks

**TELESTAR study design**

- Primary endpoint
  - Change from baseline in the number of daily bowel movements (BMs) averaged over the 12-week double-blind portion (treatment period) of the trial in patients inadequately controlled on SSA therapy
- Secondary endpoints
  - Changes in urinary 5–HIAA levels, flushing episodes, abdominal pain and QOL measures
Substantial Market Opportunity for Telotristat Etiprate in Patients Not Adequately Controlled on Current Therapy

U.S. Carcinoid Syndrome Treatment Flow (Typically 7–10 Years After Diagnosis)

1,600 New Carcinoid Syndrome Patients/Year → 13,700 Carcinoid Syndrome Patients In The U.S. → 98% Treated With Octreotide (Sandostatin) or Lanreotide (Somatuline)

79% of Patients Fail to Control Symptoms → Carcinoid Syndrome Typically Controlled For Less Than 3 Years

Telotristat Etiprate Will Be The Only Approved Therapy For These Patients

Note: Segment sizes in 2012
Sources: EPI Research, NET Claims data from IMS, Lexicon–sponsored market research with 45 oncologists (August 2013).
Note: Somatuline® Depot is an SSA approved for carcinoid syndrome in the E.U. and for GEPNET in the U.S.
Existing Therapy Fails to Maintain Adequate Control for the Significant Majority of Carcinoid Syndrome Patients

The current treatment paradigm for these patients includes:

- Titration to higher doses of octreotide LAR beyond label recommendations
- Increase in frequency of immediate release octreotide injections

No new therapy options exist for patients not adequately controlled.

Source: Lexicon-sponsored market research with 45 oncologists, August 2013
Lexicon is Preparing for the Commercialization of Telotristat Etiprate in the U.S.

Initial assessment of U.S. NET market suggests that Lexicon can be very targeted in its promotional effort and can reach the opportunity with a modest sales force and supplement efforts via non personal promotion and peer to peer education.

---

Lexicon will be able to leverage SSA prescribing data to focus promotional efforts.

---

* Metropolitan Statistical Area as defined by the US Office of Management and Budget
** Represents OnCs with 2 or more Carcinoid or PNET patients

Sources: NET Physician Level Claims data from IMS

© 2015 Lexicon Pharmaceuticals, Inc.
Collaborating with Ipsen to Commercialize Telotristat Etiprate in Europe, Canada and Other ROW Markets

Lexicon to retain rights in the U.S. and Japan

Ipsen to commercialize Telotristat Etiprate in EU, Canada and ROW

Lexicon benefits commercially from Ipsen’s substantial market presence in Europe, Canada and other countries in the licensed territory, and benefits globally from coordination with Ipsen on medical and scientific matters.

- Lexicon will potentially receive up to $150 million in upfront and milestone payments during the course of the collaboration, plus future royalties
  - Upfront payment of $23 million
  - Contingent future development and regulatory milestone payments, together with Canada up-front payment, totaling more than $35 million relating to regulatory filings and approvals and first commercial sales in Europe
  - Euro-denominated sales milestone payments of up to €72 million based on Ipsen’s net sales throughout the licensed territory
- Lexicon will receive royalties on net sales of telotristat etiprate in the licensed territory (from low 20s to mid-30s percent inclusive of supply)
Sotagliflozin: First-in-Class Dual SGLT1/SGLT2 Inhibitor for Diabetes

• SGLT1 is the primary transporter for absorption of glucose and galactose in the GI tract

• Reduction of glucose absorption in the proximal intestines leads to more glucose being delivered distally

• L cells respond by releasing GLP-1 and PYY

• SGLT2 is expressed in the kidney where it reabsorbs 90% of filtered glucose

• Enhancing glucose excretion in the kidney will enhance glycemic control

• This mechanism is independent of insulin and may be pancreas-sparing
Sotagliflozin’s Dual SGLT1 / SGLT2 Mechanism Offers Differentiating Advantages in Type 1 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>SGLT1/2 Sotagliflozin</th>
<th>Selective SGLT2 Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin-independent mechanism of action</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>A1C reduction</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Postprandial glucose reduction</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Increase in time spent in target glucose range</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Decrease in time spent in hyperglycemic range</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Bolus (mealtime) insulin requirements reduced</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Mechanism avoids hypoglycemia</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Benefit despite reduced kidney function/CKD</td>
<td>√√</td>
<td></td>
</tr>
<tr>
<td>Relatively less urinary glucose excretion</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Blood pressure reduction</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td>Elevates GLP-1 reducing post-prandial glucose</td>
<td>√√</td>
<td></td>
</tr>
</tbody>
</table>
Sotagliflozin Has Been Studied in More than 600 T1DM and T2DM Patients and Healthy Subjects, in 14 Clinical Trials

- Key studies:
  - 36-patient Phase 2a study of sotagliflozin monotherapy in type 2 diabetics
  - 299-patient Phase 2b study of sotagliflozin in type 2 diabetics on background metformin therapy
  - 20-patient study of sotagliflozin in patients with moderate to severe renal impairment
  - 36-patient Phase 2 study of sotagliflozin in type 1 diabetics

- All studies required before initiation of Phase 3 development have been completed

- No cases of euglycemic DKA to date
Sotagliflozin Type 1 DM Proof of Concept Endpoints

Primary Goal
- To establish safety and mechanistic proof-of-concept
  - First co-administration of sotagliflozin with insulin

Primary Endpoint
- To assess the effect of sotagliflozin on the total amount of bolus insulin required

Secondary Objectives (partial list)
- To assess multiple parameters of glycemic control
- To assess the effect of sotagliflozin on basal and total insulin use
- To assess other metabolic, pharmacodynamic and pharmacokinetic parameters
Sotagliflozin Met Primary Endpoint in Phase 2 Study in Type 1 Diabetes, Significantly Reducing Bolus Insulin Use

Bolus (Mealtime) Insulin

<table>
<thead>
<tr>
<th></th>
<th>Change from baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
<td>-6.4</td>
</tr>
<tr>
<td><strong>Sotagliflozin</strong></td>
<td>-32</td>
</tr>
</tbody>
</table>

* p = 0.007 relative to placebo
Sotagliflozin Produced a Significant Reduction in A1C of Subjects with Type 1 Diabetes at Four Weeks

* p = 0.002 relative to placebo

A1C

Change from baseline (%)

-0.6
-0.5
-0.4
-0.3
-0.2
-0.1
0

Placebo

Sotagliflozin

-0.06

-0.55

*
Sotagliflozin Improved Glycemic Control in Subjects with T1DM as Measured by Continuous Glucose Monitoring

Percentage of Time in Blood Glucose Range

- Baseline Placebo: 8.5% > 180 mg/dl, 55.9% 70-180 mg/dl, 35.6% <70 mg/dl
- Treatment Placebo: 5.8% > 180 mg/dl, 54.0% 70-180 mg/dl, 40.2% <70 mg/dl
- Baseline Sotagliflozin: 7.9% > 180 mg/dl, 56.4% 70-180 mg/dl, 35.7% <70 mg/dl
- Treatment Sotagliflozin: 6.7% > 180 mg/dl, 68.2% 70-180 mg/dl, 25.1% <70 mg/dl

p=0.002 vs placebo

p=0.003 vs placebo
Sotagliflozin Produced a Significant Reduction in Body Weight of Subjects with T1DM at Four Weeks

Body Weight

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Sotagliflozin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>+0.50</td>
</tr>
<tr>
<td>0.5</td>
<td>-1.72*</td>
</tr>
</tbody>
</table>

* p = 0.005 relative to placebo
Lexicon’s Collaboration with JDRF in Type 1 Diabetes is Underway

- Collaboration involves JDRF funding to support a Phase 2 clinical trial to evaluate the efficacy and safety of sotagliflozin in a younger population with T1DM

- Study design
  - Phase 2, randomized, placebo-controlled, double-blind study
  - Up to 84 individuals with T1DM younger than 30 years of age and with A1C levels greater than 9.0%
  - Treatment period: 12 weeks

- Objectives
  - Primary endpoint
    - Reduction in A1C at 12 weeks of once-daily 400 mg sotagliflozin versus placebo as an adjunct to insulin treatment
  - Secondary endpoints
    - Reduced variability in blood glucose levels
    - Lower insulin needs
Lexicon Has Advanced Sotagliflozin into Phase 3 for Type 1 Diabetes

<table>
<thead>
<tr>
<th>Pivotal Studies in T1DM</th>
<th>Two studies</th>
<th>Primary endpoint</th>
<th>Additional objectives</th>
</tr>
</thead>
</table>
|                         | • 750 patients each study  
• 2 doses (200mg and 400mg once-daily) and placebo | Reduction of A1C vs placebo on optimized insulin | • Reduced variability in blood glucose levels  
• Lower insulin needs  
• Weight loss  
• Patient-reported outcomes |

| Additional Study in T1DM (purpose: safety exposure) | 1,400 subjects with type 1 diabetes  
• 400 mg once-daily vs. placebo | Glycemic control endpoint | Safety exposure |

Phase 3 enrollment underway
Type 1 Diabetes: An Area of High Unmet Medical Need

- **Substantial majority of type 1 diabetics are not achieving A1C targets**
  - ~75% of adult T1DM patients have A1C above the ADA target of 7%\(^1\)
  - More than 50% of all T1DM patients have A1C > 8%\(^1\)

- **Significant percentage of people with type 1 diabetes experience severe hypoglycemic events\(^1\)**
  - Reports indicate 4% to 10% of T1DM patients die of hypoglycemia\(^2\)

- **Weight control is an increasing challenge for people with type 1 diabetes**
  - More than 25% of T1DM patients over the age of 25 are obese\(^1\)

- **Significant intraday glucose variability poses risks to T1DM patients and is challenging for them to manage**
  - Resulting in hyperglycemia and hypoglycemia

Sotagliflozin’s Target Profile is Directed towards Key Unmet Needs in Type 1 Diabetes

U.S. Type 1 Diabetes Treatment Flow

1.09 Million Diagnosed & Treated T1DM Patients

A1C Not At Goal (>7%)
Low Engagement (40%)
- Don’t appreciate long-term consequences
- Don’t want to gain weight
- Too much work
- Reduce severe hypoglycemia

A1C Not At Goal (>7%)
High Engagement (35%)
- Constantly trying to be at goal without success
- Fearful of severe hypoglycemia

A1C At Goal (<7%)
Active Engagement (25%)
- Tremendous patient burden coupled with fear of severe hypoglycemia

Diagnosed, Treated and Actively Monitored By Endocrinologist and Select Primary Care Physicians

Treatment Options
Insulin
Diet & Exercise
Off Label (OADs, GLPs)

Sotagliflozin’s target profile is designed to help more patients get to goal, stay at goal, and make it easier, while reducing risk of hypoglycemia

Source: ¹T1D Exchange ²Lexicon–sponsored market research
Advancing Lexicon’s Late–Stage Pipeline towards Market

- Pivotal Phase 3 study TELESTAR enrollment completed
- Commercial preparations underway for U.S.
- Collaboration with Ipsen established for commercialization of telotristat etiprate in Europe, Canada and other markets outside U.S. and Japan

Telotristat etiprate for carcinoid syndrome

- Phase 3 and Phase 2 studies progressing for type 1 diabetes, with enrollment underway

Sotagliflozin for diabetes

Strong financial position: $315.1 million in cash and investments at March 31, 2015
Lexicon is Poised to Achieve a Series of Important Value Creating Events

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q3 2015</td>
<td><strong>Phase 3 top-line data</strong> for telotristat etiprate in carcinoid syndrome</td>
</tr>
<tr>
<td>Q1 2016</td>
<td>Potential <strong>NDA filing</strong> for telotristat etiprate in carcinoid syndrome</td>
</tr>
<tr>
<td>Q1 2016</td>
<td><strong>JDRF study data</strong> for sotagliflozin in high unmet-need type 1 diabetes population</td>
</tr>
<tr>
<td>Q3/4 2016</td>
<td>Potential <strong>FDA approval</strong> and <strong>commercial launch</strong> of telotristat etiprate for carcinoid syndrome</td>
</tr>
<tr>
<td>Q4 2016</td>
<td><strong>Phase 3 top-line data</strong> for sotagliflozin in type 1 diabetes</td>
</tr>
</tbody>
</table>
Breakthrough Treatments for Human Disease

NASDAQ: LXRX

www.lexpharma.com