Lixisenatide (Lyxumia®): A novel once-daily GLP-1 agonist and lead Zealand drug invention, partnered with Sanofi in Type 2 diabetes
by/ David Solomon, President and CEO

Capital Markets Day, NYC — 29 November 2012
Predicted diabetes prevalence in 2030 (% of total population 20-79 years)*

The number of diabetes patients is expected to increase to > 550 million globally in 2030, highest growth in Emerging Markets

NATIVE GLP-1 PLAYS A KEY ROLE IN GLUCOSE CONTROL

<table>
<thead>
<tr>
<th>Food intake</th>
<th>The gut</th>
<th>Blood</th>
<th>GLP-1 targets</th>
<th>Physiological effects</th>
<th>Therapeutic effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>GLP-1 is released into the blood stream</td>
<td>Pancreas</td>
<td>Insulin Glucagon</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stomach</td>
<td>Gastric emptying</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Brain</td>
<td>Appetite</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Heart</td>
<td></td>
</tr>
</tbody>
</table>
The treatment paradigm in Type 2 diabetes (from diagnosis to advanced stage treatment in 7-10 years)

- **Diagnosis**
  - First line of treatment: Diet and exercise

- **Disease progression**
  - Second line of treatment: Oral medication

- **Disease progression**
  - Third line of treatment: Insulin therapy

**Use of GLP-1 drug:**
- Monotherapy
- Add-on to OADs
- In combination with insulin

**GLP-1 drugs have broad potential for use**
- Mimics the body’s natural glucose response
- Improves glycemic control
- Delays the use of insulin
- Good safety and Low risk of hypoglycemic event
  - Episodes of too low blood sugar levels
- Improves weight management
- Improves glycemic control in combination with insulin
- Reduces the use of insulin
- Easy to use
OVERVIEW OF THE GLP-1 MARKET

**GROWING USE OF GLP-1 AGONISTS IN DIABETES THERAPY;**

- As **mono-therapy**, as **add-on to OADs** and as **add-on to basal insulin** (About 35% of GLP-1 use today is in combination with insulin) ¹)
- Has shown **suggestive protective CV effects** in clinical studies
- Increased use with every new compound introduced to the market

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<table>
<thead>
<tr>
<th>Product</th>
<th>Dosing</th>
<th>Approval date / Status</th>
<th>Projected 2013 sales (US$m)*</th>
<th>Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Victoza (liraglutide)</td>
<td>Once daily</td>
<td>EMA 2009 FDA 2010</td>
<td>2,072</td>
<td>Novo Nordisk</td>
</tr>
<tr>
<td>Byetta (exenatide)</td>
<td>Twice daily</td>
<td>2005</td>
<td>360</td>
<td>BMS/AZ (Amylin)</td>
</tr>
<tr>
<td>Bydureon (exenatide XR)</td>
<td>Once weekly</td>
<td>2012</td>
<td>379</td>
<td>BMS/AZ (Amylin)</td>
</tr>
<tr>
<td>Lyxumia (lixisenatide)</td>
<td>Once daily</td>
<td>Nov’12: Positive CHMP opinion Dec’12: Exp US filing</td>
<td>55</td>
<td>Sanofi (Zealand Pharma)</td>
</tr>
<tr>
<td>Albiglutide</td>
<td>Once weekly</td>
<td>Filing expected in Q1 2013</td>
<td>n.a</td>
<td>GSK</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>Once weekly</td>
<td>Under investigation</td>
<td>n.a</td>
<td>Lilly</td>
</tr>
</tbody>
</table>

* Bloomberg and analyst estimates

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**Current penetration of GLP-1 agonist therapy in diabetes:**
- Europe ~ 6%
- US ~ 7%
NOT ALL GLP-1 AGONISTS ARE ALIKE

GLP-1 AGONISTS CAN BE DIVIDED INTO TWO CLASSES WITH DIFFERENT PHARMACO-KINETIC PROFILE

**Short-acting:**
- Byetta (exenatide) – twice-daily
- Lixisenatide – once-daily

**Long-acting:**
- Victoza (liraglutide) – once-daily
- Bydureon (exenatide XR) – once-weekly
- Albiglutide – once-weekly
- Dulaglutide – once-weekly

Overview of clinical differences between long- and short-acting GLP-1 agonists:

<table>
<thead>
<tr>
<th>Product</th>
<th>Fasting glucose (FPG) control</th>
<th>Post-prandial (PPG) control</th>
<th>Weight loss</th>
<th>Gastric emptying</th>
<th>CV effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting</td>
<td>✓✓✓</td>
<td>✓</td>
<td>✓✓</td>
<td>✓</td>
<td>(+/0/-) ??</td>
</tr>
<tr>
<td>Short-acting</td>
<td>✓✓</td>
<td>✓✓✓</td>
<td>✓</td>
<td>✓✓</td>
<td>(+/0/-) ??</td>
</tr>
</tbody>
</table>

Source: Dr. Filip Knop, MD, Ph.D., Head of Diabetes Research Division, Gentofte Hospital, University of Copenhagen, published clinical study results, meta-analyses of clinical data
LIXISENATIDE (LYXUMIA®) – UNIQUE THERAPEUTIC PROFILE

LIXISENATIDE FULFILLS ALL CRITERIA FOR A RELEVANT GLP-1 DRUG

• Significant and sustained improvement of glycemic control ✔
  -- consistent HbA1c reduction of 0.7-0.9 %

• Beneficial effect on body weight ✔
  (weight loss of 1.8 – 3 kg in combination with OADs/insulin)

• Favorable safety profile with relatively low risk of hypoglycemic events ✔
  -- 6-fold fewer symptomatic hypoglycemic events vs exenatide
  -- better gastrointestinal tolerability vs exenatide

AND DISPLAYS THE FOLLOWING ADDITIONAL CHARACTERISTICS

• Pronounced prandial effect (PPG) in addition to lowering of fasting glucose levels (FPG)

• Simple once-daily dosing regimen:
  One step to maintenance dose, one pen per dose

~90% of patients in GetGoal reached and stayed on the maintenance dose of 20 μg/once daily
## STUDY NAME

<table>
<thead>
<tr>
<th>STUDY NAME</th>
<th># of pts</th>
<th>Top-line results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GetGoal-Mono</td>
<td>361</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-Mono Japan</td>
<td>69</td>
<td>Positive ✓</td>
</tr>
<tr>
<td><strong>Add-on to oral anti-diabetic drugs (OADs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GetGoal-F1 (metformin)</td>
<td>482</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-S (sulfonylurea)</td>
<td>859</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-M (metformin)</td>
<td>680</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-M Asia (metformin)</td>
<td>232</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-P (pioglitazone)</td>
<td>484</td>
<td>Positive ✓</td>
</tr>
<tr>
<td><strong>Non-inferiority study</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GetGoal-X versus exenatide</td>
<td>639</td>
<td>Positive ✓</td>
</tr>
<tr>
<td><strong>Add-on to basal insulin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GetGoal-L Asia (basal insulin)</td>
<td>311</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal-L (basal insulin)</td>
<td>495</td>
<td>Positive ✓</td>
</tr>
<tr>
<td>GetGoal Duo 1 (insulin glargine)</td>
<td>446</td>
<td>Positive ✓</td>
</tr>
</tbody>
</table>
**RESULTS FROM 9 GETGOAL PHASE III STUDIES IN TYPE 2 DIABETES:**

- **GetGoal Mono**
- **GetGoal Mono-JP** *
- **GetGoal -M**
- **GetGoal -F1**
- **GetGoal -X**
- **GetGoal -S**
- **GetGoal -P**
- **GetGoal -M Asia**
- **GetGoal -L (BI)**
- **GetGoal -L Asia (BI)**
- **GetGoal Duo1 (IG)**

LIXISENATIDE - SIGNIFICANT AND CONSISTENT HbA1c REDUCTION

* 24 week data, longer term data was pooled

Source: Previous GetGoal sources, Sanofi unpublished data
LIXISENATIDE - STRONG PRANDIAL EFFICACY PROFILE

PHASE IIb: Lixisenatide vs. liraglutide on postprandial glucose
More pronounced effect of lixisenatide vs liraglutide

“IMPACT OF LIXISENATIDE ON PPG IS SUBSTANTIAL FOR THE FIRST MEAL OF THE DAY AND WITH EFFECT ALSO FOR SUBSEQUENT MEALS” 1)

1) Lorenz et al, ADA 2012

Postprandial glucose excursion after a standardized breakfast test in patients with Type 2 diabetes inadequately controlled with metformin (n=143)

(1) ClinicalTrials.gov identifier: NCT01596504
Source: Sanofi, IR Thematic Conference Call on Diabetes, 12 June 20120
THE RELEVANCE OF PRANDIAL GLUCOSE REDUCTION

BOTH FASTING AND PRANDIAL GLUCOSE CONTROL IS IMPORTANT IN THE TREATMENT OF DIABETES

Un-controlled post-prandial glucose (PPG) levels is the Main contributor to T2D patients on basal insulin not reaching HbA1c target of < 7%
SIGNIFICANT EFFECT FOR LIXISENATIDE ON TOP OF BASAL INSULIN +/- ORALS

**GETGOAL–L**
Lixisenatide + basal insulin ± ME

**GETGOAL–L-ASIA**
Lixisenatide + basal insulin (60% Lantus®) ± SU

Source: Sanofi, IR Thematic Conference Call on Diabetes, 12 June 2012
LIXISENATIDE IN FREE COMBINATION WIT LANTUS®: SIGNIFICANTLY IMPROVES GLYCEMIC CONTROL

GETGOAL DUO 1
Lixisenatide + Lantus® + OAD, 446 insulin naïve patients

Mean A1c (%) by visit

Lixisenatide OR Placebo

SIGNIFICANT HbA1c & PPG REDUCTION ACHIEVED WITH LIXISENATIDE ON TOP OF LANTUS® IN T2D UNCONTROLLED WITH ORALS

Source: Sanofi, IR Thematic Conference Call on Diabetes, 12 June 2012
Approximately 50% of Type 2 diabetes patients on basal insulin are not well controlled (HbA1c > 7%)

Strong clinical evidence from 3 GetGoal studies (> 1,250 patients), evaluating lixisenatide in free combination with basal insulin (including Lantus®)

- Significant effect on HbA1c
- Pronounced PPG lowering
- Acceptable safety and tolerability profile
NEXT STEP: SINGLE PEN DEVICE FOR LIXISENATIDE AND LANTUS®

FIX-FLEX DEVICE FOR JOINT ADMINISTRATION OF LIXISENATIDE AND LANTUS®

- Convenience of a single injection per day with possibility to adjust the Lantus® dosing

- Entering phases for industrialization, validation, usability and manufacturing

- Fix/flex combination device expected to be available mid-2013 for initiation of Phase III studies

Lixisenatide + LANTUS

NEW FIX/FLEX COMBINATION DEVICE
A randomized, double-blind, placebo-controlled multicenter study to evaluate cardiovascular outcomes during treatment with lixisenatide in Type 2 Diabetic Patients After an Acute Coronary Syndrome

- Initiated mid-2010: Expected to enrol ~6,000 patients globally
- Event driven study
- The study is estimated to complete mid-2014

Primary study objective

Demonstrate that lixisenatide can reduce cardiovascular morbidity and mortality compared to placebo in Type 2 diabetic patients who recently experienced an acute coronary syndrome event.

- The study will provide extensive clinical CV safety data on lixisenatide.
- Interim ELIXA results to be included in the FDA filing package for lixisenatide in the U.S.
LIXISENATIDE (LYXUMIA®) – IN REGISTRATION PHASE

2003
Licensed to Aventis

2007
Phase II completed

2009
Completed Phase III patient enrollment

2010
First GETGOAL Phase III results
Initiation of CV safety study (ELIXA)

2011/2012
GetGoal Phase III program completed
12 regulatory filings
Positive CHMP opinion
US filing in Dec ’12

2013/2014
Ph III with LixiLan fix-flex device
Complete ELIXA

LIXISENATIDE – Status summary

• A potent and selective GLP-1 agonist \(^1\) (20 μg once-daily) invented by Zealand Pharma/licensed to Sanofi

• Consistent, positive results throughout the global Phase III GetGoal program (+5,000 patients), including three Phase III studies (>1,250 patients) on top of basal insulin

• Positive CHMP opinion in Nov 2012 – 11 other registrational filings – US filing planned for Dec 2012

• IP protection until 2020 (US and Europe) + up to 5 years of PT extension