American Diabetes Association
65th Annual Scientific Sessions

Investor Reception
June 12, 2005
Safe Harbor Statement

This presentation contains forward-looking statements about Amylin. Our actual results could differ materially from those discussed due to a number of factors, including that our BYETTA and/or SYMLIN may not prove to be important new therapeutic options or may be affected by unexpected new data or technical issues; our dependence on others; and inherent scientific, regulatory and other risks in the drug development and commercialization process. Reimbursement and pricing decisions, the pace of market acceptance, or manufacturing and supply issues may also affect the potential of BYETTA and/or SYMLIN. These and additional risks and uncertainties are described more fully in our SEC filings, including our Form 10-K. We disclaim any obligation to update these forward-looking statements.
Agenda

> Amylin at ADA

> BYETTA™ (exenatide) injection
   > Review of key BYETTA presentations
     Dr. David Kendall, International Diabetes Center, Minneapolis MN
   > A Physician’s Experience
     Dr. Carol Wysham, Rockwood Clinic, Spokane WA

> SYMLIN® (pramlintide acetate) injection

> Questions and Answers
Amylin at ADA

> Oral presentations and abstracts in scientific sessions
  > BYETTA (7 presentations)
  > SYMLIN (3 presentations)
  > Pipeline (2 presentations)

> Grant support for 2 symposia

> Commercial exhibits supporting SYMLIN and BYETTA

> Opportunities to network with and learn from leading researchers and clinicians
BYETTA™ (exenatide) injection
Now Available

> First-in-class – incretin mimetic

> Approved for type 2 diabetes as adjunct to metformin and/or sulfonylurea
  > Stimulates insulin secretion only in the presence of elevated blood glucose, providing self-regulating control
  > Restores first-phase insulin response
  > Long-term improvements observed in indicators of beta-cell function

> Fixed dose – no daily dose adjustment

> Full prescribing information available at www.BYETTA.com
Review of Key BYETTA Presentations

Dr. David Kendall
Chief of Clinical Services and Medical Director
International Diabetes Center - Minneapolis, MN
Exenatide Achieves Equivalent Glycemic Control, with Weight Reduction and Less Nocturnal Hypoglycemia in MET and SU-treated Type 2 Diabetes Patients: A 26 Week Comparison Study with Insulin Glargine

Robert J. Heine¹, Luc Van Gaal², Don Johns³, Michael J. Mihm³, Mario H. Widel³, Robert G. Brodows³

Amsterdam, the Netherlands¹
Antwerp, Belgium²
Indianapolis, IN, US³
Primary Hypothesis

Glycemic control achieved with exenatide is non-inferior to that of insulin glargine in patients inadequately responding to metformin + sulphonylurea

- 26 week treatment, BID fixed dose exenatide vs QD insulin glargine titration
- Primary endpoint: Change in HbA1c
- Intent-to-treat sample: N=549 randomized patients with >1 post-baseline measurement
Time Course of $\text{HbA}_{1c}$

- Exenatide, 10µg BID
- Insulin Glargine, mean dose at endpoint = 25.0 U/day

ITT sample shown
Mean ± SE shown
7-Point Self-Monitored Blood Glucose Profiles

Exenatide

Baseline (Week 0)  
Endpoint (Week 26)

Blood Glucose (mg/dL)

100 120 140 160 180 200 220 240

Pre-Breakfast  
Pre-Lunch  
Pre-Dinner  
3 AM

Insulin Glargine

Baseline (Week 0)  
Endpoint (Week 26)

ITT sample shown
Mean ± SE shown
Time Course of Change in Body Weight

EXENDI 

ITT sample shown
Mean ± SE shown

* p<0.0001, exenatide vs insulin glargine at same time point

Change in Body Weight (lbs)

Weeks

Exenatide
Insulin Glargine

+4.0 lbs

-5.1 lbs
Conclusions

• In this study, fixed-dose exenatide was as effective as titrated insulin glargine in improving glycemic control in type 2 diabetes patients

• Exenatide was associated with:
  – Tighter postprandial control
  – Less nocturnal hypoglycemia
  – Progressive reductions in body weight

• Insulin glargine was associated with:
  – Greater reductions in FPG
  – Less daytime hypoglycemia
  – Progressive weight gain

• The most common adverse effects of exenatide were GI-related, and decreased in incidence throughout the study, with low dropout

• Exenatide can be an effective alternative to starter basal insulin for type 2 diabetes sub-optimally controlled with MET + SFU therapy
Improvements in Cardiovascular Risk Factors Accompanied Sustained Effects on Glycemia and Weight Reduction in Patients with Type 2 Diabetes Treated with Exenatide for 82 Weeks

David M. Kendall¹, Dennis Kim², Terri Poon², Jenny Han², Catherine Schnabel², Mark Fineman², Michael Trautmann³, David Maggs²

¹Minneapolis, MN, ²San Diego, CA, ³Hamburg, Germany
Introduction

- **GLP-1**: important incretin hormone regulating glucose homeostasis
- **Exenatide**: incretin mimetic for treatment of type 2 diabetes with multiple mechanisms of action:
  - Enhances glucose-dependent insulin secretion
  - Suppresses elevated glucagon secretion
  - Reduces food intake and body weight
  - Slows gastric emptying
  - Increase in beta-cell mass (in animal studies) and measures of beta-cell function
Summary: Three Phase 3 Trials
30-Week Placebo-Controlled (AMIGOs)

Patients with type 2 diabetes treated with 10 µg exenatide BID and maximally-effective MET and/or SFU:

• **Metabolic Measures:**
  - A1C reduction ~ 1%
  - ~ 40% achieved A1C ≤7%
  - Weight reduction ~1.9 kg

• **Safety and Tolerability**
  - Generally well tolerated
    - Mild to moderate nausea most common adverse event
    - Nausea mostly seen during initiation of therapy
  - Hypoglycemia
    - No increase with MET
    - Mild to moderate hypoglycemia increased with SFU.
Open Label Extension
Basic Study Design

- Three 30 week randomized, triple-blind, placebo-controlled, multi-center studies followed by open-label extensions
- All patients continued maximally-effective doses of metformin (MET) and/or SFU

<table>
<thead>
<tr>
<th>Treatment (weeks)</th>
<th>Placebo-Controlled Clinical Trial</th>
<th>Open Label Extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5 µg Exenatide BID</td>
<td>10 µg Exenatide BID</td>
</tr>
<tr>
<td>4</td>
<td>10 µg Exenatide BID</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>5 µg Exenatide BID</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>Placebo BID</td>
<td></td>
</tr>
<tr>
<td>82</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Screening
### Demographics and Baseline Characteristics

#### 82 Week Exenatide Cohort (N=265)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>56 ± 10</td>
</tr>
<tr>
<td>Sex (% male/female)</td>
<td>63/37</td>
</tr>
<tr>
<td>Race: Caucasian/Black/Hispanic/Other (%)</td>
<td>78/11/9/2</td>
</tr>
<tr>
<td>A1C (%)</td>
<td>8.3 ± 1.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100 ± 21</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34 ± 6</td>
</tr>
<tr>
<td>Fasting Plasma Glucose (mg/dL)</td>
<td>170 ± 42</td>
</tr>
<tr>
<td>Duration of Diabetes (y)</td>
<td>7 ± 6</td>
</tr>
</tbody>
</table>

Mean ± SD
Sustained A1C Reduction
Exenatide-Treated Patients

Mean ± SE
N = 265

Placebo-Controlled Trials
Baseline A1C 8.3%

-1.2 ± 0.1%

Open-Label Extension

Change in A1C (%)
Duration of Treatment (Weeks)
Progressive Body Weight Reduction
Exenatide-Treated Patients

Mean ± SE
N = 265

Placebo-Controlled Trials
Open-Label Extension

No special diet or exercise counseling was provided

Change in Body Weight (kg)

Duration of Treatment (Weeks)

Baseline weight: 100 kg

-4.6 ± 0.4 kg
## Effects on Cardiovascular Risk Factors
### 82 Weeks of Exenatide
(N=265)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline ±SE</th>
<th>Mean change from Baseline ±SE</th>
<th>95% Confidence Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (TC) (mg/dL)</td>
<td>185.9 ± 2.4</td>
<td>-2.5 ± 2.0 (-0.1%)</td>
<td>-6.4 to +1.4</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>38.0 ± 0.6</td>
<td>+4.5 ± 0.4 (+13.3%)</td>
<td>+3.6 to +5.3</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>115.1 ± 2.2</td>
<td>-1.4 ± 1.8 (-2.9%)</td>
<td>-5.0 to +2.2</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>91.6 ± 1.5</td>
<td>-1.3 ± 1.3 (-2.8%)</td>
<td>-3.8 to +1.2</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>239 ± 11</td>
<td>-37 ± 10 (-5.7%)</td>
<td>-56 to -18</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>128.6 ± 0.8</td>
<td>-1.5 ± 1.0</td>
<td>-3.5 to +0.5</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>78.7 ± 0.5</td>
<td>-3.2 ± 0.6</td>
<td>-4.4 to -2.1</td>
</tr>
</tbody>
</table>
Change in Weight

Weight Change Quartile at 82 Weeks

- Mean+SE
- 83% of subjects lost weight
- For entire cohort, weight change was -4.6± 0.4 kg

N=67
N=66
N=66
N=66

83% of subjects lost weight
For entire cohort, weight change was -4.6± 0.4 kg
<table>
<thead>
<tr>
<th>Weight Quartile</th>
<th>Δ A1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>-1.8</td>
</tr>
<tr>
<td>II</td>
<td>-1.2</td>
</tr>
<tr>
<td>III</td>
<td>-0.9</td>
</tr>
<tr>
<td>IV</td>
<td>-1.0</td>
</tr>
</tbody>
</table>

Mean ± SE
Change in Blood Pressure
Weight Change Quartile at 82 Weeks

Systolic BP

Diastolic BP

Mean+SE
Change in Triglycerides and HDL-C

Weight Change Quartile at 82 Weeks

<table>
<thead>
<tr>
<th>Weight Quartile</th>
<th>Triglycerides</th>
<th>HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>↓ 40%</td>
<td>+7.4</td>
</tr>
<tr>
<td>II</td>
<td>-92</td>
<td>+3.5</td>
</tr>
<tr>
<td>III</td>
<td>-58</td>
<td>+3.0</td>
</tr>
<tr>
<td>IV</td>
<td>+7</td>
<td>+3.8</td>
</tr>
</tbody>
</table>

Mean+SE
Change in Triglycerides and HDL-C for Quartile 1 (N=67)

Range of weight change -42.9 to -7.3 kg

Placebo-Controlled Trials

- HDL-C +7.4 mg/dL

Open-Label Extensions

- Triglycerides -92 mg/dL

Duration of Treatment (Weeks)
Safety and Tolerability in the Open-Label Extensions

- Exenatide generally well-tolerated
- Adverse events in open-label extensions generally consistent with placebo-controlled trials
  - Nausea:
    - Most frequent adverse event (46%)
    - Generally mild to moderate in intensity
    - Withdrawals due to nausea low (3.6%)
Conclusions

82 weeks of exenatide treatment results in:

• Sustained improvements in glycemic control
• Progressive weight reduction
• Clinically meaningful improvements in triglycerides, HDL-C, and blood pressure

Improvements in cardiovascular risk factors greatest in patients who experienced greatest weight reduction
A1C and Body Weight Reductions: Preliminary Analysis for Subjects Treated with Exenatide for 2 Years

2 yr data for 82-wk cohort N = 146

Mean ± SE

No special diet or exercise counseling was provided
BYETTA Commercial Update
BYETTA Commercial Progress

> Amylin/Lilly sales forces fully trained two weeks after approval
  > Field promoting BYETTA in May
  > BYETTA in first position

> Reimbursement activities exceeding expectations
  > Unique code received from First Data Bank
    > Antihyperglycemic, Incretin Mimetic (GLP-1 Receptor Agonist)
  > Clinical data dossier available -- fulfilled 100+ requests

> Medical education focus
  > Speaker Bureau providing trained physician speakers
    > 500+ speakers trained by end of August
    > 40,000+ medical education interactions by year end
  > National satellite educational event in late June

> Patient education
New BYETTA improves acute beta-cell responsiveness for self-regulating glycemic control

- Mimics natural physiology for self-regulating glucose control
- Improves glycemic control and helps many patients reach their A1C goal
  - Along with improvements in A1C, most patients lost weight in clinical trials
- Provides simple, fixed BID dosing before the morning and evening meal
- Most common adverse events include hypoglycemia (with a sulfonylurea) and nausea, both mild-to-moderate
BYETTA – A Physician’s Experience

Dr. Carol Wysham
Clinical Endocrinologist
Rockwood Clinic – Spokane, WA
Session Goals

1. To review the indication of use for BYETTA™ (exenatide) injection
2. To present on-label case studies of patients in the exenatide phase 3 trials
AMIGO Trials (MET, SFU, MET + SFU + Extensions)

- Recruitment

- Barriers to patient acceptance
  - Injections
  - Side effects
    - Nausea
    - Hypoglycemia

- Experiences with compound
  - Glycemic response
  - Weight loss
Recruitment

- Recruited most patients through our multispecialty clinic
  - One person called about the “monster spit” study
  - Reviewed basics of protocol with patients over the telephone, including use of injectable study drug

- Twenty patients total randomized – retention was very high
Barriers to Patient Acceptance

- Injectable medication
  - Only 3 patients declined the study due to injections
  - Only 1 patient has expressed significant dissatisfaction with ongoing injections
  - Minimal to no site reactions

- Nausea
  - Minor, especially with small initial doses
  - Usually in late morning
  - Eating usually helped
  - 2 patients used meclizine

- Hypoglycemia
  - Symptoms were uncommon and rarely associated with glucose <70
Experience With Compound

- Glycemic response has been excellent – near 100% response rate
  - A1C reduction 1-3%

- Weight loss is frequent
  - Usually modest, but 1 patient has lost 30 pounds
  - Many report decreased appetite
Exenatide Pivotal Studies: Study Design

- Study methods

- Exenatide or placebo was added to maximally effective doses of metformin (MET) and/or a sulfonylurea (SFU) in patients with type 2 diabetes
  - Study MET: MET (at least 1500 mg/day)
  - Study SFU: SFU (at least maximally effective dose of an SFU)
  - Study MET+SFU: MET dose (1500 mg/day) and at least maximally effective dose of an SFU
## Mean Change in Clinical Measures at End of Core Studies

<table>
<thead>
<tr>
<th>Group</th>
<th>Δ A1C (%)</th>
<th>Δ TG (mg/dL)</th>
<th>Δ Weight (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET</td>
<td>-1.5</td>
<td>-121</td>
<td>-16</td>
</tr>
<tr>
<td>SFU</td>
<td>-1.4</td>
<td>-65</td>
<td>-4.3</td>
</tr>
<tr>
<td>MET+SFU</td>
<td>-1.8</td>
<td>-44</td>
<td>-13</td>
</tr>
</tbody>
</table>
## Change in Weight and A1C by Group During Extension Trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>( \Delta ) A1C (% \pm 95% CI)</th>
<th>( \Delta ) Weight (lbs \pm 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo switched to 10 mcg exenatide</td>
<td>-1.7 (-1.0,-2.9)</td>
<td>-13.5 (-7,-18)</td>
</tr>
<tr>
<td>5 or 10 mcg exenatide continued on 10 mcg exenatide</td>
<td>-0.2 (+0.9,-1.6)</td>
<td>-9.8 (+1.0,-19)</td>
</tr>
</tbody>
</table>
Case 1
Background (MET+SFU)

- 65-year-old white female with 17 years of type 2 diabetes mellitus
- Entered study on glimepiride 2 mg BID, MET 500 mg AM and 1000 mg PM
- Baseline measurements: weight = 233, BMI = 36.5 kg/m², A1C = 8.5%
- She had been treated with insulin until 1995, when she was started on MET and troglitazone (changed to pioglitazone) and glimepiride; pioglitazone discontinued 1 year prior to entry due to edema and weight gain
- Weight fluctuated between 218-232 over 12 years
- Confounding medical conditions / medications (if impact diabetes management)
Case 1
Patient Outcomes

- She was randomized to placebo during the core study
  - Patient had no trouble accepting nor learning injection technique
- Glycemic control
  - A1C dropped from 8.5% at visit 1 to 7.9% at week 30
  - At end of MET+SFU (extension), A1C dropped to 6%
  - 9 months into LTE, A1C stable at 6%
- Weight
  - Baseline 233; 226 at end of MET+SFU
  - Weight dropped to 200 lbs at end of MET+SFU (extension)
  - At 9 months of LTE, weight 189
  - Joined Weight Watchers after losing first 20 pounds
- Had onset of “tingling” in feet shortly before starting the trial; she reported that these symptoms had resolved by V3E
- At V10E: “I feel the best I have in many, many years”
Case 1
Ongoing Use of Exenatide

- During the first few weeks of blinded medication (placebo), she suffered from frequent hypoglycemia with glucose levels as low as 45 mg/dL

- Side effects
  - Hypoglycemia resolved with reduction (and eventual discontinuation) of glimepiride
  - Mild nausea and early satiety

- A major effect of participation in the study was the patient’s perception of her improved ability to follow a weight-reduction diet; she previously had tried countless diets, but stopped after a few months because “I got bored” with slow weight loss
Case 1
Clinical Interpretation

- Patient experience has been very favorable
  - Glycemic control (8.5-6.0), sustained over 24 months
  - Weight control (233-189), continued loss up to 24 months
- Patient is thrilled with the results of weight loss, glycemic control, and general improvement in quality of life
Case 2
Background (SFU)

- 65-year-old female (retired school teacher) with 5-year history of type 2 diabetes, on glipizide extended release 10 mg daily; she was unable to tolerate MET; she maintained an A1C between 6.9-7.5% for the duration of her treatment; she struggled with her weight all of her life, having lost up to 20 lbs on various diets, but unable to keep weight off for more than a few months; since her retirement from teaching, she maintains an extremely busy schedule with civic and social activities

- Confounding medical conditions
  - Poorly controlled hypertension (unable to tolerate side effects from medications)
  - Hyperlipidemia

- Baseline A1C = 7.5%
- Baseline weight = 229 lbs, BMI = 43
Case 2
Initiation of Exenatide

- This patient had no trouble learning the injection technique; injections were not a barrier to starting the medication, but she missed her PM injection about once weekly (due to lifestyle issues); she did “tire” of the injections by the end of SFU, nonetheless, she opted to enter both extensions

- Side effects
  - Mild, transient nausea – usually early AM after injection; did not require any symptomatic treatment
  - Mild hypoglycemic symptoms, necessitating reduction and eventual discontinuation of SFU
Case 2
Patient Outcomes

- During the core study, she was randomized to 5 mcg dose of active drug
  - This patient had no trouble learning the injection technique

- Glycemic control – A1C
  - Baseline = 7.5%
  - At end of core study = 6.2%
  - At end of SFU (extension) = 5.9% with discontinuation of SFU
  - Currently = 6.4 (11/19/04)

- Weight
  - Baseline = 229 lbs, BMI = 43
  - At end of core study = 222 lbs
  - At end of SFU (extension) = 209 lbs
  - Currently = 204 lbs (11/19/04)

- The weight loss attributed to the study medication encouraged her to begin a regular exercise program with her husband
Case 2
Clinical Interpretation

- Patient and her provider hoped that enrollment in this study would provide her improved control and weight loss.

- These goals were met as evidenced by continued loss of weight (now almost 3 years since screening for study) and good glycemic control.

- Patient and her husband are both very pleased with the improvement in her health.

- As of most recent visit, her blood pressure has finally been controlled (without additional medication).
Case 3
Patient Background (MET)

- 62-year-old male with diabetes for 7 years, on MET 850 mg TID; his A1C ranged between 7.3 and 7.7% over the past 2 years; he had no known complications of diabetes; his blood pressure and cholesterol were well-controlled on medical management

- Since retiring from his occupation as a pipefitter, he enjoys traveling on fishing expeditions

- On entry, weight 227 lbs and A1C 8.2%
Case 3
Patient Outcomes

- During the core study, he was randomized to placebo
  - Patient had no trouble accepting nor learning injection technique; he was extremely compliant

- Glycemic control
  - Baseline A1C = 8.0%
  - End of core study = 8.2%

- Weight
  - Baseline 227 lbs
  - End of core study – 227 lbs
Case 3
Ongoing Use of Exenatide

- **During extension**
  - A1C dropped to 6.9% by 3 months and 5.3% by 12 months
  - Weight dropped steadily until month 12, with total loss of 16 lbs

- **During long-term extension**
  - A1C 5.3% and weight stable at 9 months (total of 24 months)

- He denies any intentional changes in his diet or activity
  - He continues to report no side effects
Case 3
Clinical Interpretation

- Our goals for his treatment were to improve his control, avoiding hypoglycemia and weight gain; we have been most pleased with his outcomes.

- He remains very satisfied with the results of treatment and hopes to continue it when available.

- He has demonstrated excellent compliance, despite challenges from his travels.
Summary

- Our experience with exenatide has been very favorable.

- Patients in our studies were very accepting of the mode of delivery; many in “120” study were sorry to see study come to an end.

- One patient in MET+SFU stopped the study because of social issues; she returned 2 months after termination with substantial deterioration of control on standard orals; she has required multidose insulin therapy to achieve the same control she had during the extension study; her weight decreased by 16 lbs during the study; she has regained that and an additional 7 pounds over 6 months; she expresses the desire to go back to exenatide, when it becomes available.
No one dropped out of the study because of gastrointestinal side effects or hypoglycemia

Dropouts (5)
- 2 moves
- 1 loss of glycemic control (1 was likely an overweight LADA)
- 1 “tired” of study visits (no objection to injections)
- 1 “tired” of shots
SYMLIN® (pramlintide acetate)
SYMLIN® (pramlintide acetate)
Approved for Two Distinct Indications

> First-in-class – amylinomimetic

> Approved for insulin-using type 2 and type 1 diabetes patients
  > Reduces postprandial hyperglycemia and glucose fluctuations
  > Improves glycemic control with weight loss
  > Nausea most common adverse event; generally mild to moderate and dissipates over time
  > Boxed warning highlights increased risk of insulin-induced severe hypoglycemia, particularly in type 1 diabetes

> Full prescribing information and medication guide for patients available at www.SYMLIN.com
SYMLIN Commercial Progress

> Specialty sales force trained and fully deployed
  > Targeted launch to highest insulin prescribers
  > Entire Amylin field force trained to answer SYMLIN questions

> Reimbursement activities ahead of plan
  > Unique code received from First Data Bank
    > Antihyperglycemic, Amylin Analogue Type
  > Early feedback is very positive
    > SYMLIN and BYETTA being reviewed together
SYMLIN
What Doctors Are Hearing From Us

SYMLIN offers patients with type 2 and type 1 diabetes not properly controlled with optimal mealtime insulin therapy:

- Reduction of postprandial glucose levels
- Reduction of glucose fluctuations
- Reduction in A1C values compared to insulin alone
- Reduction in mealtime insulin usage
- Weight neutral or weight reduction in most patients
- Boxed warning highlights increased risk of insulin-induced severe hypoglycemia, particularly in type 1 diabetes
> Two first-in-class diabetes products – NOW AVAILABLE
Questions and Answers