June 2015

Lexicon pharmaceuticals

Progressing from Late-Stage Development to Commercialization

Jefferies 2015 Healthcare Conference

Lonnel Coats

President and Chief Executive Officer

Discovering Breakthrough Treatments for Human Disease

Forward-looking Statements

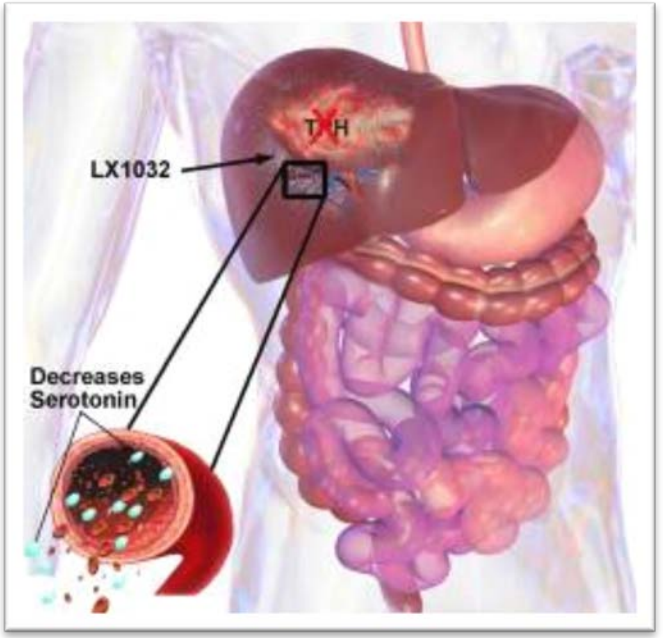
This presentation contains "forward-looking statements," including statements about Lexicon's strategy and operating performance, events or developments that we expect or anticipate will occur in the future, such as projections of our future results of operations or of our financial condition, the status 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

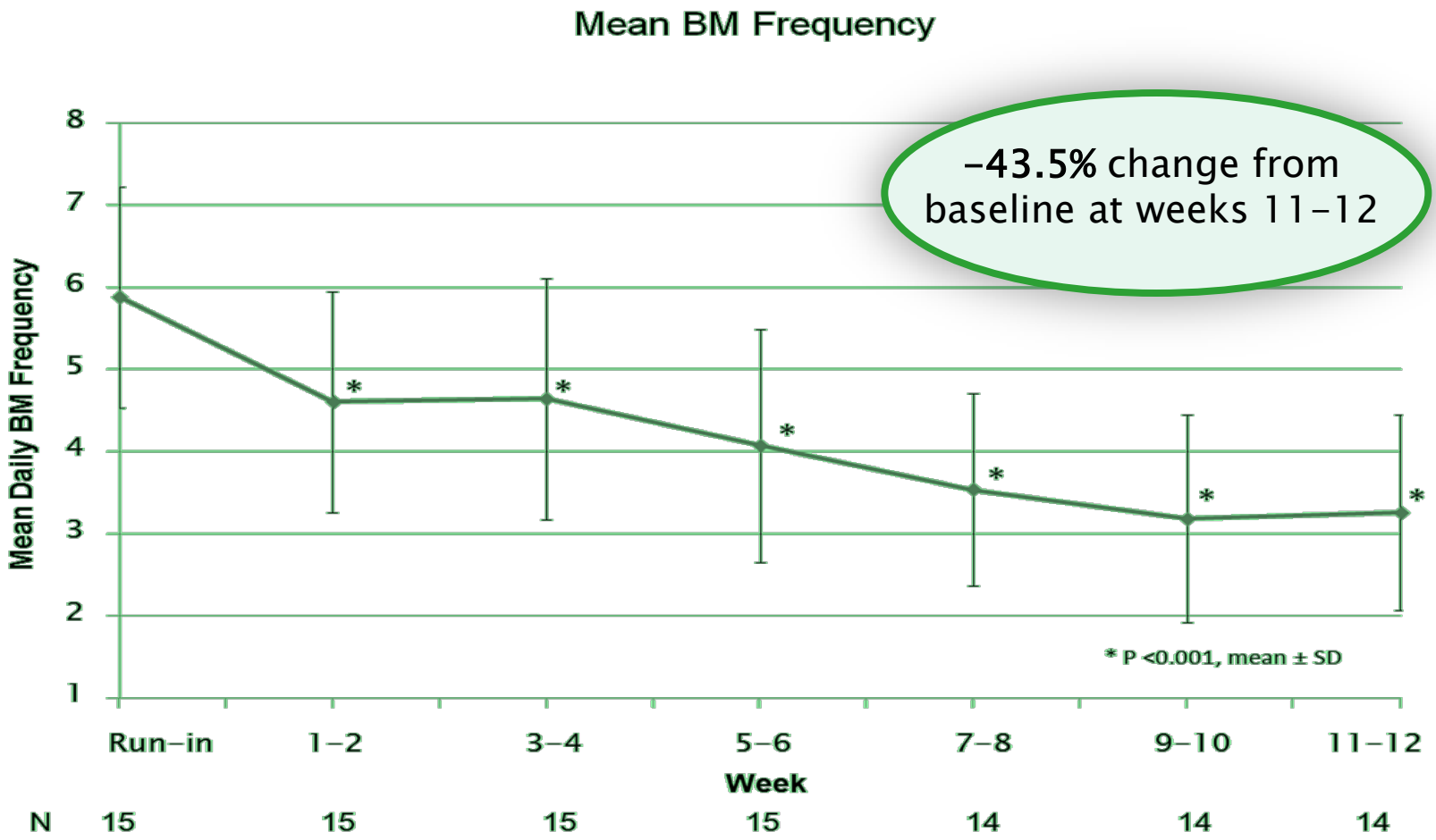
Telotristat Etiprate:
A Peripherally-Acting Serotonin Synthesis Inhibitor

- **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



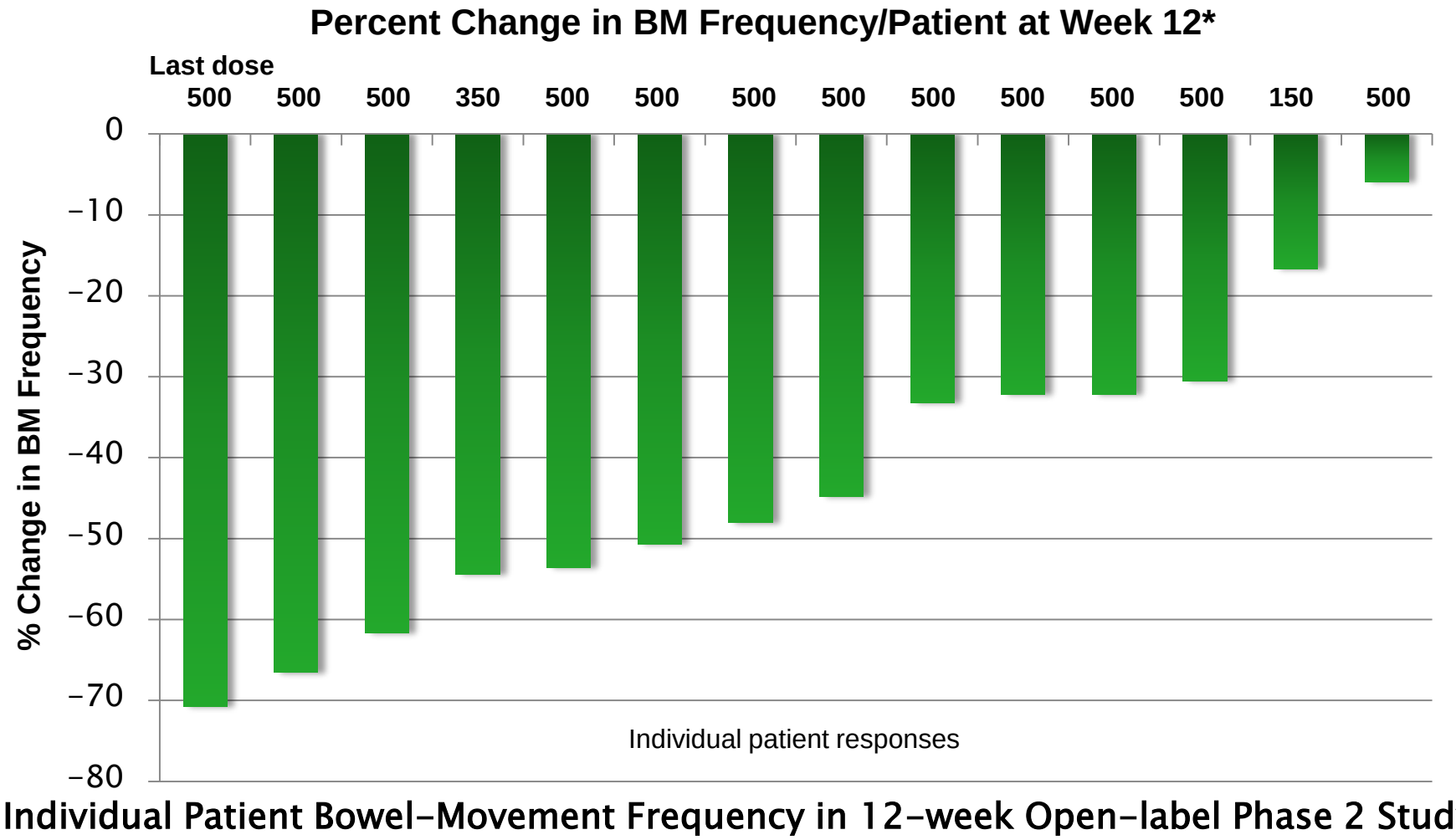
Carcinoid syndrome results from metastatic carcinoid tumor, a life-threatening neuroendocrine tumor that produces large amounts of serotonin; associated with diarrhea, flushing, pain, and valvular disease

12-Week Phase 2 Results Correspond to Duration of Placebo-Controlled Portion of Pivotal Phase 3 Study



Change in Mean Bowel-Movement Frequency in 12-week Open-label Phase 2 Study

Patients in Phase 2 Achieved Clinically Meaningful Benefit



Telotristat Etiprate Progressing Toward Market

Pivotal Phase 3 study, TELESTAR

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

TELESTAR study design

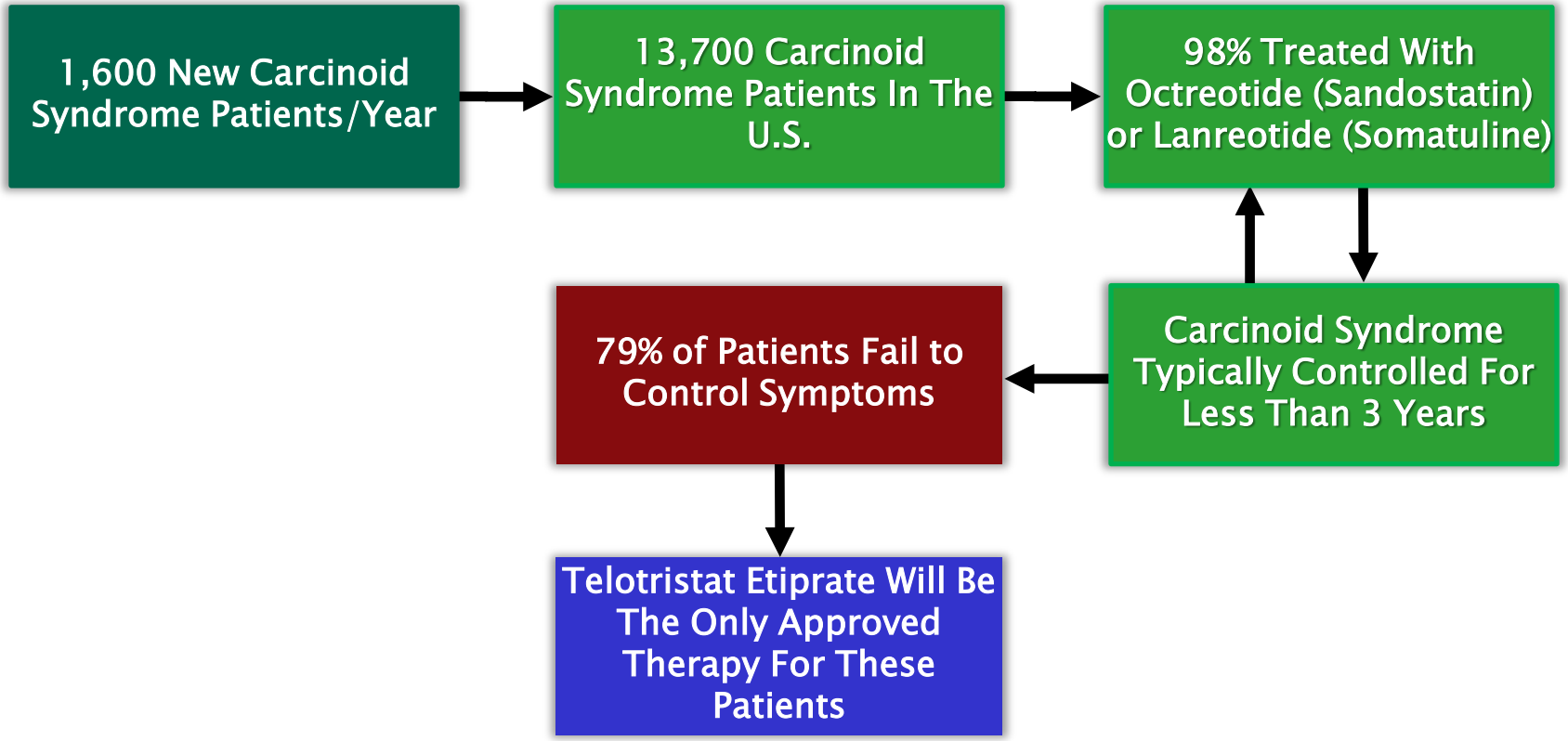
- Phase 3, randomized, placebo-controlled, double-blind study
- 135 patients on somatostatin analog (SSA) therapy
- Double-blind treatment period: 12 weeks
- Open-label extension and follow-up period: 36 weeks

TELESTAR objectives

- 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)

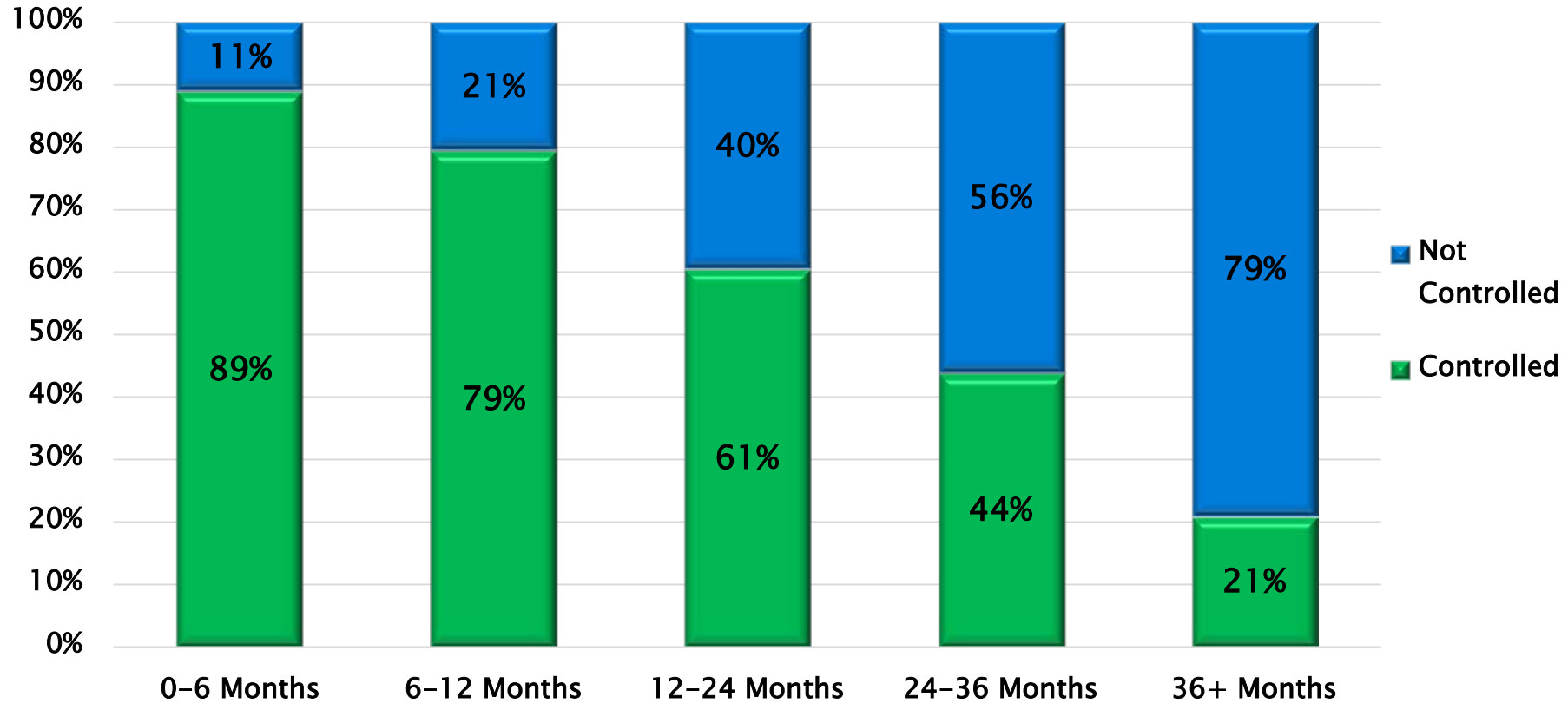


Note: Segment sizes in 2012

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



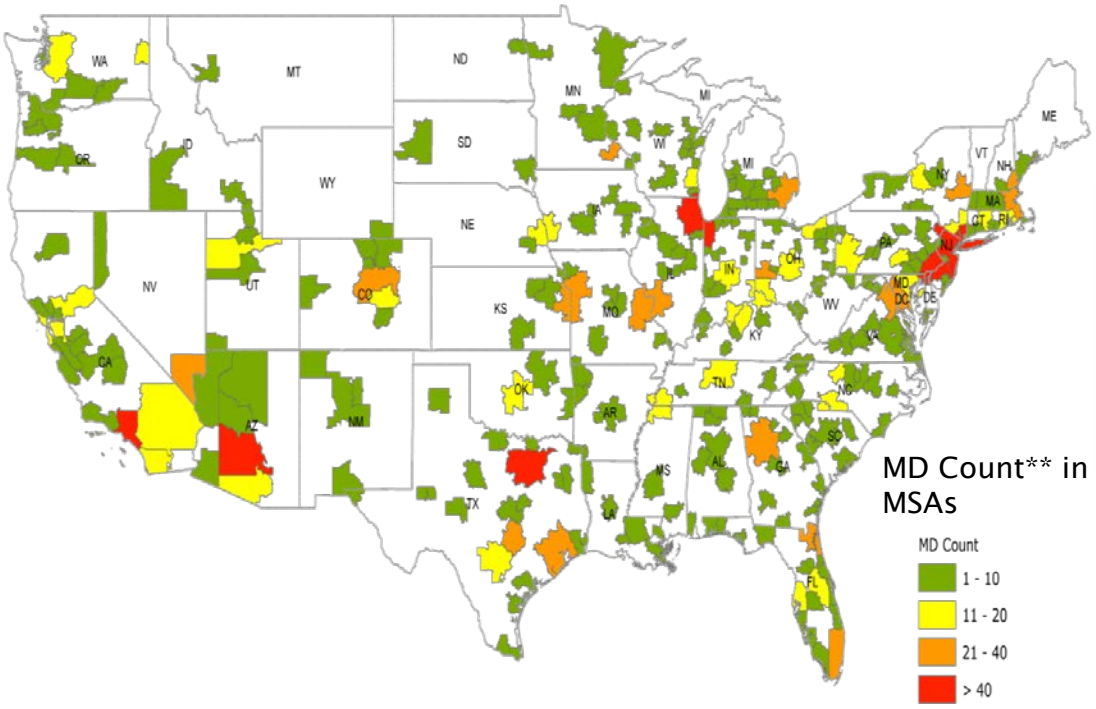
No new therapy options exist for patients not adequately controlled

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

Source: Lexicon-sponsored market research with 45 oncologists, August 2013

Lexicon is Preparing for the Commercialization of Telotristat Etiprate in the U.S.



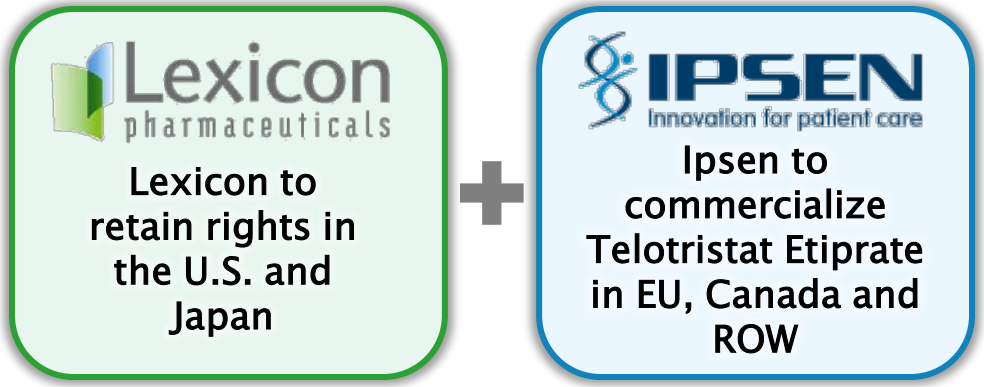
Lexicon will be able to leverage SSA prescribing data to focus promotional efforts

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

* 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

Collaborating with Ipsen to Commercialize Telotristat Etiprate in Europe, Canada and Other ROW Markets



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)

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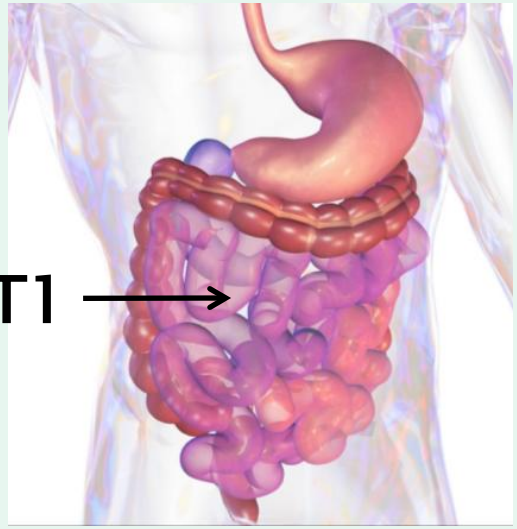
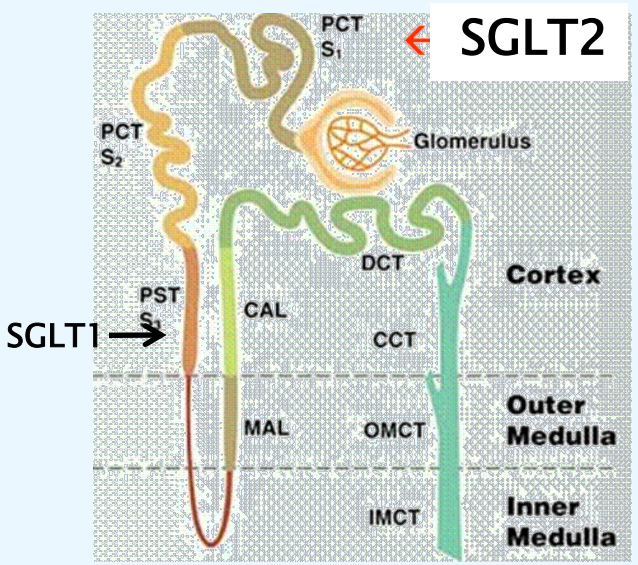
Sotagliflozin:
First-in-Class Dual SGLT1/SGLT2 Inhibitor for Diabetes



- 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

	SGLT1/2 Sotagliflozin	Selective SGLT2 Inhibitors
Insulin-independent mechanism of action	2	1
A1C reduction	√√	√
Postprandial glucose reduction	√√	√
Increase in time spent in target glucose range	√√	√
Decrease in time spent in hyperglycemic range	√√	√
Bolus (mealtime) insulin requirements reduced	√√	√
Mechanism avoids hypoglycemia	√√	√
Benefit despite reduced kidney function/CKD	√√	
Relatively less urinary glucose excretion	√	
Weight loss	√	√
Blood pressure reduction	√√	√
Elevates GLP-1 reducing post-prandial glucose	√√	

Sotagliflozin Has Been Studied in More than 600 T1DM and T2DM Patients and Healthy Subjects, in 14 Clinical Trials

11	3	271	385	36
Phase 1 clinical trials	Phase 2 clinical trials	Total healthy test subjects	Type 2 diabetes patients	Type 1 diabetes patients

- **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

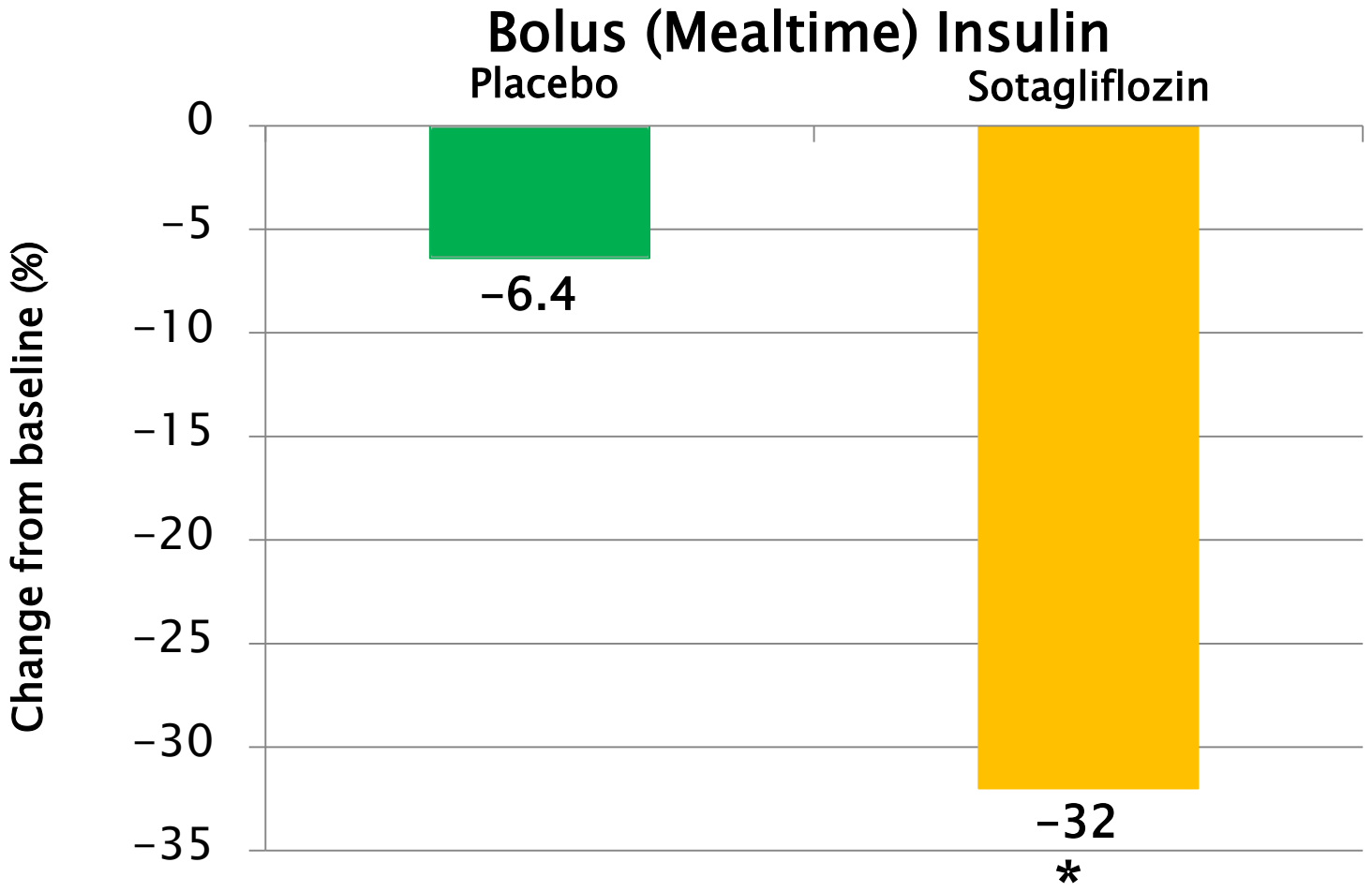
Primary Endpoint

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

Secondary Objectives (partial list)

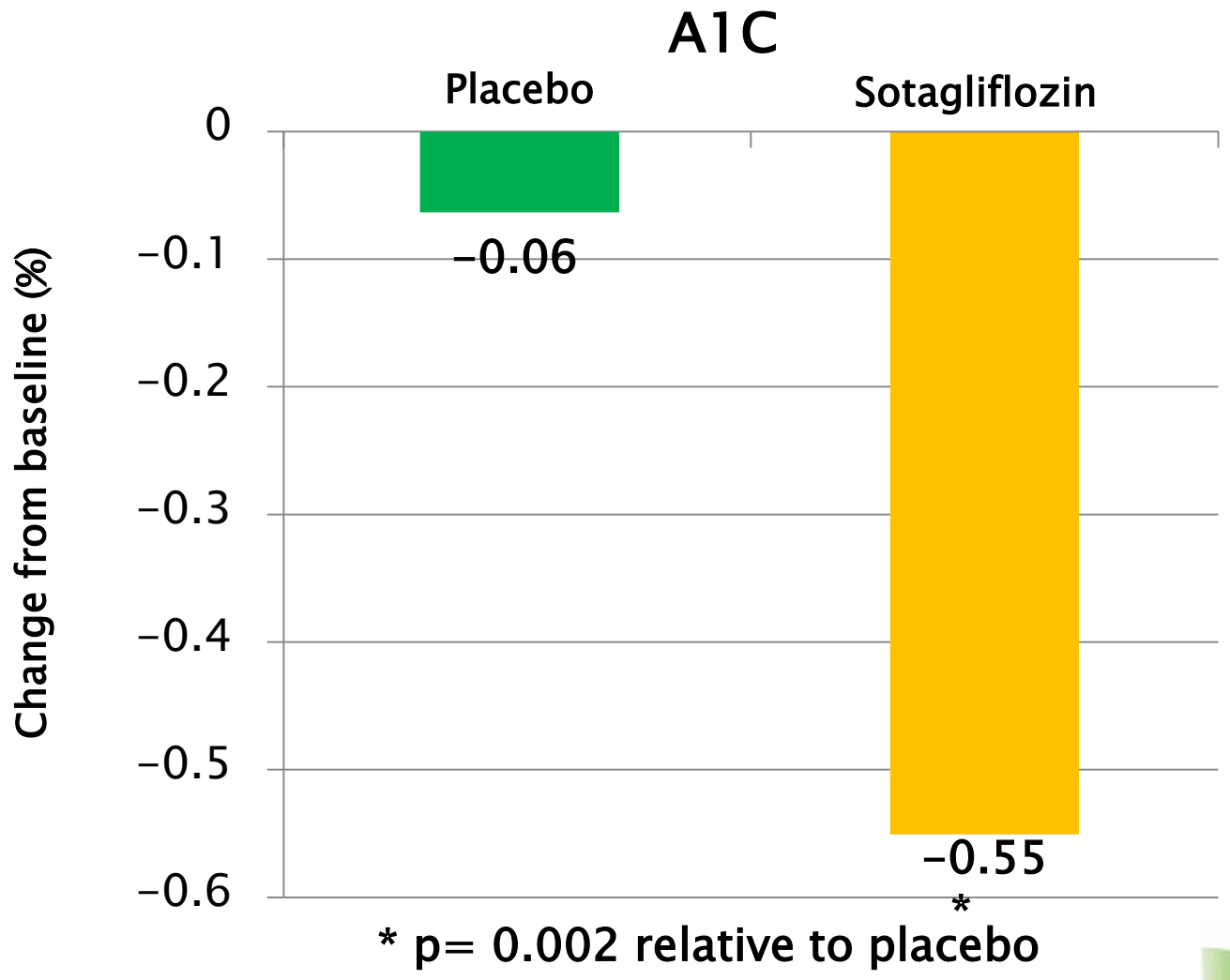
- To assess multiple parameters of glycemic control
- To assess the effect of sotagliflozin on basal and total insulin use
- To assess other metabolic, pharmacodynamic and pharmacokinetic parameters

Sotagliflozin Met Primary Endpoint in Phase 2 Study in Type 1 Diabetes, Significantly Reducing Bolus Insulin Use

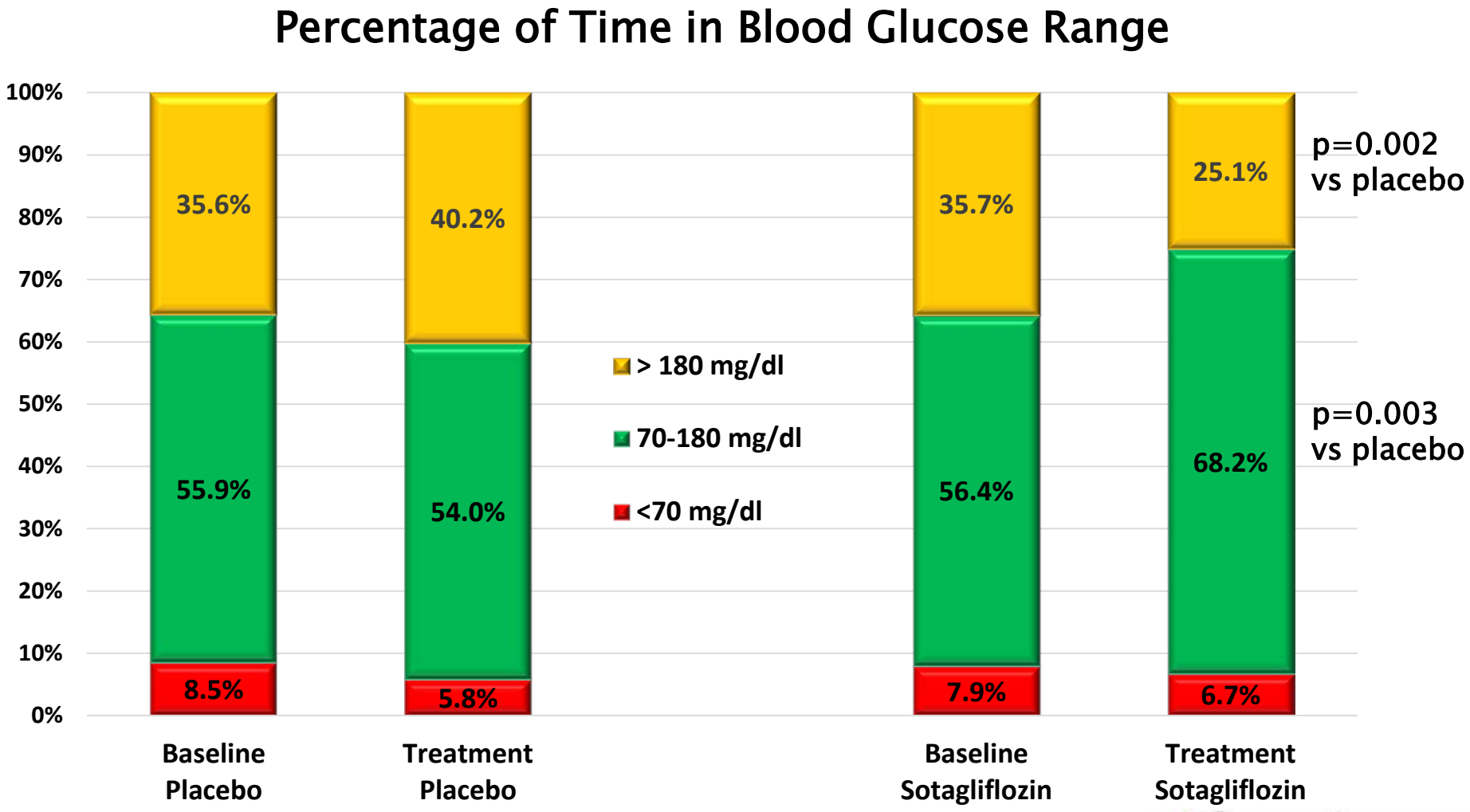


* p= 0.007 relative to placebo

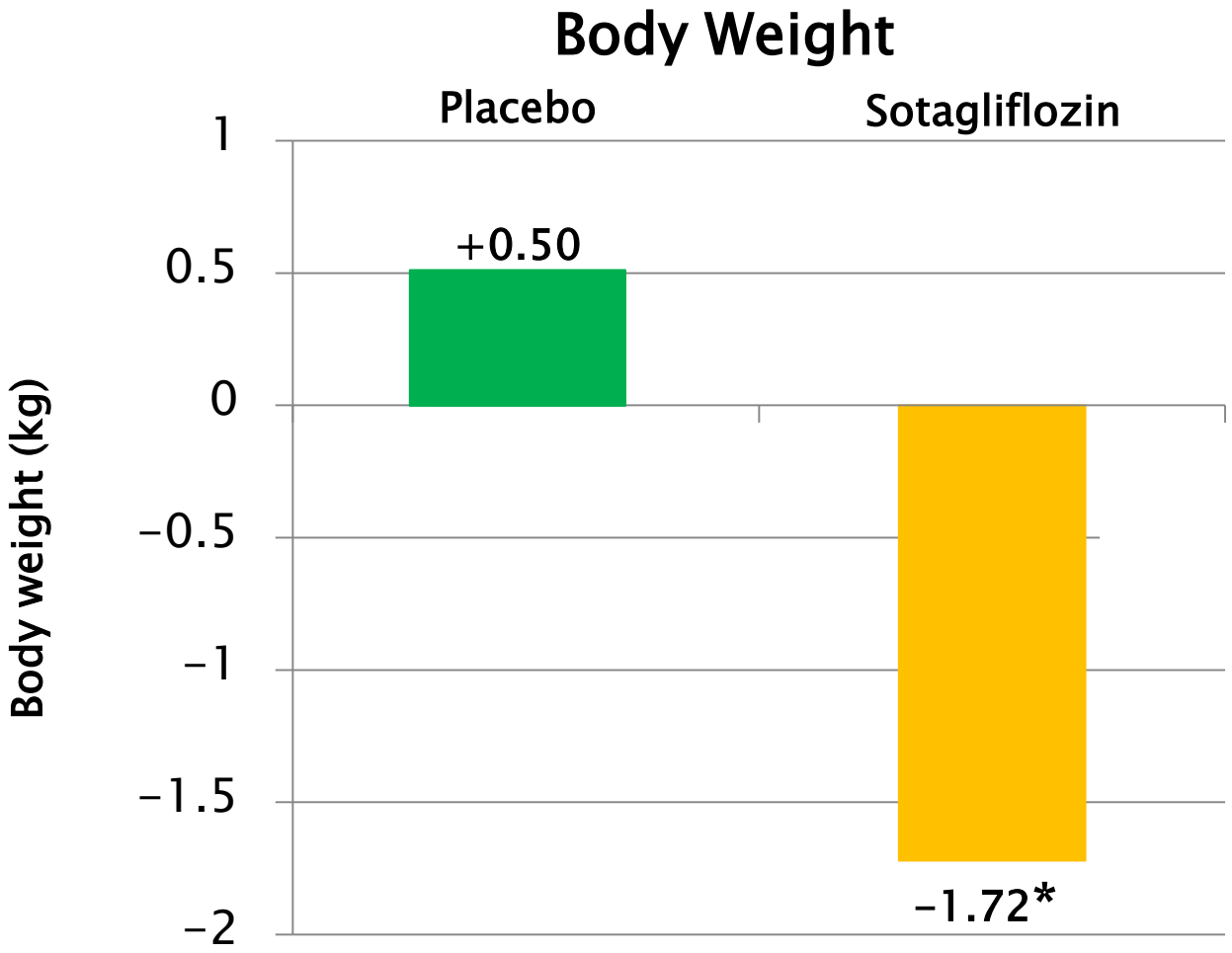
Sotagliflozin Produced a Significant Reduction in A1C of Subjects with Type 1 Diabetes at Four Weeks



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



Sotagliflozin Produced a Significant Reduction in Body Weight of Subjects with T1DM at Four Weeks



* p= 0.005 relative to placebo

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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

Pivotal Studies in T1DM	**Two studies**	**Primary endpoint**	**Additional objectives**
	• 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

Source: [1]T1D Exchange database. [2] Patterson et al, Early mortality in EURODIAB population-based cohorts of type 1 diabetes diagnosed in childhood since 1989, *Diabetologia* 2007; 50:2439-2442; Skrivarhaug et al, Long-term mortality in a nationwide cohort of childhood-onset type 1 diabetic patients in Norway, *Diabetologia* 2006; 49:298-305

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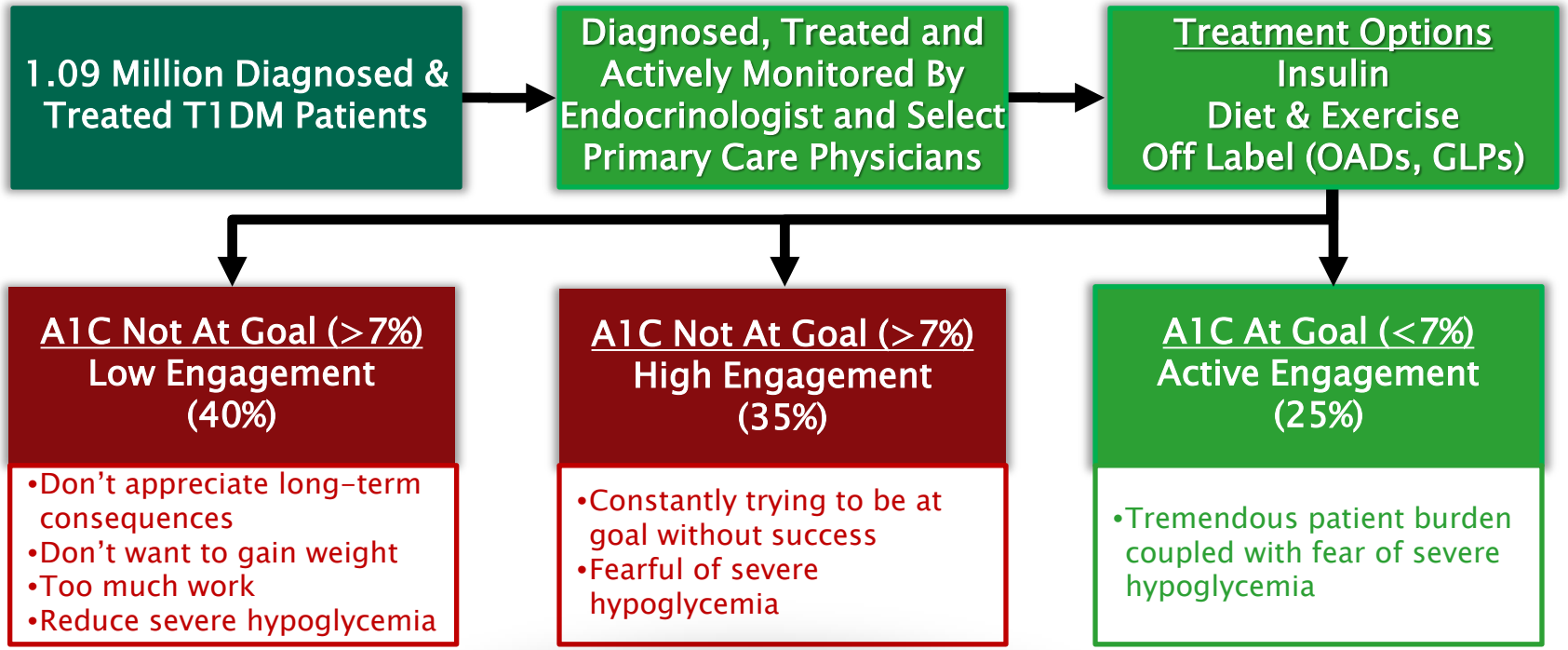
Sotagliflozin's Target Profile is Directed towards Key Unmet Needs in Type 1 Diabetes

U.S. Type 1 Diabetes Treatment Flow



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: [1]T1D Exchange [2] Lexicon-sponsored market research

Advancing Lexicon's Late-Stage Pipeline towards Market

Telotristat etiprate for carcinoid syndrome

- 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

Sotagliflozin for diabetes

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

Strong financial position: $315.1 million in cash and investments at March 31, 2015

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Lexicon is Poised to Achieve a Series of Important Value Creating Events

Timeline	Event
Q3 2015	**Phase 3 top-line data** for telotristat etiprate in carcinoid syndrome
Q1 2016	Potential **NDA filing** for telotristat etiprate in carcinoid syndrome
Q1 2016	**JDRF study data** for sotagliflozin in high unmet-need type 1 diabetes population
Q3/4 2016	Potential **FDA approval** and **commercial launch** of telotristat etiprate for carcinoid syndrome
Q4 2016	**Phase 3 top-line data** for sotagliflozin in type 1 diabetes

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Breakthrough Treatments for Human Disease

NASDAQ: LXRX

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