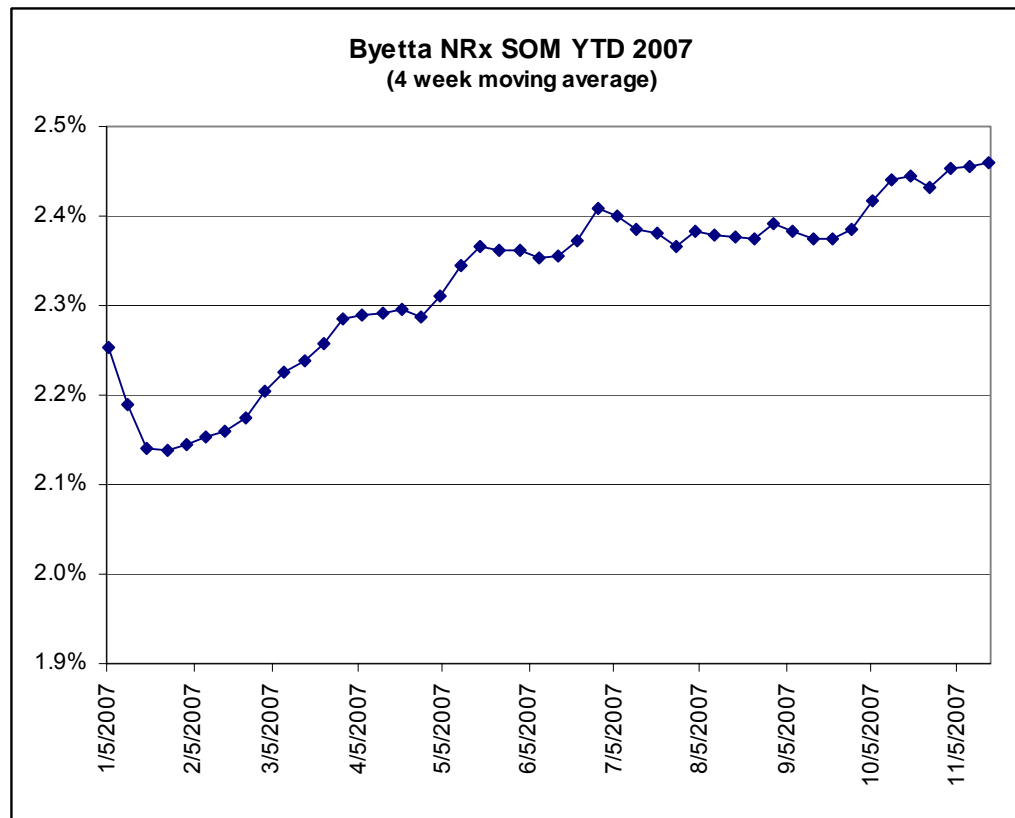


# Byetta

Gaining share in U.S.

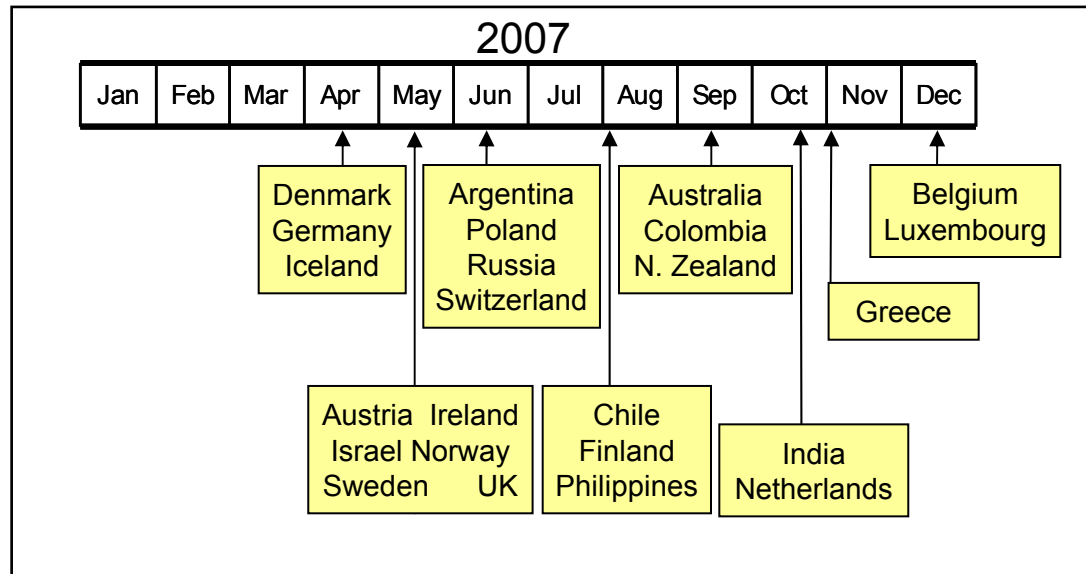


- Over 4M prescriptions written in U.S. so far
- DTC campaign launched October 2007
- New clinical data: improved beta cell function vs. glargine and weight loss instead of weight gain
- Payers
  - Greater than 80% Tier 2 access

Source: IMS Health

# Byetta

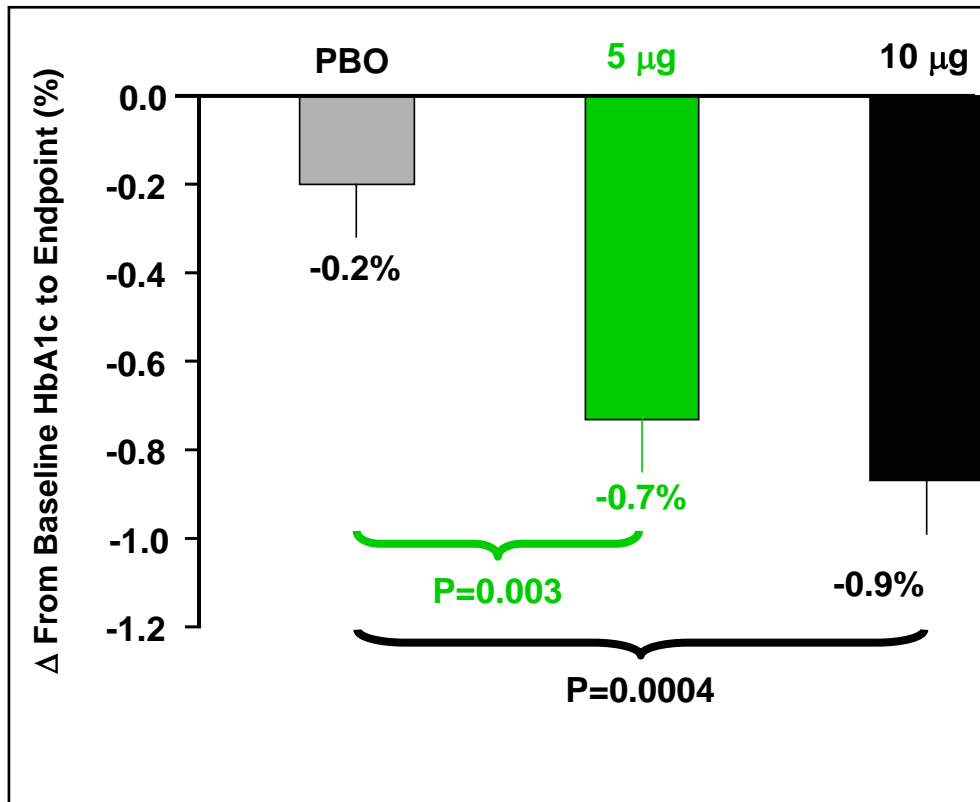
## International launches proceeding as planned



- 22 launches YTD 2007; expect 24 for full year
- Sixty (60) launches anticipated through 2008
- Promising access and reimbursement signals
  - Full access and reimbursement from Scottish Medicines Consortium (Scotland), Denmark, Sweden, Greece
  - Supportive guidelines from NICE (UK)
  - IQWiG (Germany) recommendation includes glucose control & weight loss

# Byetta

## Monotherapy results



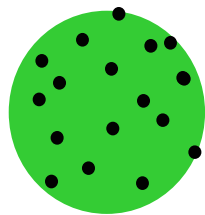
- First trial examining only monotherapy in drug naïve patients
- Efficacy
  - Byetta superior to placebo
  - Dose of 10 ug bid resulted in mean adjusted decrease of 0.9% in A1c from baseline of 7.8
  - Weight loss similar to previous Byetta studies
  - Greater than 50% of patients achieved target of  $\leq 7\%$  A1c at endpoint
- Well tolerated
  - Low drop-out rate (13%)
  - Low incidence of nausea (13%) at 10 ug dose
- FDA submission first half of 2008
  - Expect six-month review – response to approvable letter

ITT sample (N=232). Data are LS mean  $\pm$  SEM. Baseline HbA1c range: 7.8-7.9%.

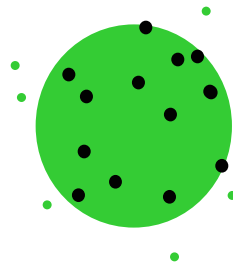
# Exenatide Once-Weekly

Alkermes' Medisorb® long-acting release technology

Initial release

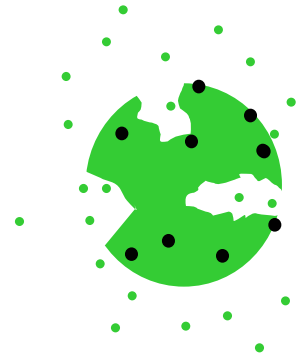


hydration

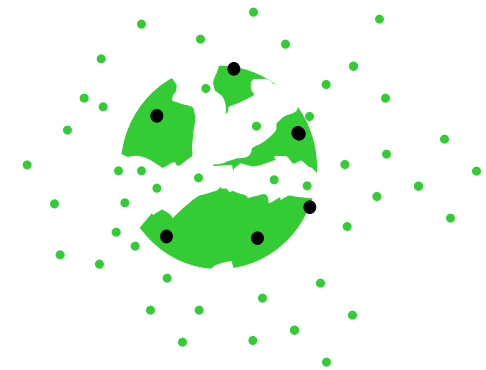


diffusion

Sustained release

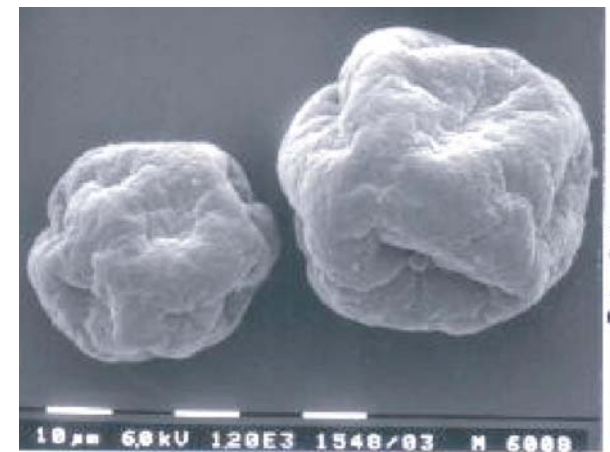


degradation



erosion

- Technology provides consistent 24-hour exposure to exenatide once-weekly
- Avoids peaks in exposure
- These characteristics should produce
  - better, more consistent glycemic control
  - enhanced tolerability, leading to better compliance and improved patient outcomes



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# Exenatide Once-Weekly Pivotal Study

## Overview

- 30-week, long-term, non-inferiority study
- 295 patients with Type 2 diabetes
- Not achieving glycemic control using diet and exercise, with or without one or more oral agents
- Patients received 2 mg. exenatide once-weekly or Byetta® twice daily
- Open-ended continuation phase included

# Exenatide Once-Weekly Pivotal Study

## Efficacy results

- HbA1c reduction from baseline of 1.9% versus 1.5% for Byetta®
- Achieved non-inferiority endpoint and met statistical criteria for superiority
- Patients achieving target HbA1c
  - 75% achieved HbA1c  $\leq$  7.0%
  - 50% achieved HbA1c  $\leq$  6.5%
- Patients with starting HbA1c  $\geq$  9% achieving target
  - 67% achieved HbA1c  $\leq$  7.0%
  - 33% achieved HbA1c  $\leq$  6.5%
- Average weight loss of 8.1 pounds

# Exenatide Once-Weekly Pivotal Study

## Safety and tolerability

- Safety
  - No major or severe hypoglycemia
  - As expected, minor hypoglycemia in patients receiving sulfonylureas
  - Antibody profile consistent with prior studies
  - Hope to leverage extensive Byetta® safety database
- Tolerability
  - 30% less nausea
  - Fewer than 1 in 5 had treatment-related nausea; predominantly mild and transient
  - Similar reduction in vomiting and other abdominal complaints

# Exenatide Once-Weekly Pivotal Study

## Compliance

- Compliance
  - Injections were self-administered
  - Nearly 90% of exenatide once-weekly patients completed the study, in line with Byetta® patients
  - Only 1 in 10 injections associated with any kind of injection site adverse event; generally mild in intensity
  - High proportion of Byetta®-treated patients crossed over to continue on exenatide once-weekly



# Exenatide Once-Weekly

## Overall clinical profile

- Outstanding glycemic control
- Substantial weight loss
- Minimal risk of hypoglycemia
- Convenient once-weekly dosing; no titration
- Lower rates of nausea than shorter-acting incretin mimetics
- Well-tolerated injection

# Exenatide Once-Weekly

## Steps toward commercialization

- We believe current pivotal trial provides safety and efficacy data necessary for NDA submission
- Commercial-scale manufacturing ready during second half of 2008
- NDA submission by the end of the first half of 2009; pursuing opportunities to accelerate
- Three superiority trials
  - Head-to-head versus TZD and versus DPP-4 with metformin background therapy
  - Head-to-head versus Lantus® with background oral anti-diabetic therapy
  - Monotherapy versus metformin