



Challenging Science.
Changing Lives.

Amylin Pharmaceuticals Inc. Research and Development Breakfast

October 24, 2006



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 risks that BYETTA and/or SYMLIN may be affected by unexpected new data, technical issues, or manufacturing and supply issues; our clinical trials may not start when planned and/or confirm previous results; our preclinical studies may not be predictive; our product candidates and/or label expansion requests may not receive regulatory approval; we may not be able to complete our manufacturing facility on a timely basis; and inherent scientific, regulatory and other risks in the drug development and commercialization process. These and additional risks and uncertainties are described more fully in the Company's SEC filings. Amylin disclaims any obligation to update these forward-looking statements.



Agenda

- > Introduction
 - > Ginger Graham, CEO
- > Clinical Development
 - > Orville Kolterman, MD – Senior Vice President, Clinical and Regulatory Affairs
 - > SYMLIN
 - > BYETTA
 - > Exenatide LAR
- > Early Development
 - > Alain Baron, MD – Senior Vice President, Research
 - > Fast-to-man Approach
 - > Approach to Obesity
 - > Approach to Diabetes
- > Discovery Research
 - > Michael Hanley, PhD – Vice President, Discovery Research
 - > Philosophy and Platform
- > Closing remarks
 - > Daniel Bradbury, President and COO



Clinical Development

Orville Kolterman, MD

Senior Vice President, Clinical and Regulatory Affairs



Supporting Two First-In-Class Medicines

- > SYMLIN[®] (pramlintide acetate)
 - > Post-approval commitments
 - > Label expansion
 - > SYMLIN Pen

- > BYETTA[®] (exenatide)
 - > Post-approval commitments
 - > Label expansion

- > Exenatide LAR



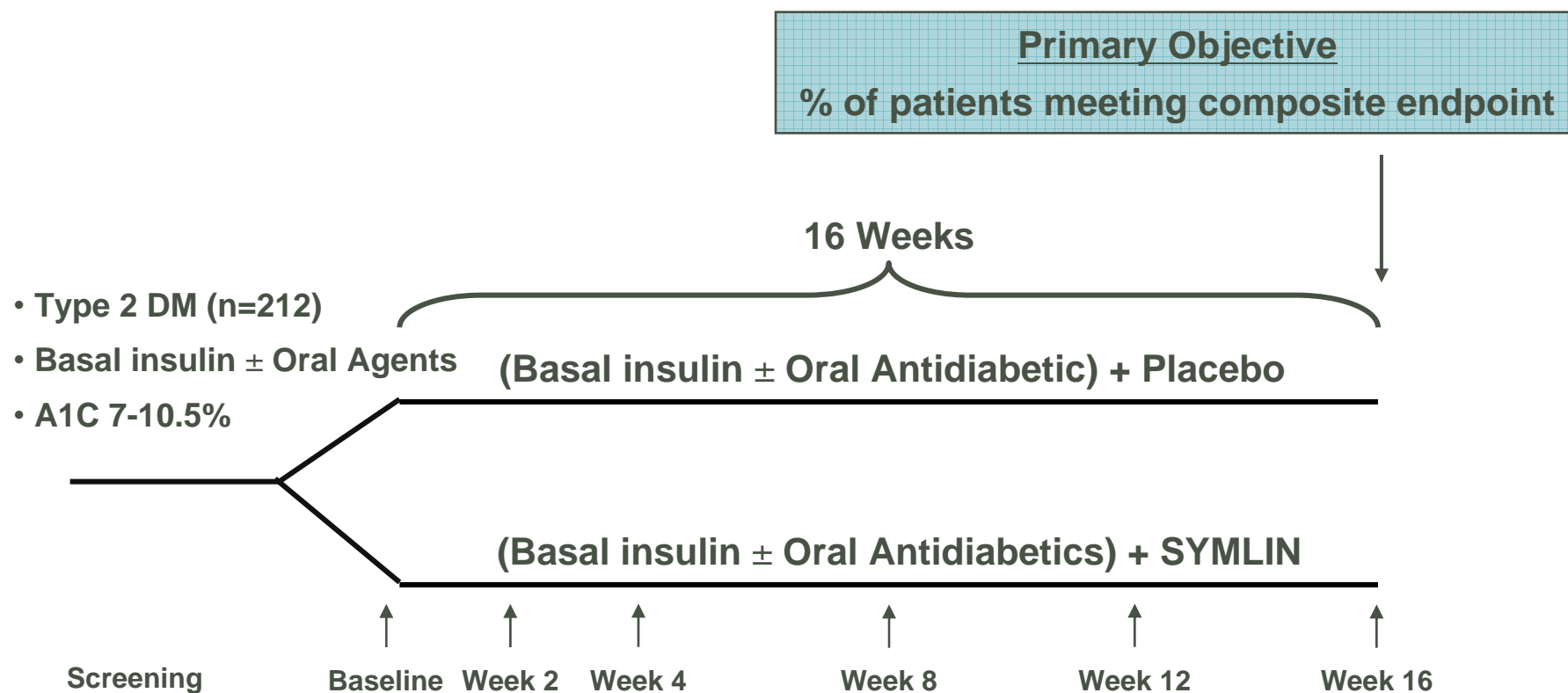
SYMLIN Market Support

- > Post-approval Commitments
 - > Observational Study
 - > Objective: Evaluate safety of SYMLIN use in the marketplace
 - > Focus on severe hypoglycemia observed during first 3 months
 - > 1250 subjects followed for 6 months
 - > Over 70% recruited to date
 - > Data confirms safe initiation of therapy
 - > Pediatric pharmacokinetic study enrollment nearing completion
- > Label expansion for use with basal insulin alone in type 2 patients
 - > Study completed
 - > sNDA submission in Q406



SYMLIN + Basal Insulin Study

STUDY DESIGN



- Weekly telephone contact with site
- 7-point glucose profiles prior to each site visit

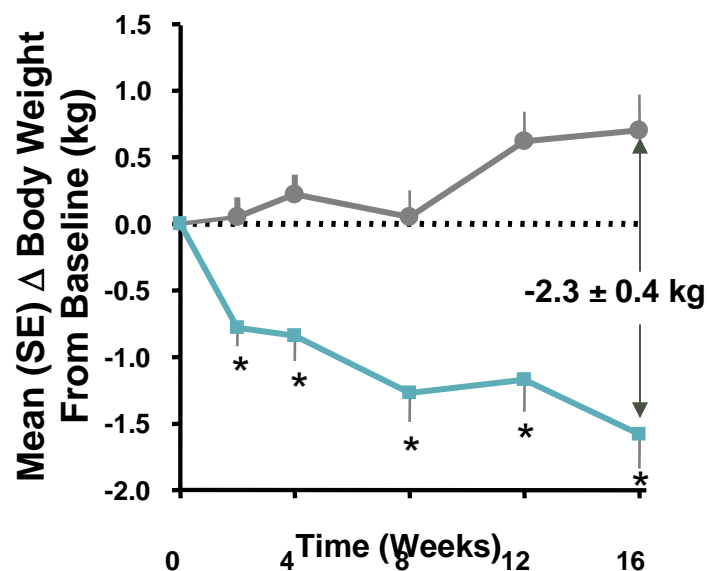
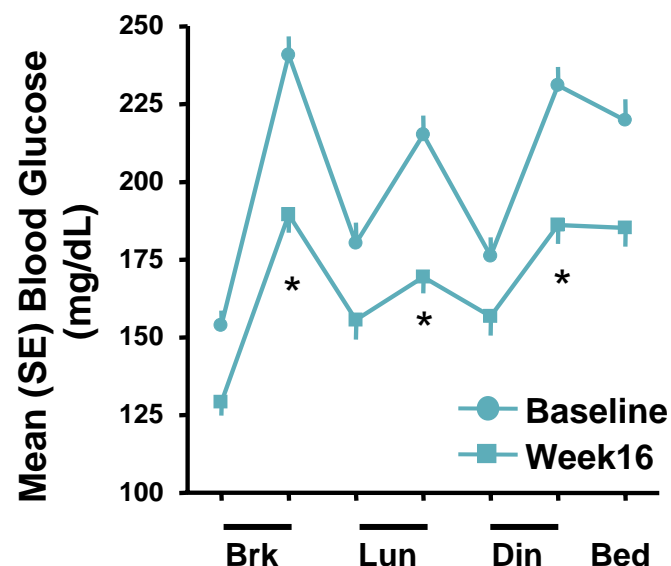
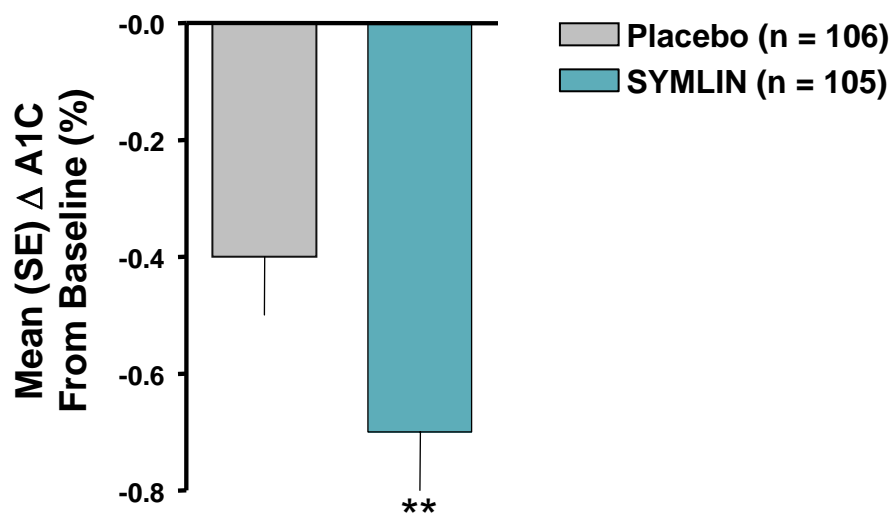


SYMLIN + Basal Insulin Study ENDPOINTS

- > Co-Primary Endpoints:
 - > Composite endpoint at Week 16
 - $A1C \leq 7.0\%$ and/or $A1C \text{ reduction} \geq 0.5\%$
 - Postprandial glucose excursions $\leq 40 \text{ mg/dL}$
 - No weight gain
 - No severe hypoglycemia
 - > Change in A1C from Baseline to Week 16
- > Secondary Endpoints:
 - > A1C and A1C targets
 - > Fasting and postprandial glucose
 - > Body weight and waist circumference
 - > Markers of CV risk
 - > Patient-reported outcomes



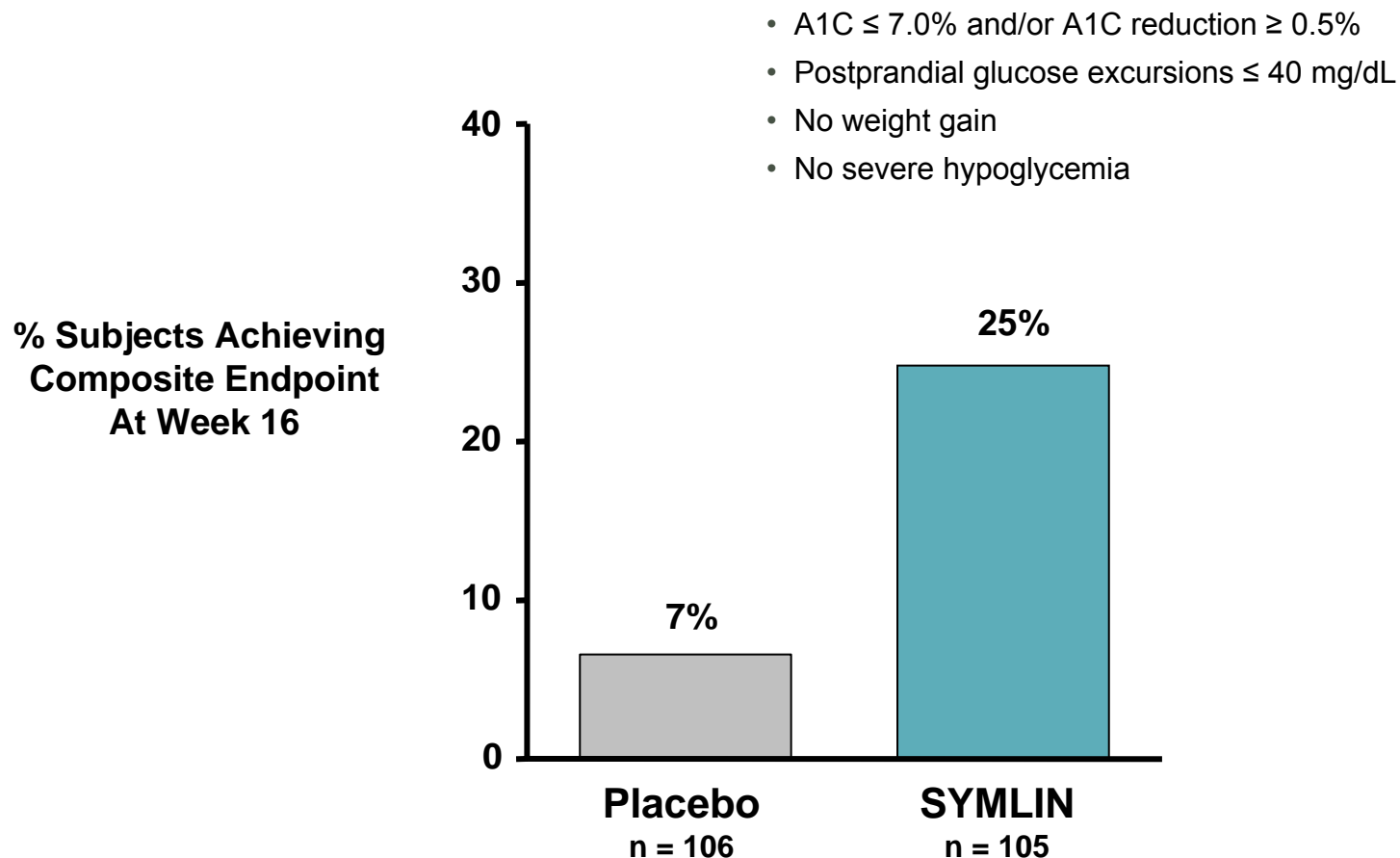
SYMLIN + Basal Insulin Safely Improved Glycemic Control With Weight Loss



- > Incidence of hypoglycemia
 - > SYMLIN + Basal insulin: 44%
 - > Placebo + Basal insulin: 47%
- > Severe hypoglycemia: 1 event in SYMLIN group



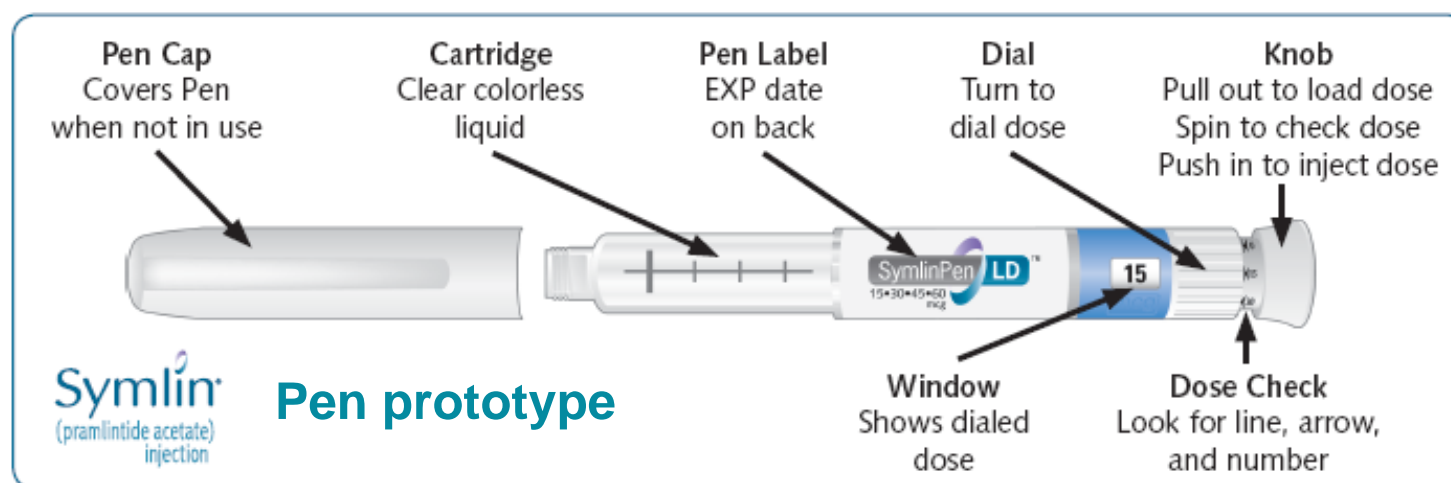
One Out of Four SYMLIN-Treated Patients Achieved Composite Endpoint





SYMLIN Pen Delivers Multiple, Fixed Doses

- > SymlinPen sNDA submitted; 2007 launch planned



- > Development work underway on more concentrated formulation
 - > Increased patient convenience + reduced COGS
 - > Supports both SYMLIN and pramlintide obesity program



BYETTA Market Support

- > Pediatric pharmacokinetics study underway
 - > Pediatric exclusivity agreement reached with FDA
- > Monotherapy indication study has initiated enrollment
 - > Target ~250 subjects not achieving glucose goals on diet and exercise
 - > 5 and 10 mcg arms (“AMIGO-like” design)
 - > Data available by end 2007 and submission planned in 2008
 - > 6-month review anticipated
- > sNDA for use in patients treated with TZDs
 - > Supported by 16-week efficacy data
 - > Submitted Q1 2006; 10-month review anticipated
- > sNDA supporting “in use” pen storage at room temperature
 - > Anticipate new usage guidelines in place in early 2007

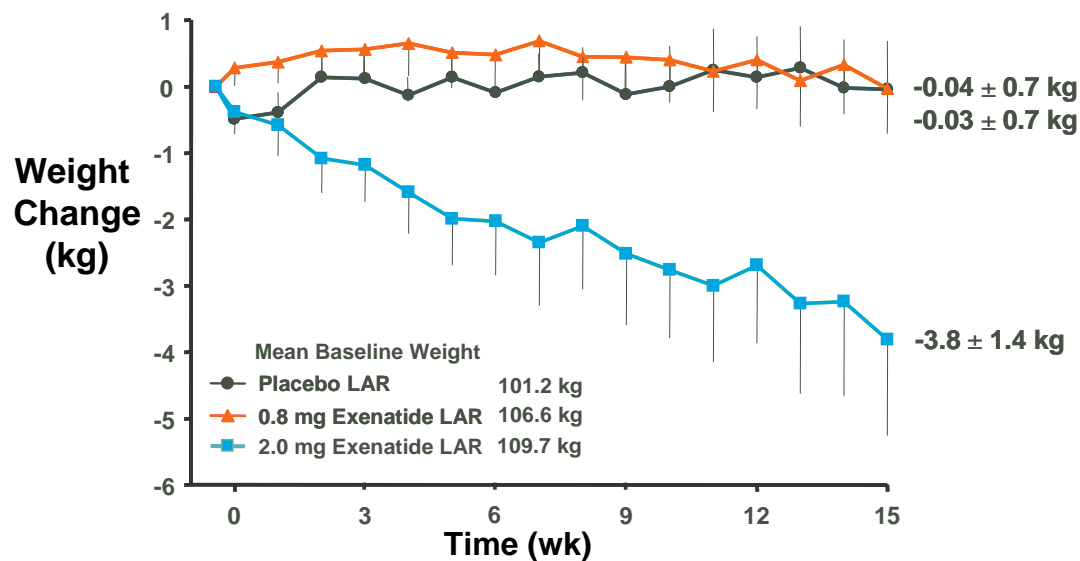
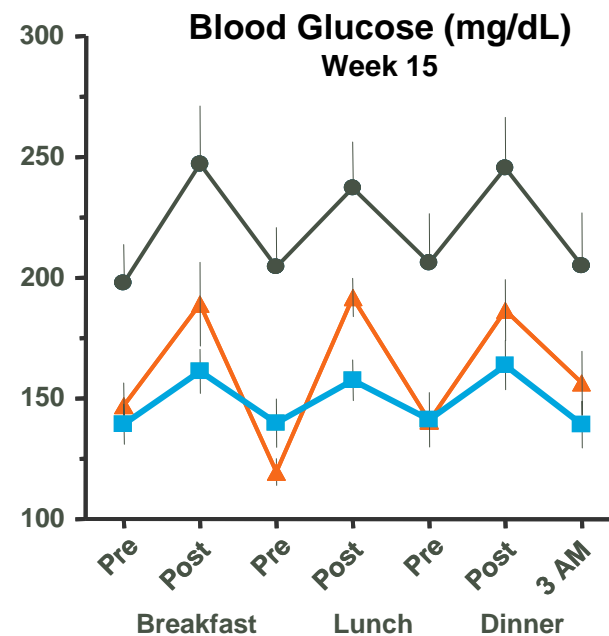
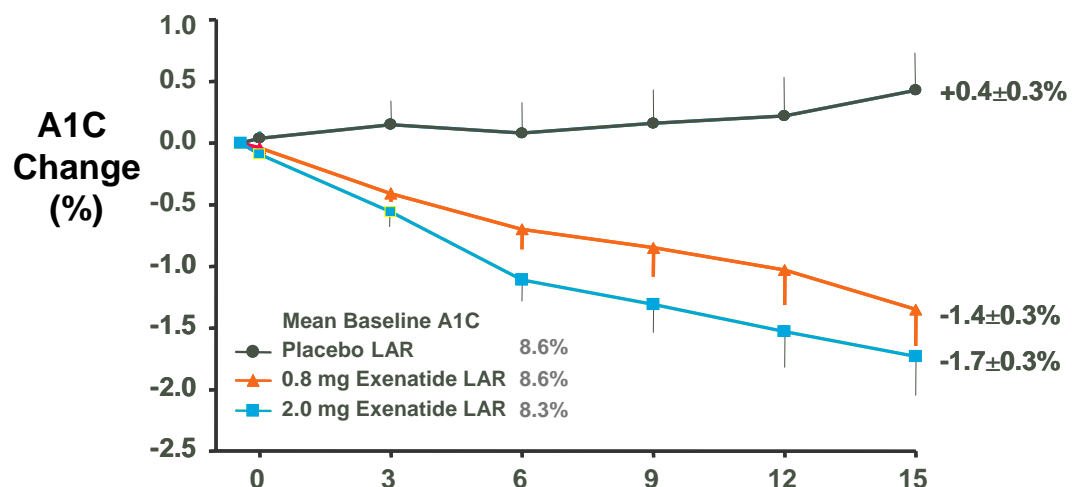


Exenatide LAR



Once-Weekly Exenatide LAR

A1C AND WEIGHT IMPROVEMENTS



- > Generally well-tolerated
 - > Mild nausea
 - > No adverse events leading to early withdrawal in LAR treatment arms



Once-Weekly Exenatide LAR

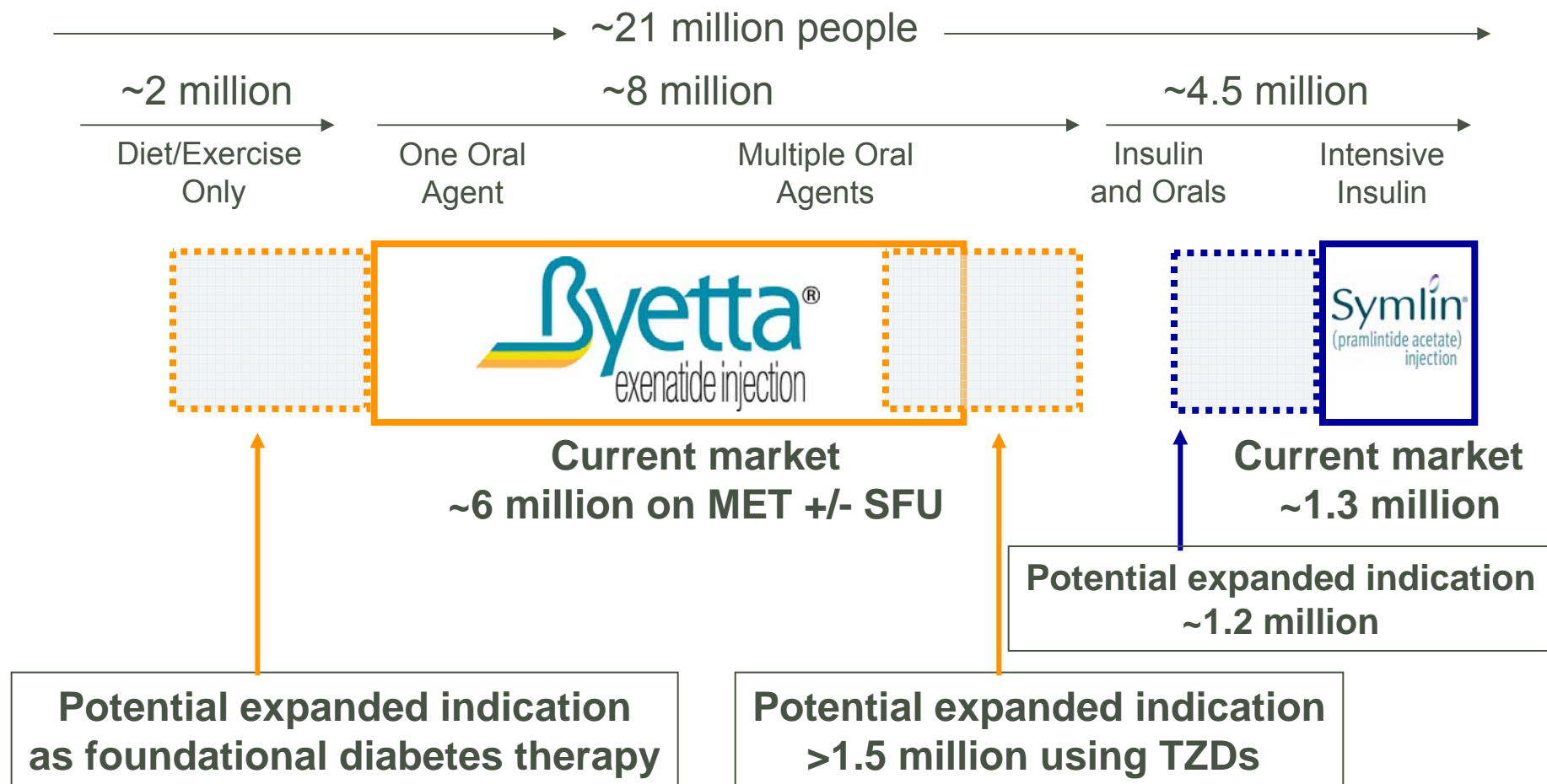
CLINICAL DEVELOPMENT ONGOING

- > Subcutaneous injection
 - > Needle size / volume to be finalized during process development
- > Long-term study of exenatide LAR safety and efficacy ongoing
 - > Open-label, randomized study of ~300 subjects
 - > Includes BYETTA twice-daily comparator group
 - > Efficacy endpoint – reduction in A1C
 - > Anticipated data available in 2H07
- > Process development and scale-up activities on track
 - > Construction of OH facility proceeding well
 - > Study enrollment plan linked to manufacturing scale-up
 - > Expect to finalize commercial manufacturing process by 2H08



Amylin's Presence Across Diabetes Spectrum

NEW OPTIONS FOR EXPANDED PATIENT GROUPS





Early Development

Alain Baron, MD

Senior Vice President, Research



Outline

- > Fast to Man Approach to Clinical Research and Development
 - > Congestive Heart Failure as an Example
- > Approach to Obesity
 - > INTO: Integrated Neurohormonal Therapy for Obesity
 - > Review of 3 Molecular Franchises: Pramlintide, PYY3-36, Leptin
- > Approach to Diabetes



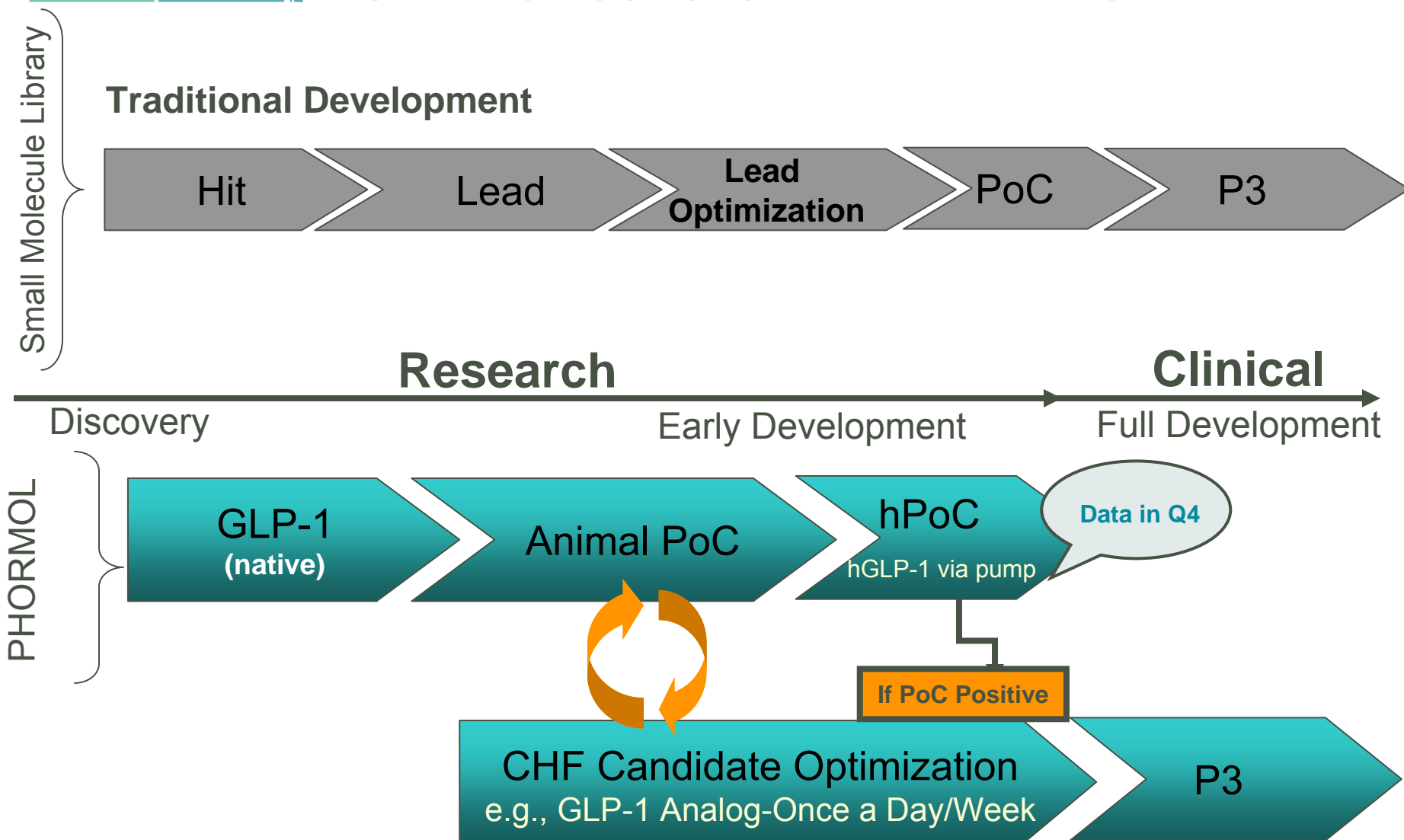
GLP-1 in Congestive Heart Failure:

Example of Amylin's Fast-to-Man
Clinical Research Approach



Fast to Man Proof-of-Concept at Amylin

GLP-1 FOR CONGESTIVE HEART FAILURE



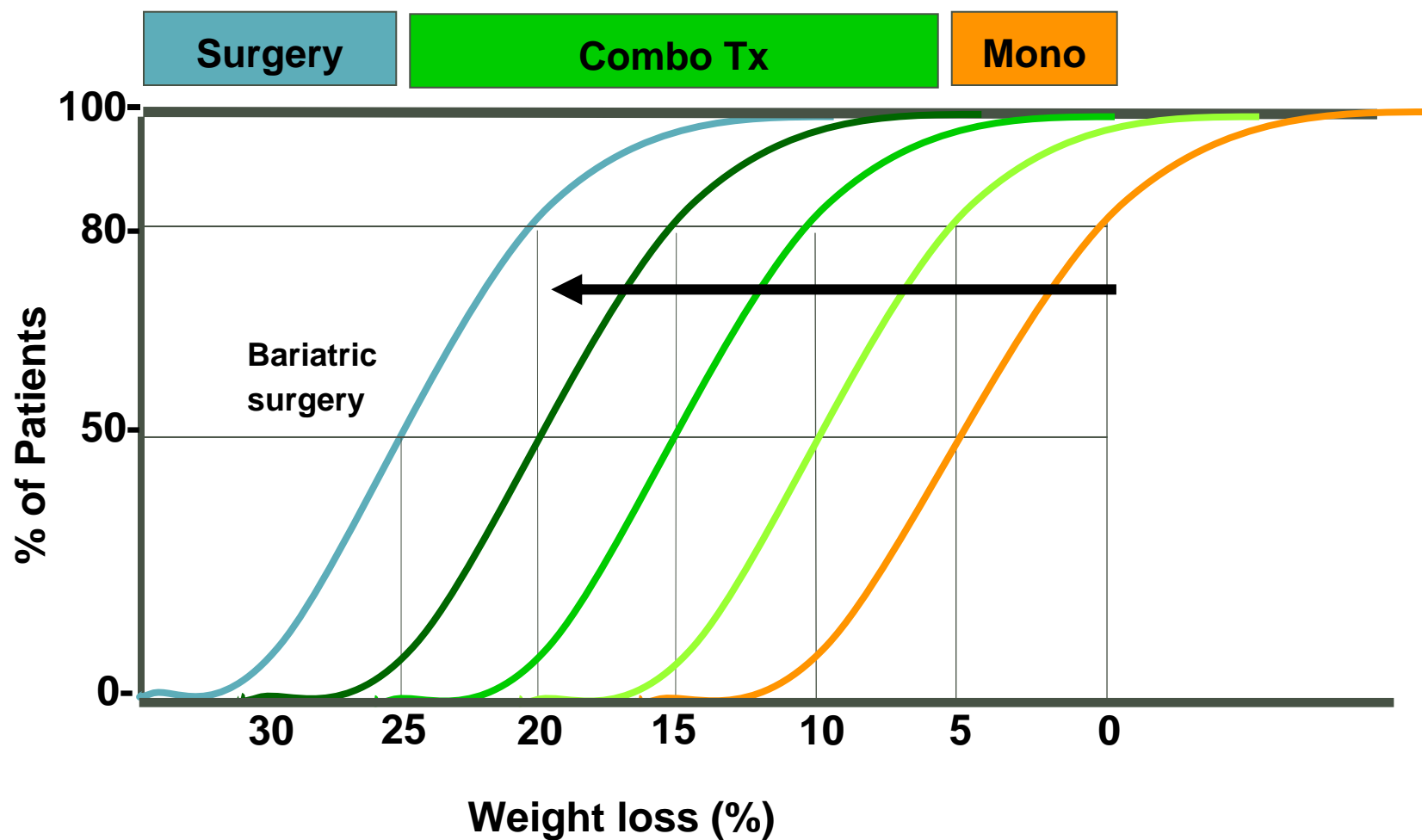


Integrated Neurohormonal Therapy for Obesity

INTO

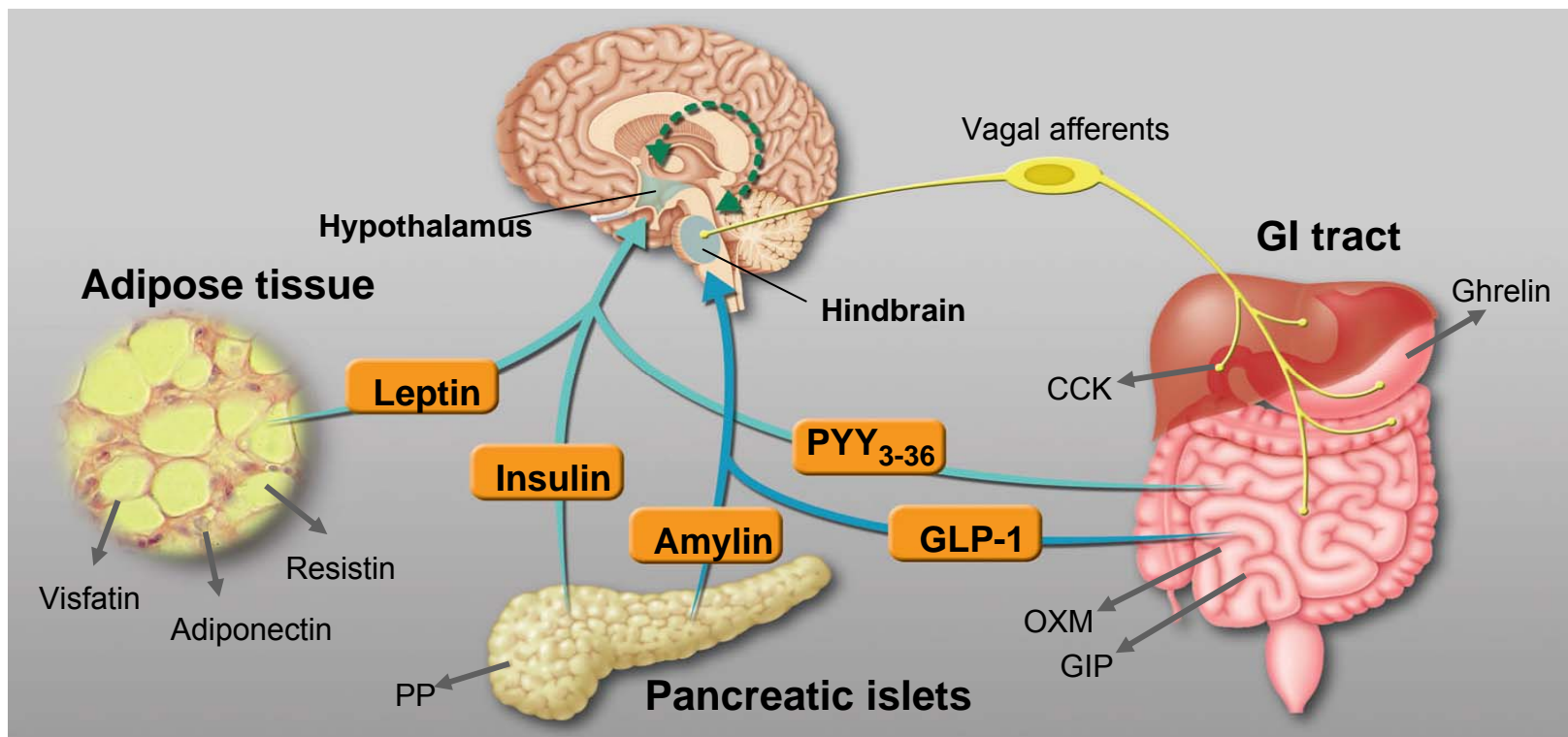


The Market Demands Better Efficacy and Safety: CAN COMBINATION THERAPY DELIVER?





Integrated Neurohormonal Therapy for Obesity: LEVERAGING PHYSIOLOGY



Clinical-Stage Compounds

AC164594
(r-met human leptin)

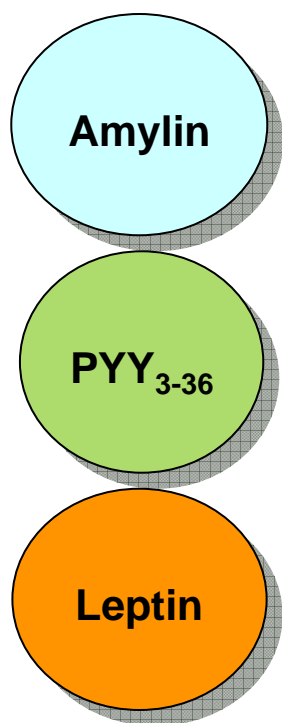
AC137
(Pramlintide)

AC162352
(synthetic PYY3-36)

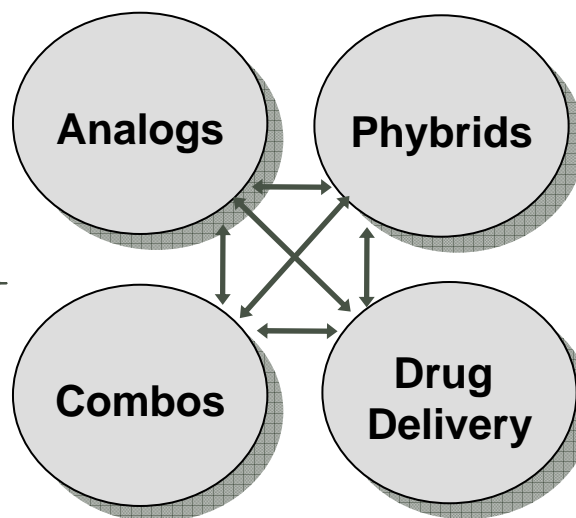


INTO Strategy: FRAMEWORK OF OPPORTUNITIES

Molecular Franchises



Research Capabilities



Potential Treatments

Products
Product Regimens

4 main goals:

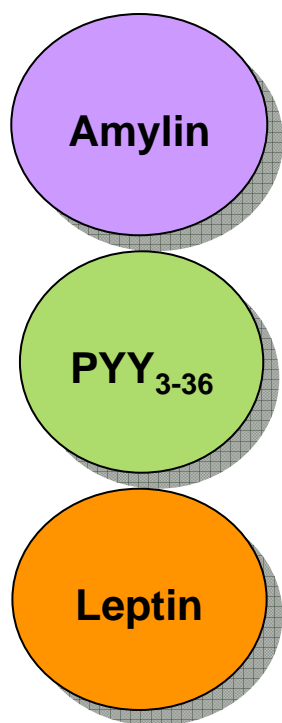
- highly efficacious
- safe
- conveniently delivered
- favorable COGS

Mono Therapy
Dual-Combo Therapy
Triple-Combo Therapy

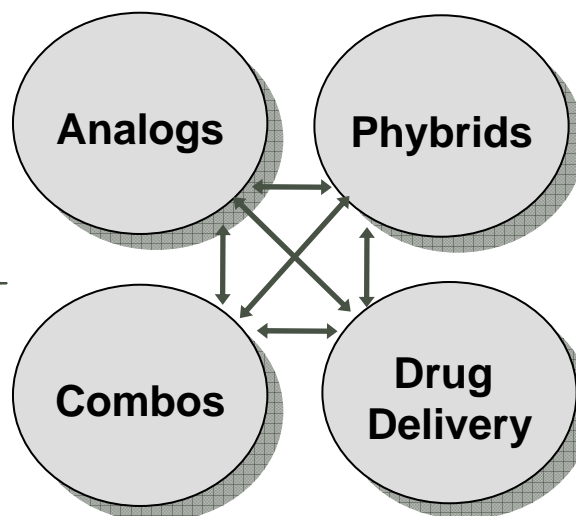


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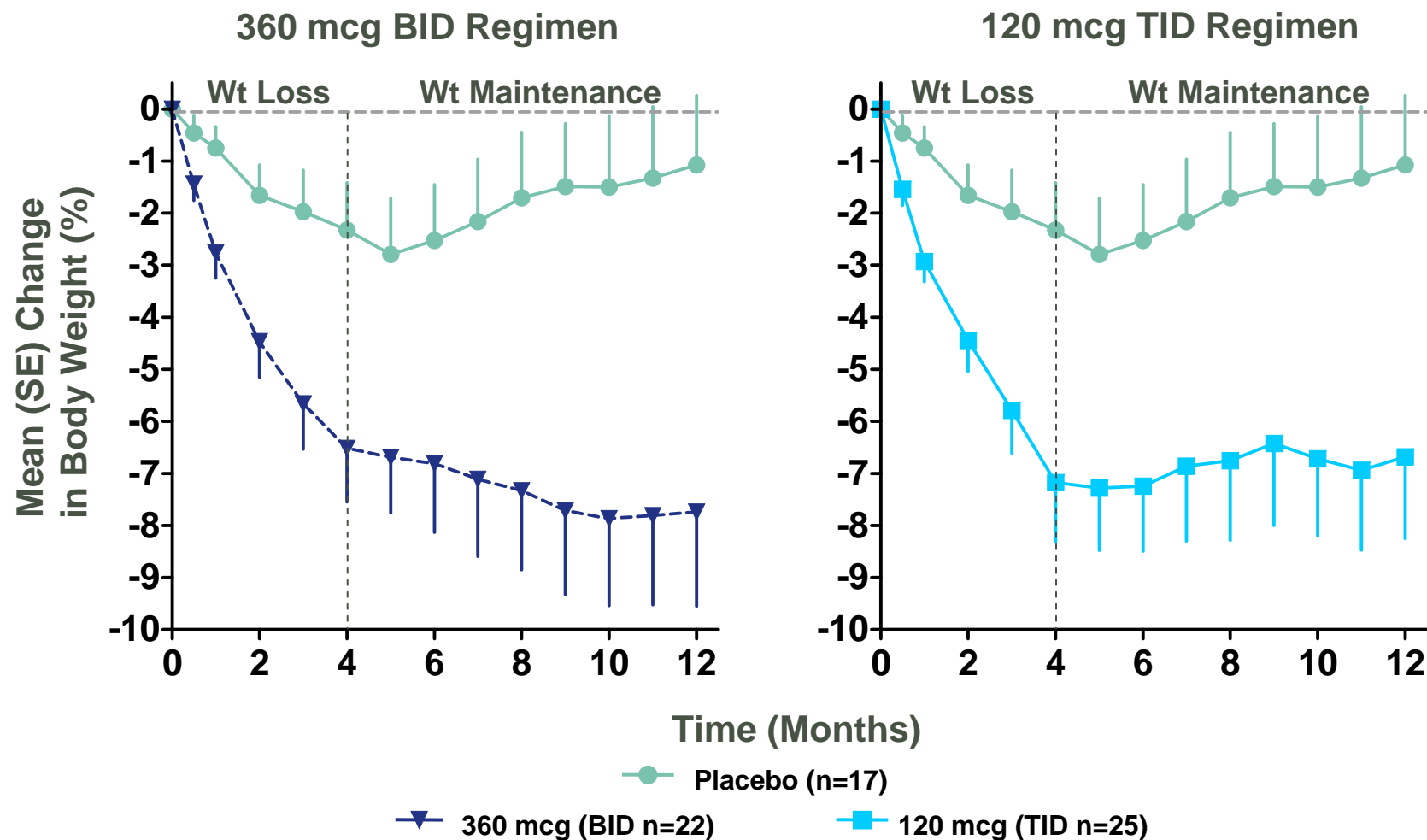
Pramlintide Obesity Program

Phase 2b + Extension trial update



Pramlintide Phase 2b and Extension Study

% CHANGE IN WEIGHT



Data shown for subjects who completed 1 year of treatment.



Pramlintide Obesity Program: STRATEGIC CONSIDERATIONS FOR PHASE 3

- > Efficacy
 - > Sustained 52-week weight loss in conjunction with lifestyle intervention
- > Safety
 - > Approved for diabetes indication
 - > Extensive nonclinical toxicology program completed
 - > No evidence of neuro-psychiatric or idiosyncratic adverse events
 - > No severe hypoglycemia observed in obesity trials
- > Product Development
 - > More concentrated formulation provides increased convenience and reduced COGS
- > Potential to become first neurohormonal therapy for obesity



Pramlintide Obesity Program

NEXT STEPS

- > Pramlintide is foundational of current INTO approach
- > Beginning preparations for Phase 3
- > Phase 3 start date and design guided by:
 - > Ongoing combination study results
 - > Clinical design strategy and regulatory discussions



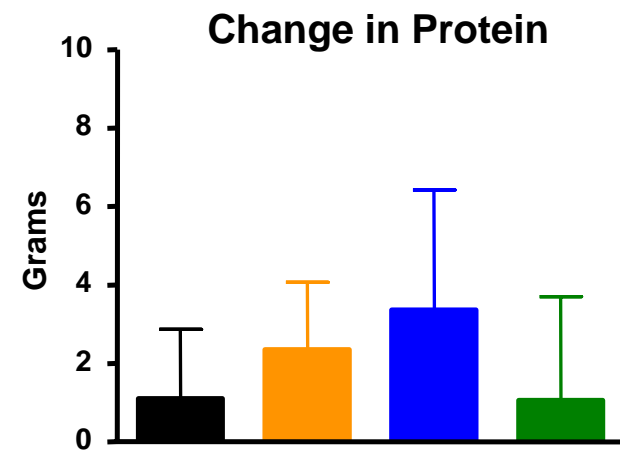
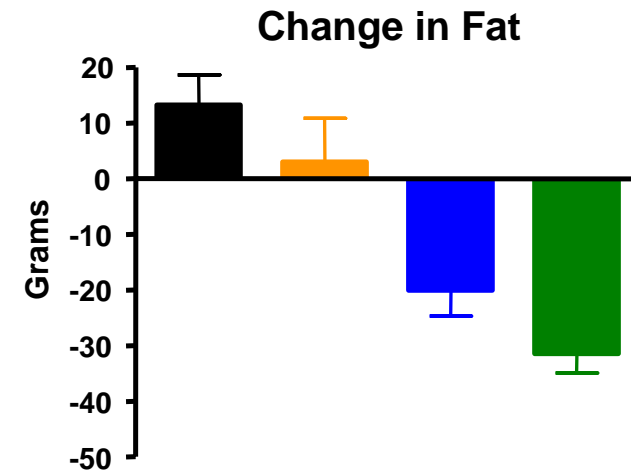
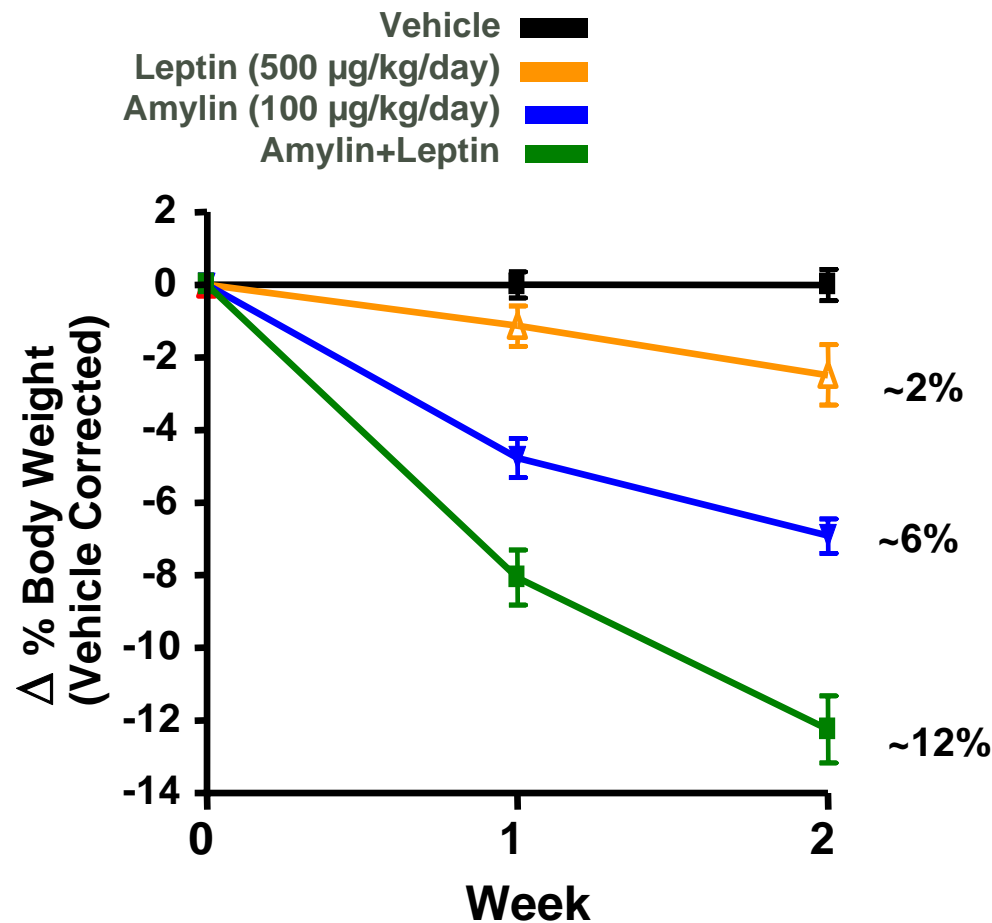
Why Did Amylin Acquire Leptin?

- > “Leptin Not Impressive in Clinical Trial”
 - *Science*, October 1999
- > “What happened to leptin?”
 - WebMD, August 1999
- > “Search for an obesity ‘cure’ fails”
 - BBC, September 2001



Amylin + Leptin: Preclinical Proof of Concept

SYNERGISTIC, FAT-SPECIFIC WEIGHT LOSS



Diet-induced obese (DIO) rats
Continuous infusion of peptides (osmotic minipump)



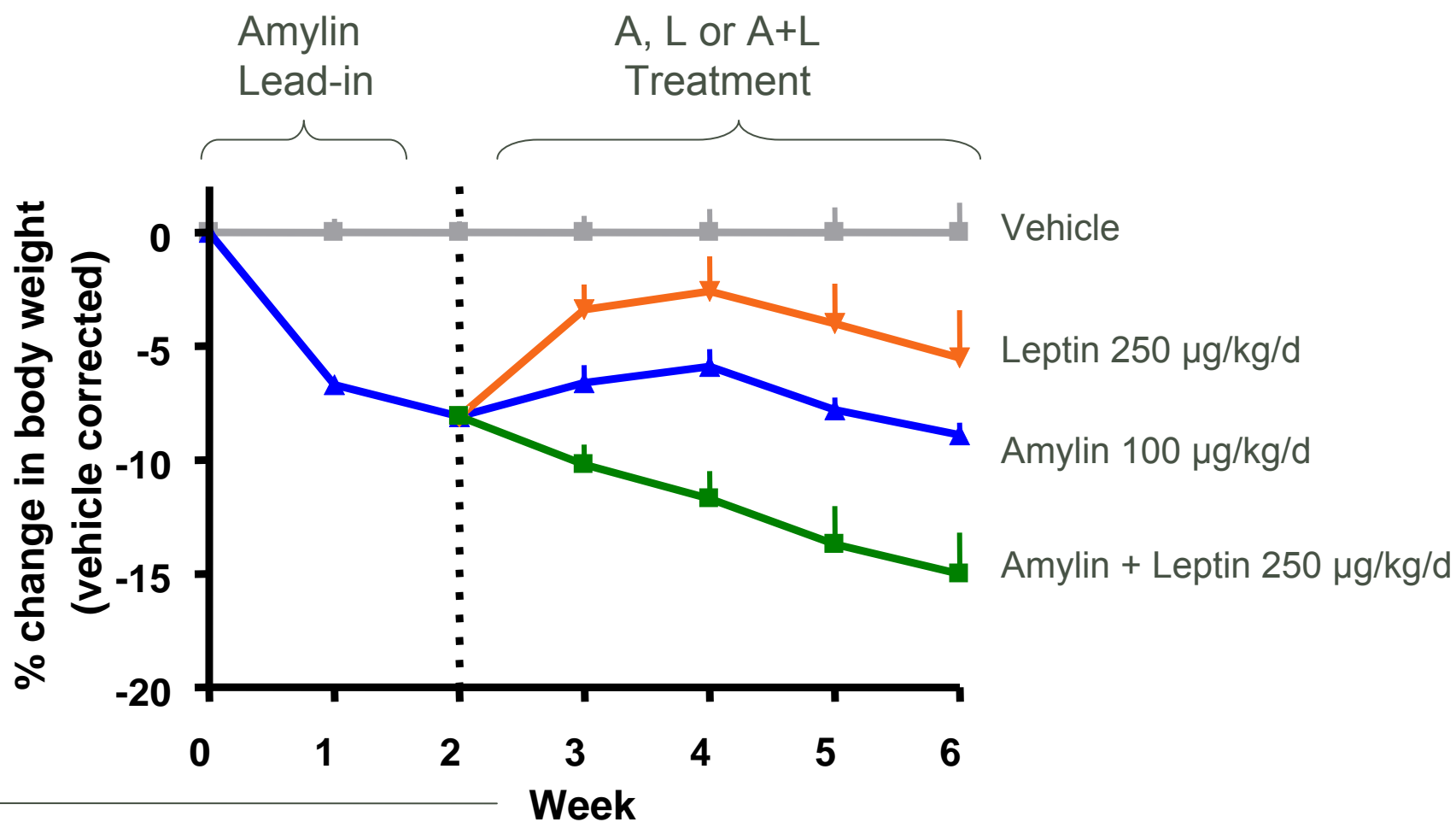
Pramlintide + Leptin

CLINICAL PROOF OF CONCEPT STUDY INITIATED

- > Randomized, controlled double-blind combination study
 - > 180 subjects target enrollment, 125 to be randomized
- > 24-week study
 - > 4-week lead-in period with diet + pramlintide
- > 3 treatment groups, BID dosing
 - > Leptin + Placebo
 - > Pramlintide + Placebo
 - > Leptin + Pramlintide
- > Evaluate effect on body weight



Amylin + Leptin: Preclinical Results Support Clinical Study Design

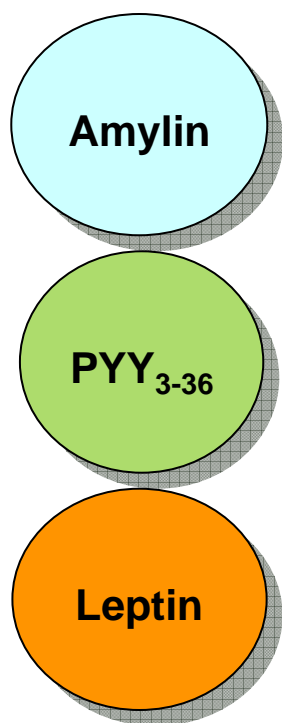


Diet-induced obese (DIO) rats

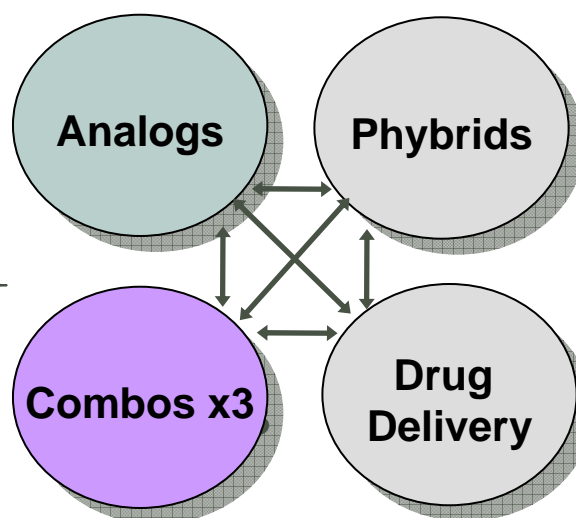


INTO Strategy: FRAMEWORK OF OPPORTUNITIES

Molecular Franchises



Research Capabilities



Potential Treatments

Products
Product Regimens

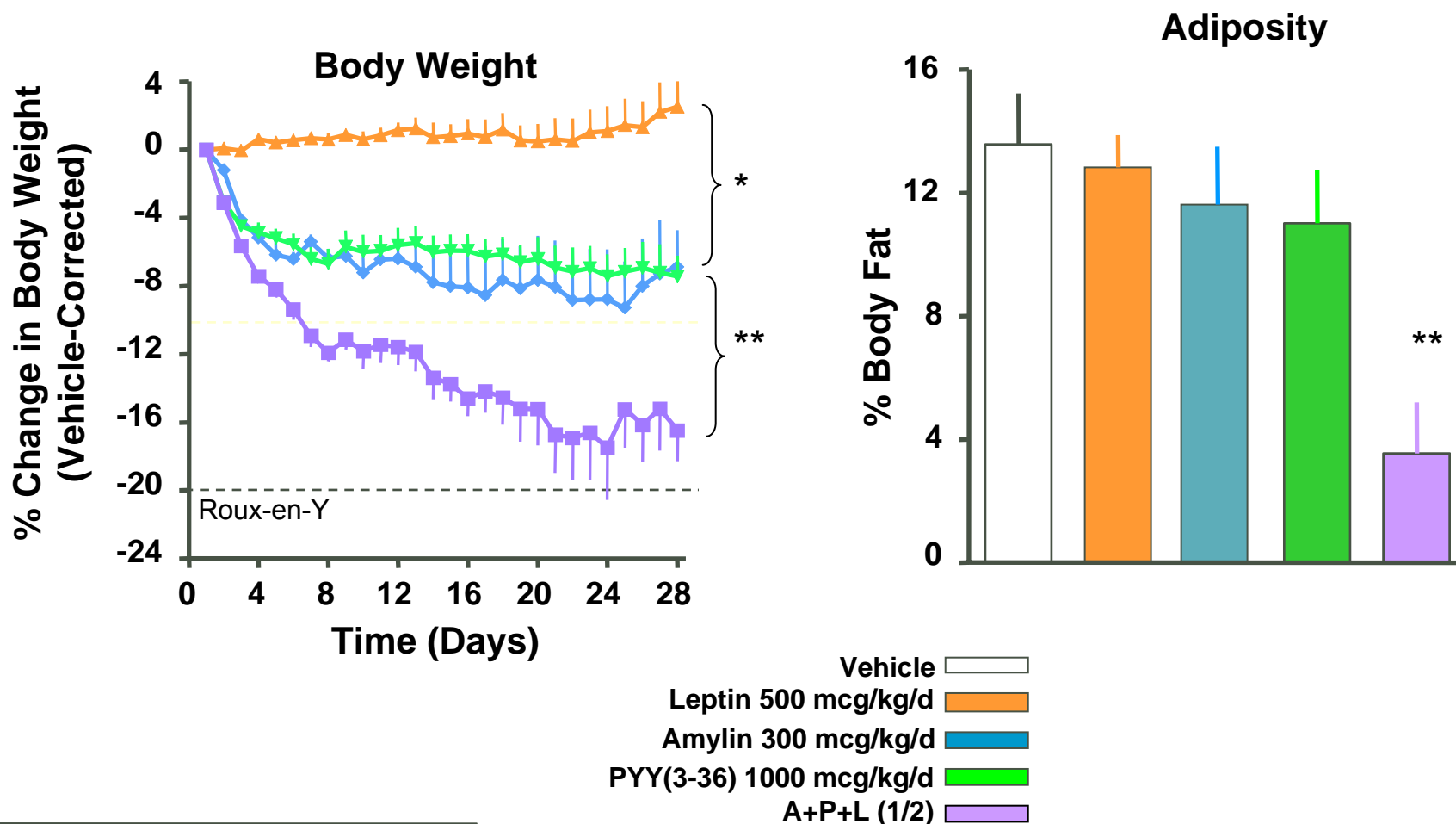
4 main goals:

- highly efficacious
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Mono Therapy
Dual-Combo Therapy
Triple-Combo Therapy



Integrated Neurohormonal Therapy for Obesity: TRIPLE COMBINATION THERAPY



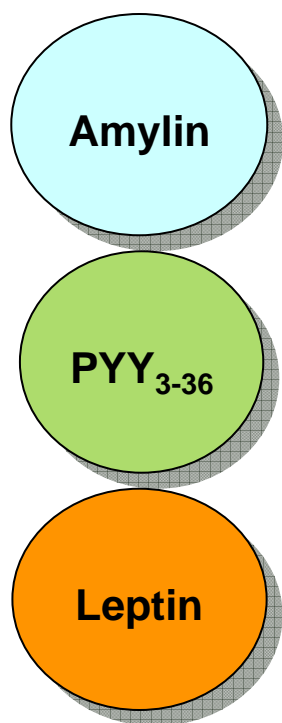
Diet-induced obese (DIO) rats
Continuous infusion of peptides (osmotic minipump)
Sources: Roux-en-Y - Stylopoulos et al, Surg Endosc 19:942-6, 2005

*p<0.05 vs. vehicle; **p<0.05 vs. all groups

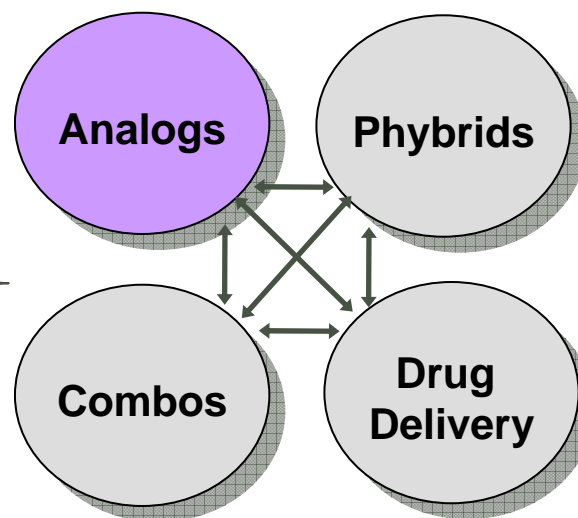


INTO Strategy: FRAMEWORK OF OPPORTUNITIES

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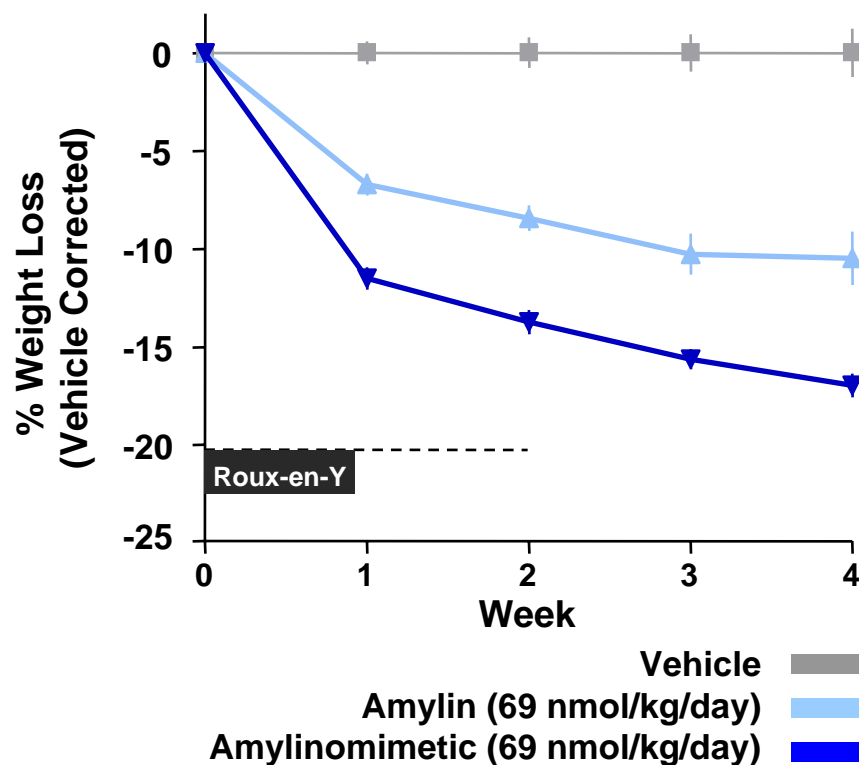
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- conveniently delivered
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Mono Therapy
Dual-Combo Therapy
Triple-Combo Therapy

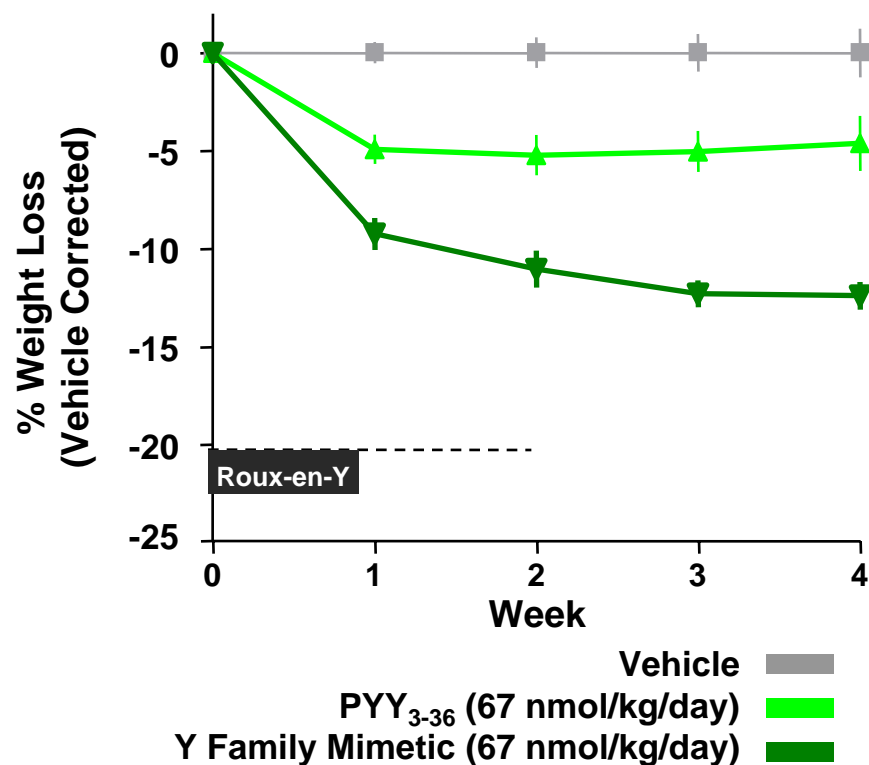


Integrated Neurohormonal Therapy for Obesity OPTIMIZED SECOND GENERATION COMPOUNDS

Amylin → 2nd Gen Amylinomimetic



PYY₃₋₃₆ → Y Family Mimetic

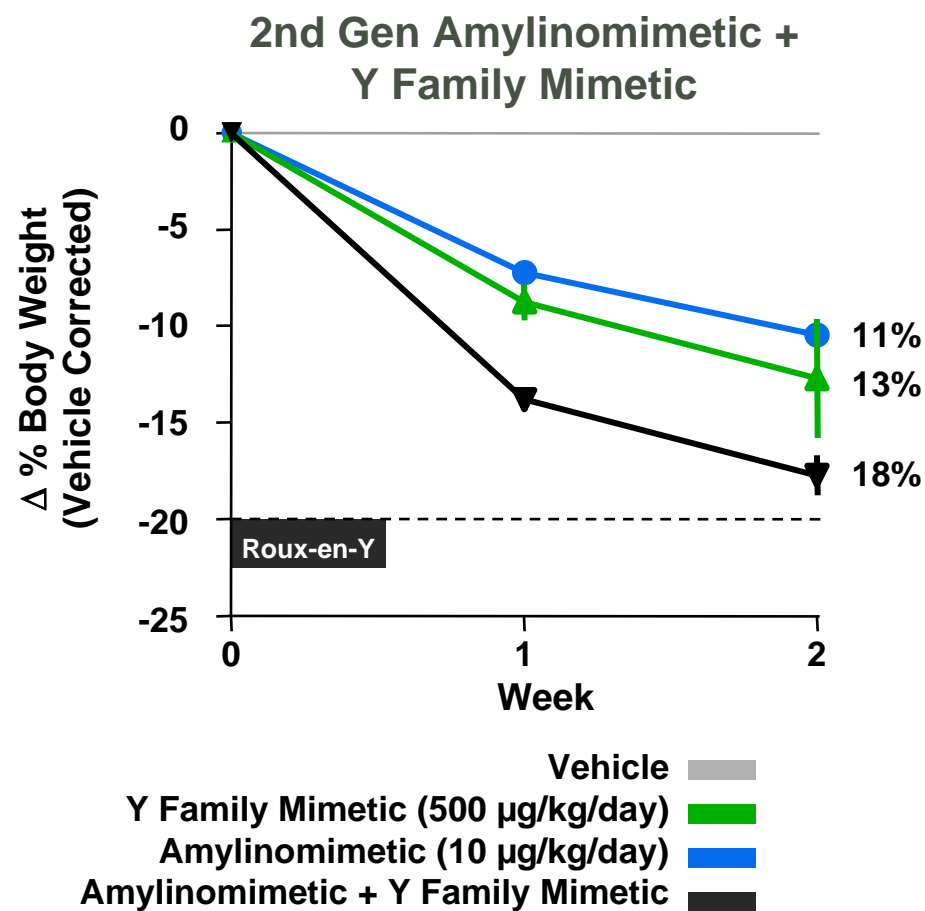
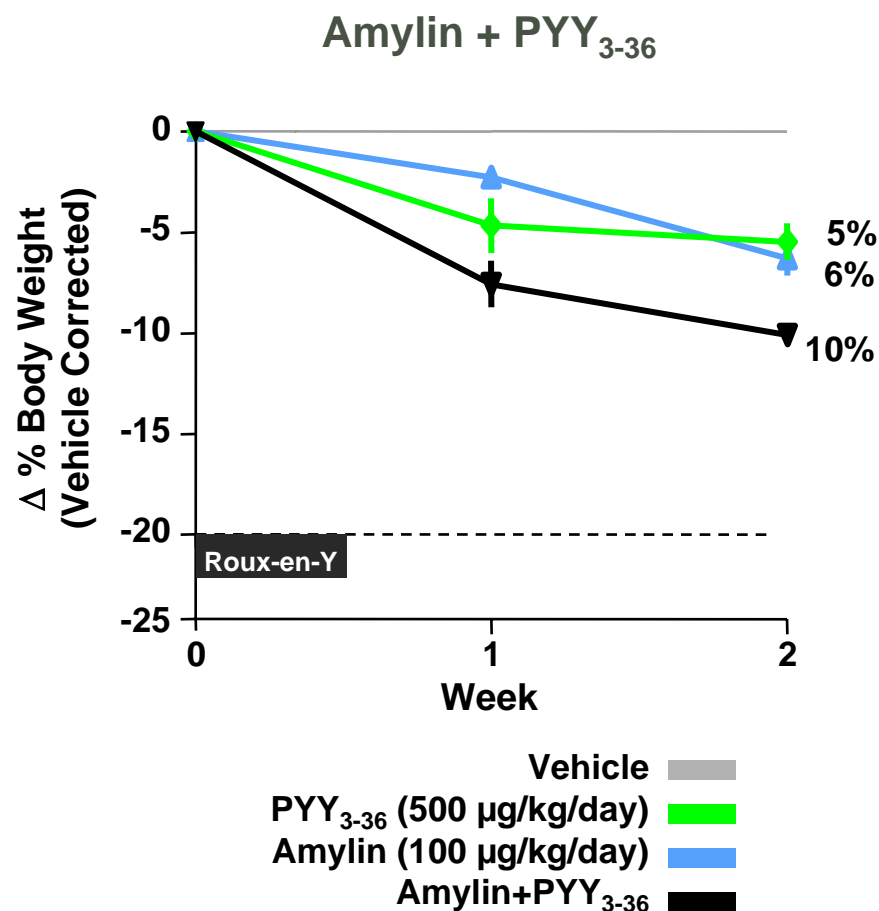


Diet-induced obese (DIO) rats
Continuous infusion of peptides (osmotic minipump)
Sources: Roux-en-Y - Kaplan L et al, Surg Endosc 19:942-6, 2005



Integrated Neurohormonal Therapy for Obesity

DUAL COMBINATION THERAPY (2ND GENERATION)



Diet-induced obese (DIO) rats
 Continuous infusion of peptides at full doses (osmotic minipump)
 Source: Roux-en-Y - Kaplan L et al, Surg Endosc 19:942-6, 2005



Obesity Clinical Research Program

Q4 2006: 4 new clinical obesity studies

- > 2nd generation amylinomimetic
 - > IND submitted, Phase 1 single-dose study initiated (safety, tolerability, PK)
- > Pramlintide + Leptin
 - > Proof of concept study initiated (weight loss)
- > Pramlintide + PYY3-36
 - > Safety/tolerability – combination multi-dose study initiated
- > Pramlintide + oral agents
 - > Combination study to be initiated (weight loss)

2007

- > Pramlintide + PYY3-36 + Leptin PoC combo study start planned

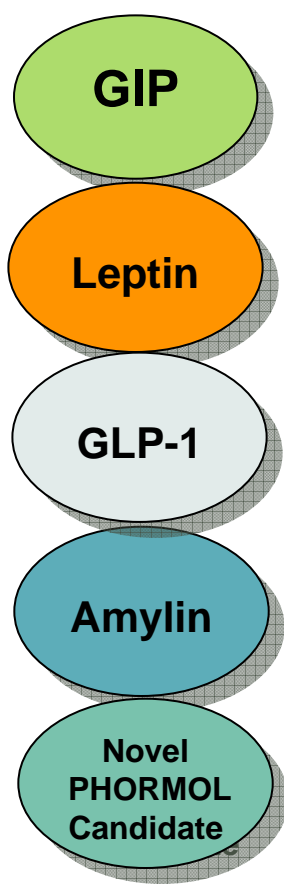


“Integrated Neurohormonal Therapy for Diabetes”

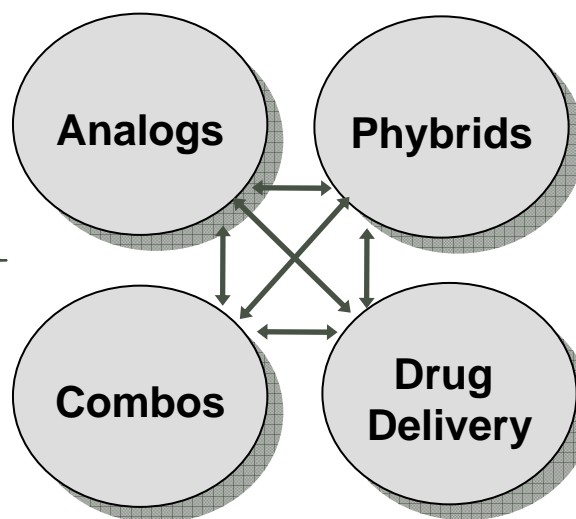


Diabetes Strategy: FRAMEWORK OF OPPORTUNITIES

Molecular Franchises



Research Capabilities



Potential Treatments

Products
Product Regimens

4 main goals:

- highly efficacious
- safe
- conveniently delivered
- favorable COGS

Mono Therapy
Dual-Combo Therapy
Triple-Combo Therapy



Integrated Neurohormonal Therapy for Diabetes:

Role of Glucose-Dependent Insulinotropic Polypeptide

GIP



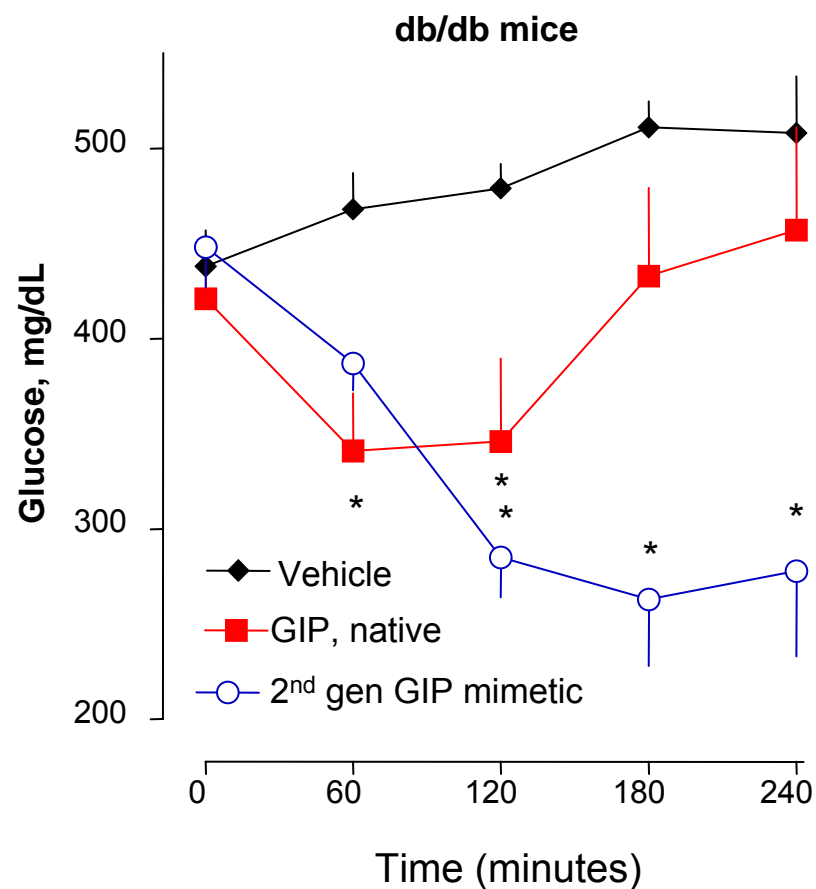
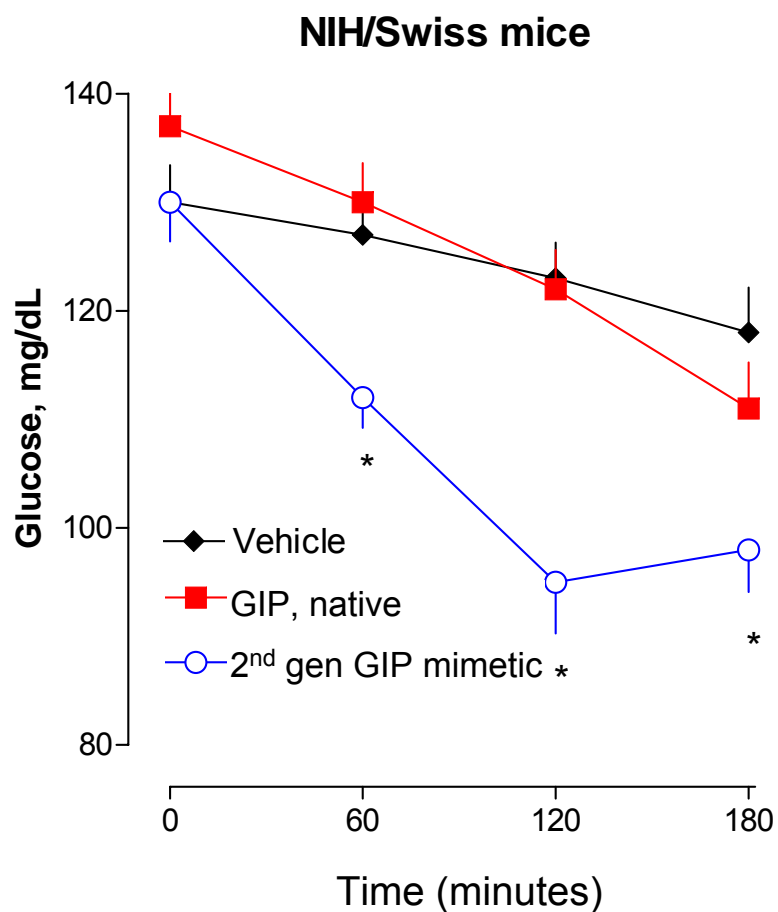
Glucose-dependent Insulinotropic Polypeptide

- > GIP is the “second incretin”
- > 42 amino acids
- > Released by nutrients from K cells in the gut
- > DPP IV sensitive
- > Augments glucose-dependent insulin secretion as well as GLP-1 in healthy humans
- > Poor efficacy in type 2 diabetes – GIP “Resistance”?
- > **Second generation GIP mimetic**
 - > **Peptidic analog of mammalian GIP with an extended half-life**



2nd Generation GIP Mimetic Produces Sustained Glucose Lowering

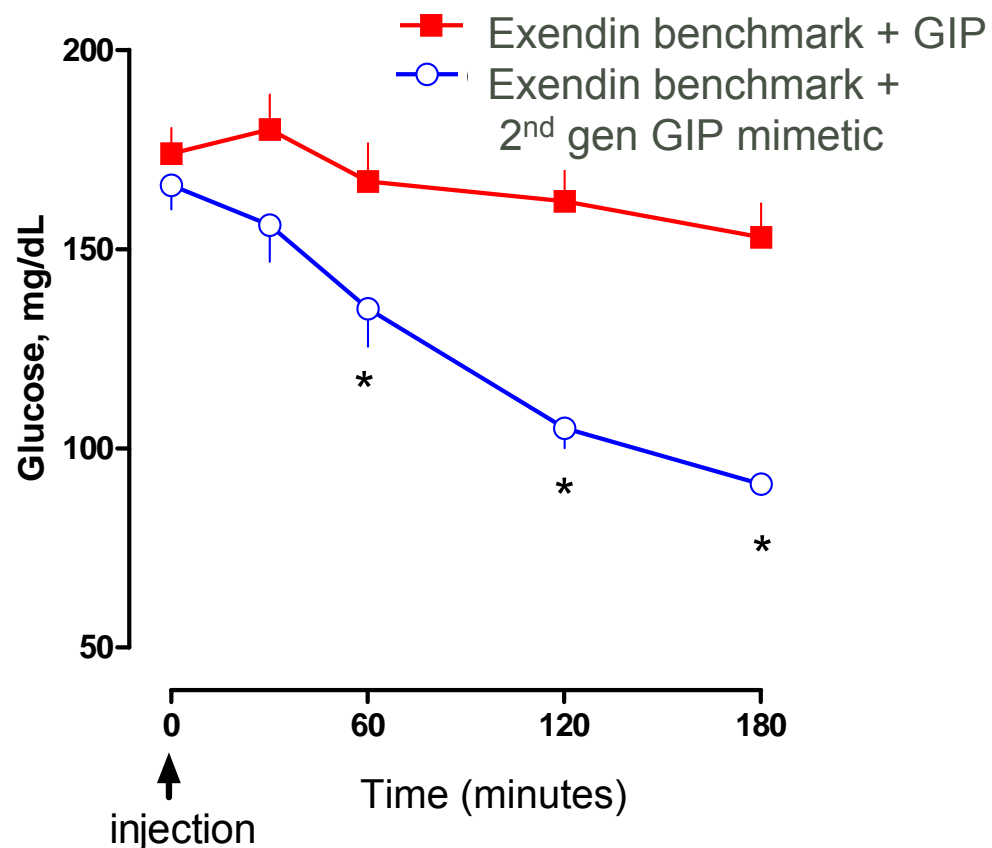
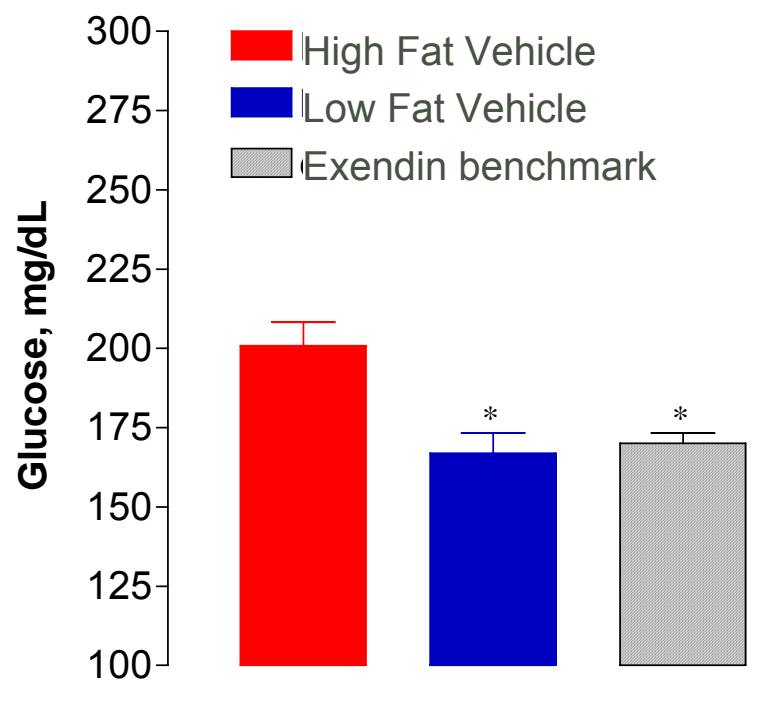
- > Favorable activity for acute glucose lowering in 2 mouse models





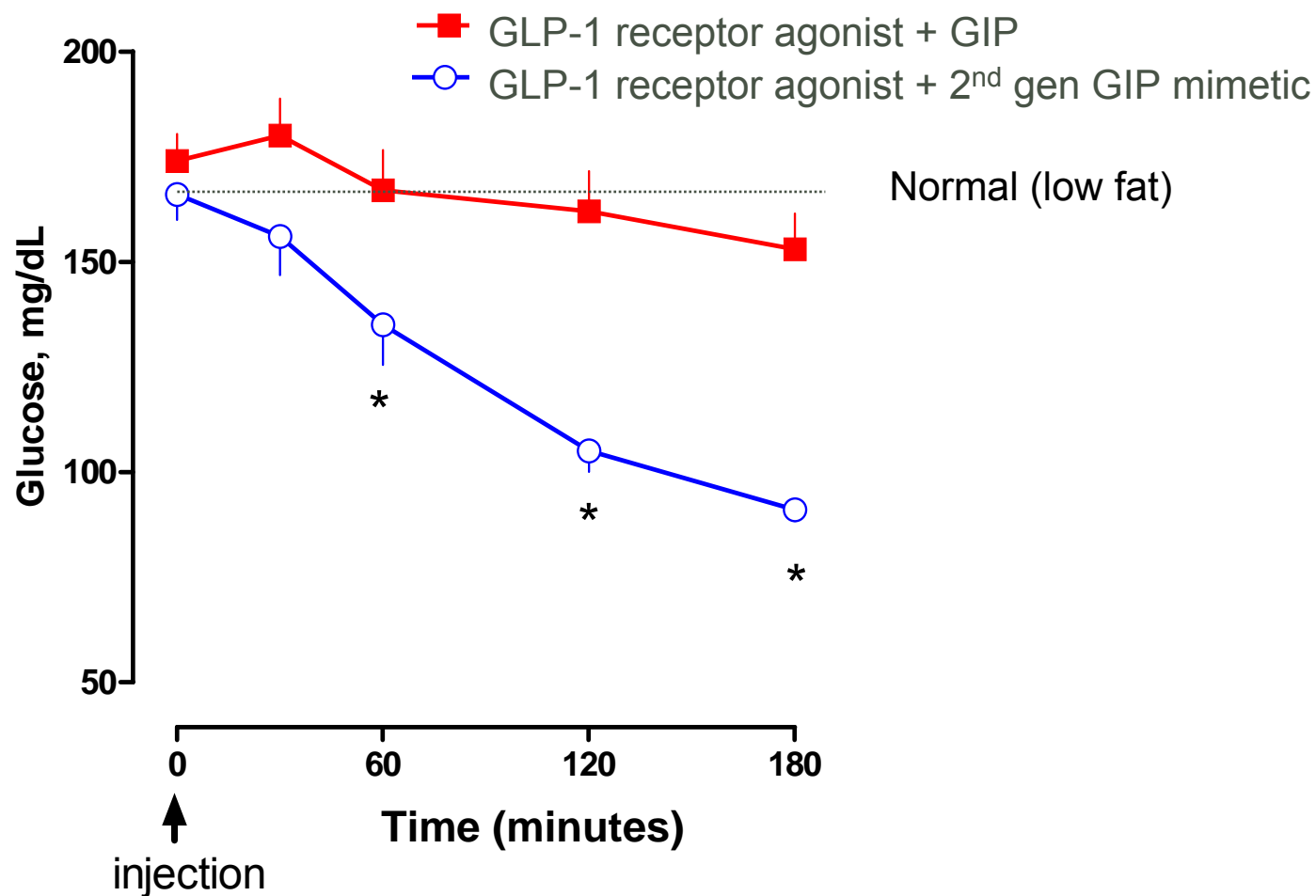
2nd Generation GIP Mimetic Enhances Glucose Lowering Effect

> Fasting blood glucose after 4 weeks' continuous infusion of exendin analog





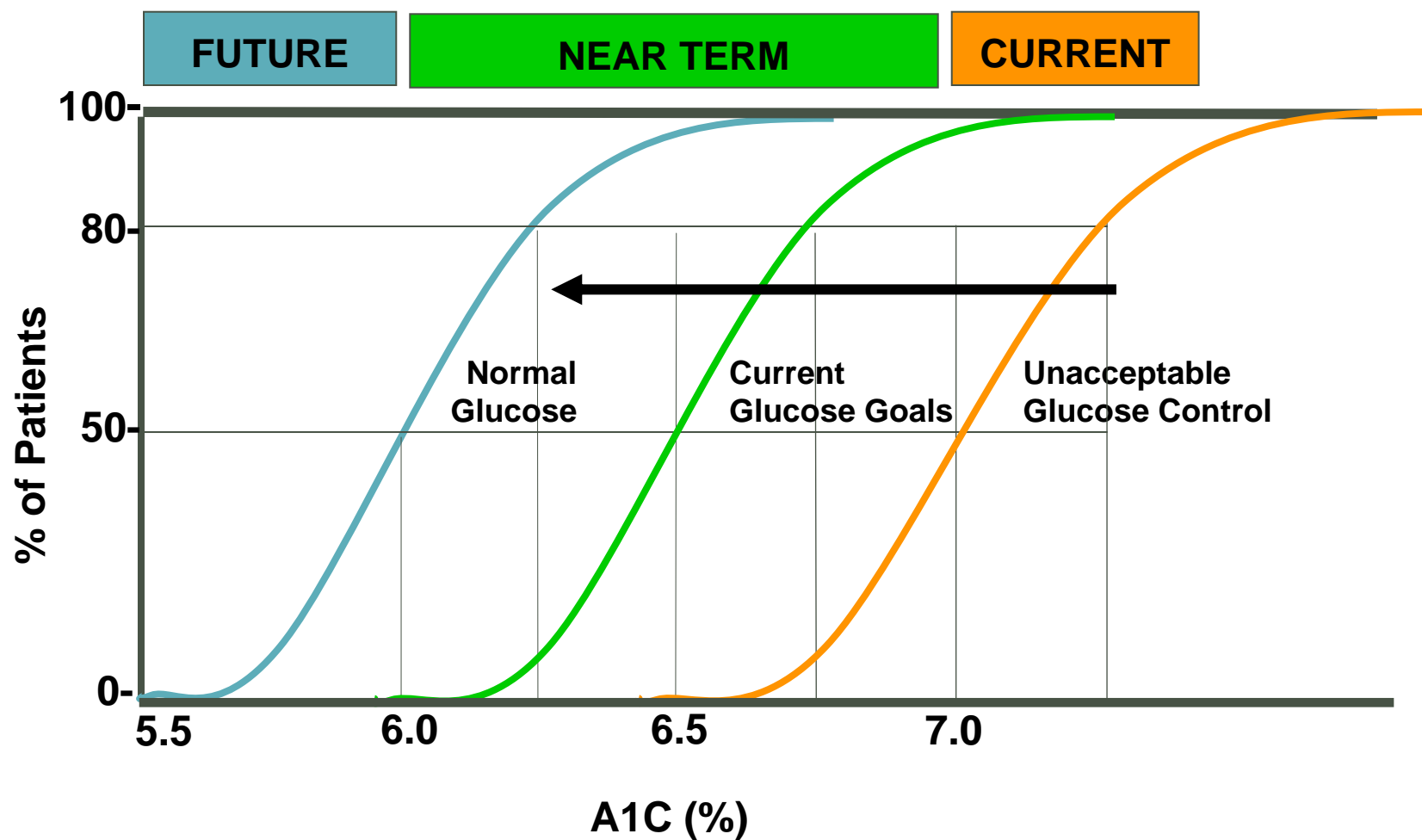
2nd Generation GIP Mimetic Enhances Glucose Lowering Effect





Unmet Market Need For Diabetes Therapy

ROLE OF INTEGRATED NEUROHORMAL APPROACH





Early Development Conclusions

- > Fast-to-Man
- > Integrated Neurohormonal Therapies:
 - > Addresses complex diseases – more effective than mono-therapies
 - > Enhanced through targeted analoging



Discovery Research

Michael Hanley, PhD
Vice President, Discovery Research



Outline

- > Philosophy
- > Platform
- > Enabling Technology



Philosophy of Drug Discovery and Development at Amylin

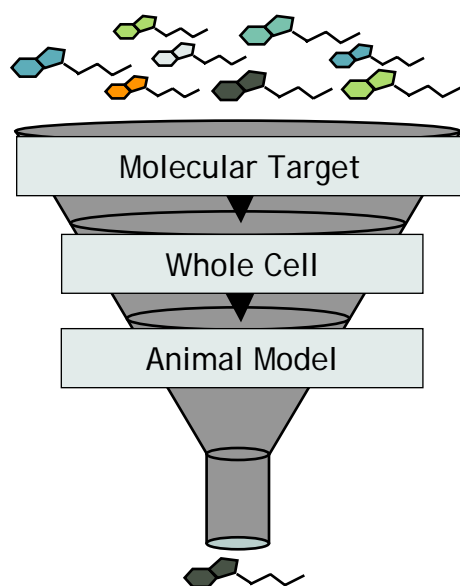
- > Peptide and protein hormones can make ideal drugs because they integrate physiological systems
- > Most diseases are potentially treatable with peptide therapeutics
- > Peptide hormone therapeutics are generally potent and largely devoid of idiosyncratic toxicities
- > Adverse events are most often predicted and manageable
- > If highly effective and safe, injectables can compete in “oral agent space”
- > Evolution promotes peptide hormone optimization according to species-specific needs – a shortcut to discovery



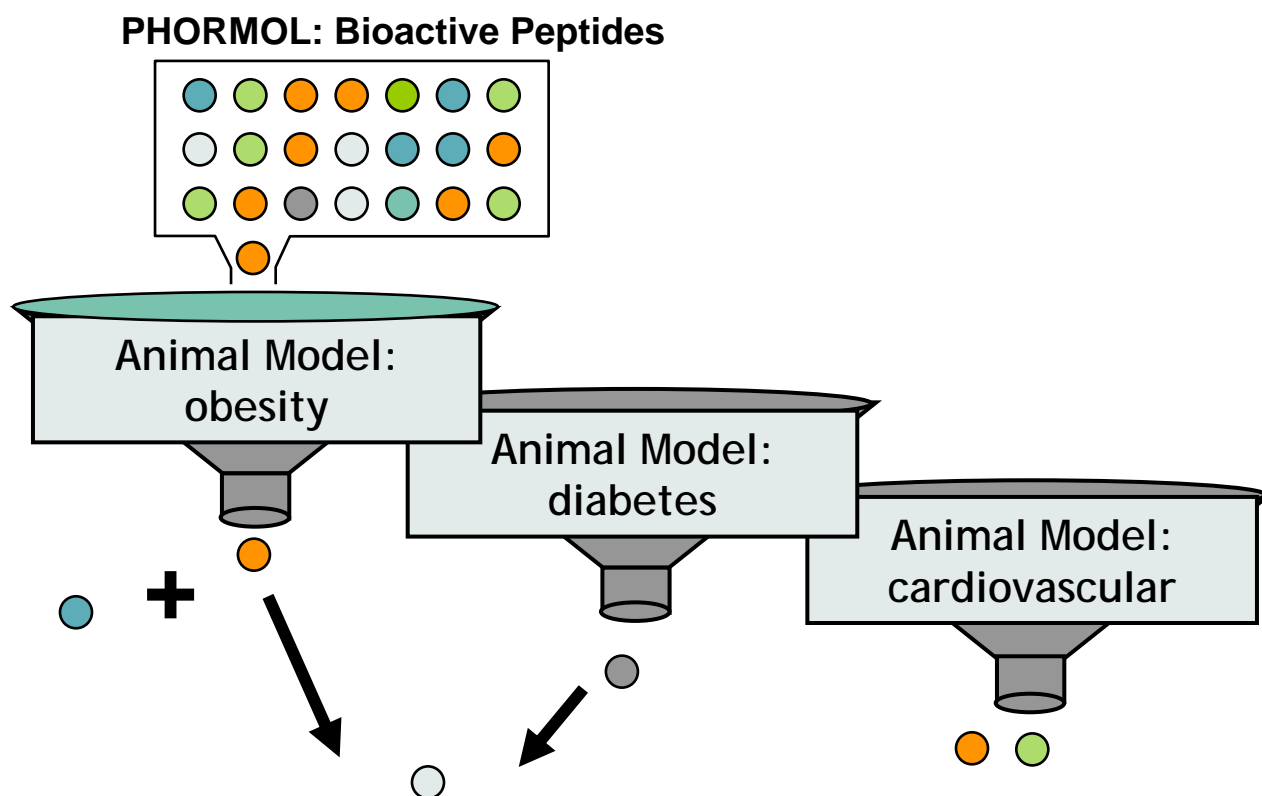
Amylin Screening Path

DIRECT SCREENING IN ANIMAL MODELS

Target Driven



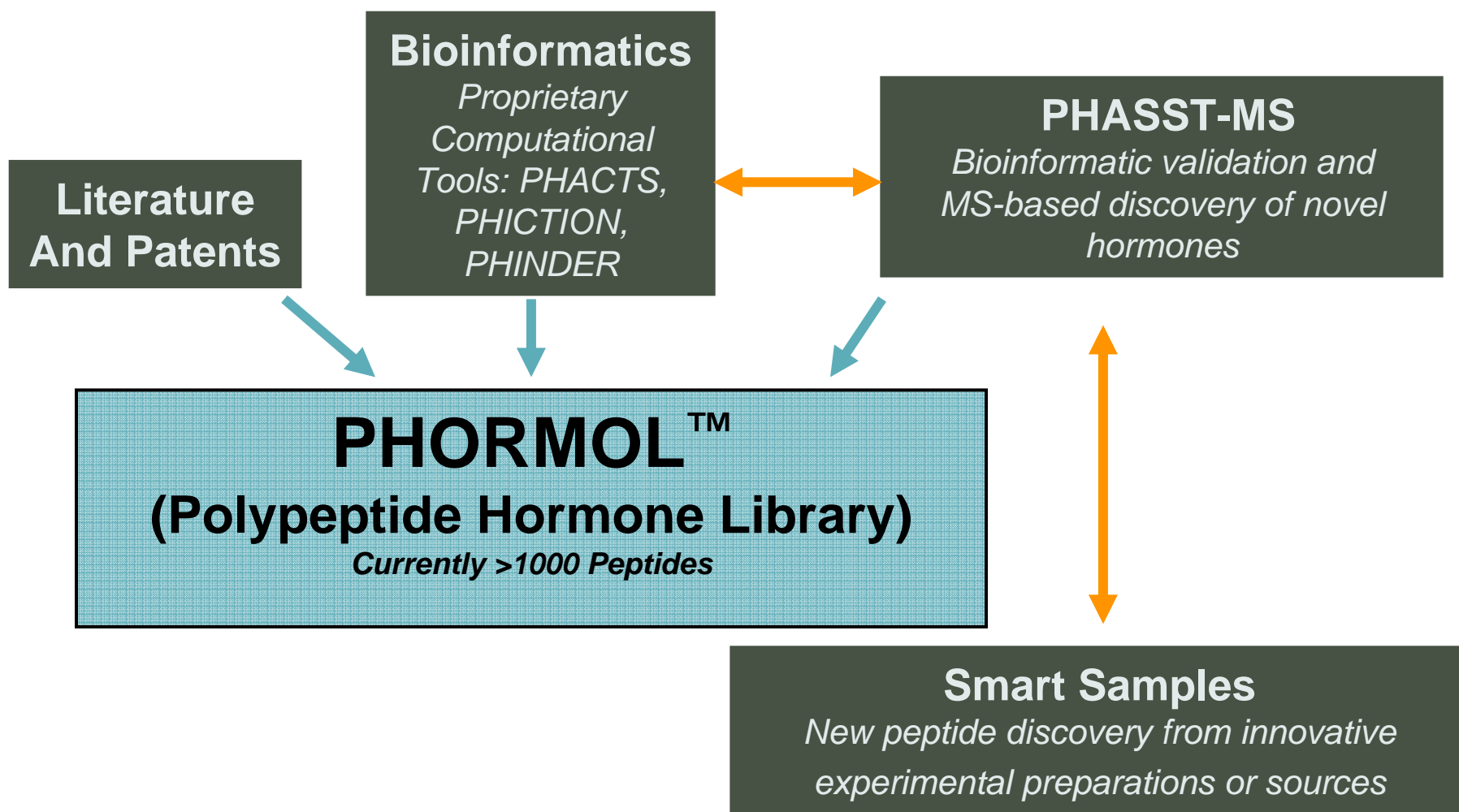
Amylin Approach





Building Value

PHORMOL: A KEY DISCOVERY ASSET





Research Informatics

PHINDER™

- > Identifies “harmonicity™”: basis of predictive “hormone code”
- > Analyzes and optimizes sequences
- > Mines entire genomes in automated computational engine

PHORMOL™

STRUCTURE-ACTIVITY DATA SOURCES

In Vitro - CYTOCENSUS™
In Vivo
Molecular
Published

PHINDER™

PREDICTIVE MODELS

Homonicty™
Aggregation
In Vitro Profiling
Integrative Physiology

Antigenicity
Chemical Stability
Patent Novelty

More Parameters..

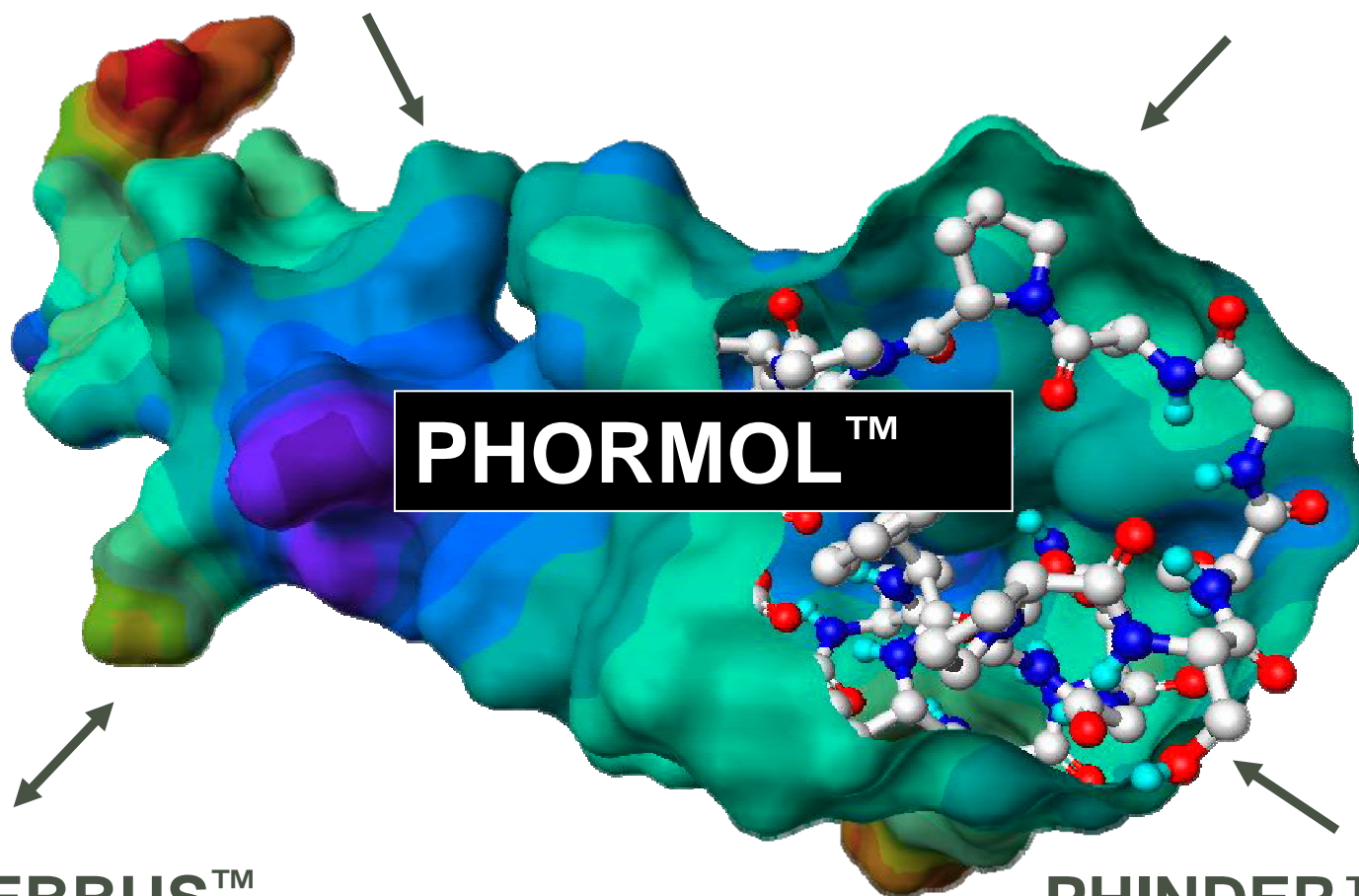
PHOEBBUS™



Research Informatics for Peptide
Therapeutics

PHACTS™ & PHICTION™

TSAR™



PHORMOL™

PHOEBBUS™

PHINDER™



Lead Optimization Built Around Target Candidate Profile

- > Can the potency or efficacy be improved?
- > Are there any pharmaceutical properties to improve?
 - > Solubility, stability, aggregation potential
 - > Metabolic stability
 - > Clearance, half-life
 - > Immunogenicity
- > What is the desired pharmacokinetic profile?
 - > Sustained
 - > Pulsatile
- > What is the desired route of delivery?



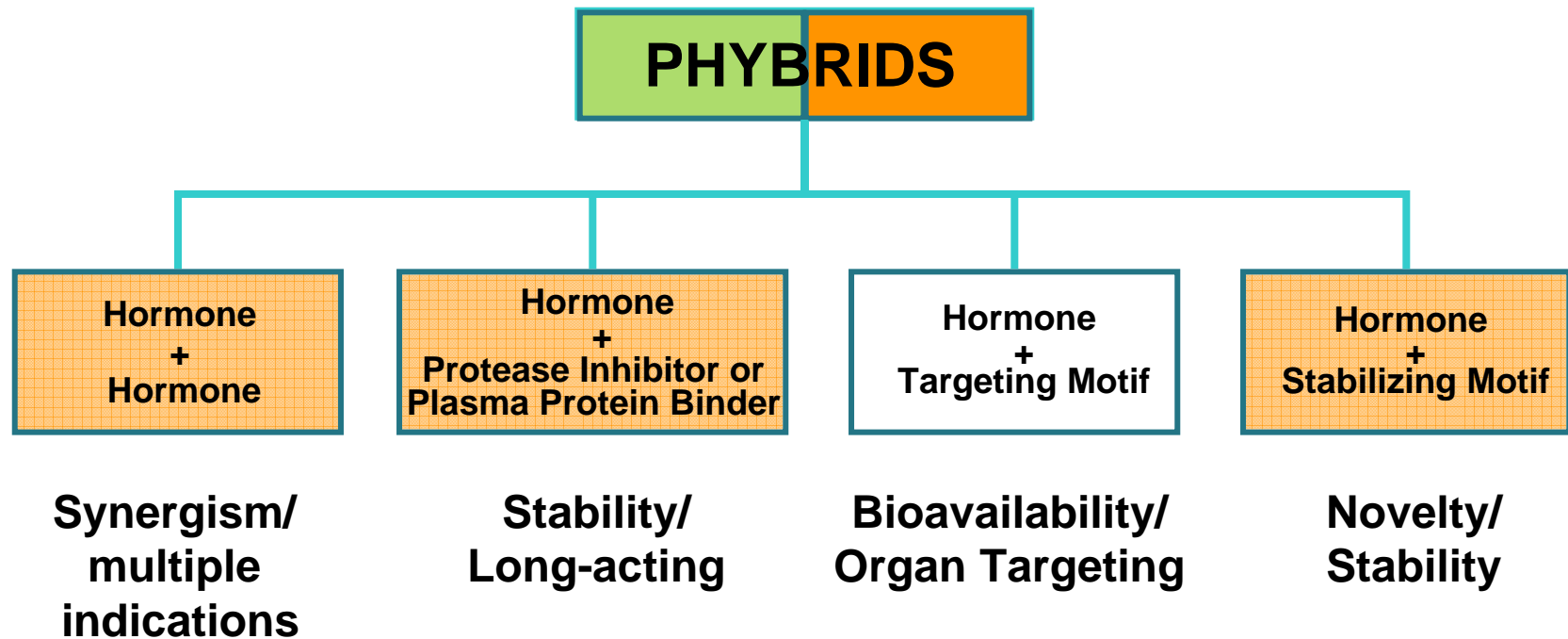
Profile of 2nd Generation Compounds

Endpoint	Y Family Mimetic	Amylinomimetic (2 nd Gen)
➤ Efficacy		
<i>Acute & Chronic Combo-Therapy</i>	↑↑	↑↑
➤ Potency		
<i>Acute</i>	=	↑
<i>Chronic</i>	↑	↑
➤ Duration of Action	↑	↑
➤ Plasma Lipids (decrease)	↑	=
➤ Body Composition	=	=
➤ Stability		
<i>Plasma</i>	↑	↑
<i>Chemical</i>	↑	↑↑
<i>Physical</i>	↑	↑↑
➤ Off Target Profiling		
<i>Telemetry</i>	=	=
<i>Locomotor</i>	=	=
➤ Intellectual Property	Applications filed	Applications filed



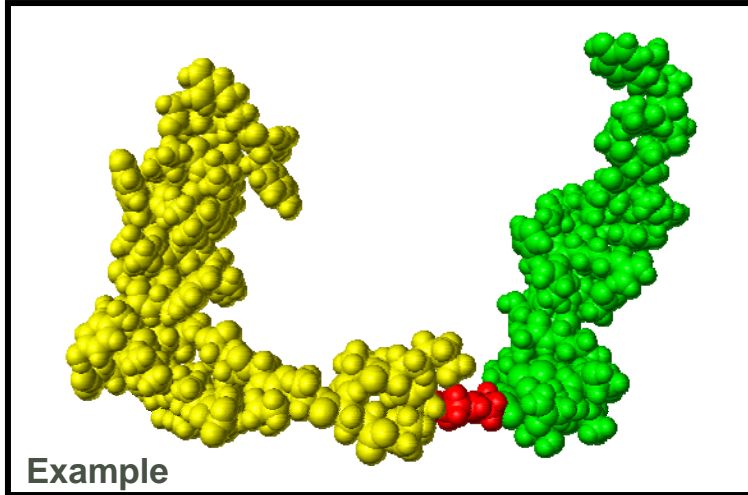
Towards Peptide Therapeutic Design

CREATE FUNCTIONAL PEPTIDE HYBRIDS (“PHYBRIDS”)



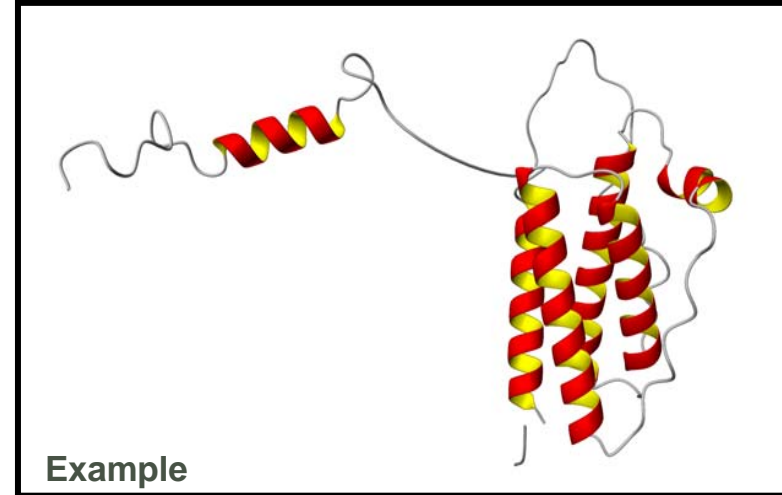


Phybrid Approach: Potential to Enable Obesity Combo-Tx in a Single NME



— 2°-Gen Amylinomimetic
— 2°-Gen Y Family Mimetic

- ☒ dual receptor action
- ☒ *in vivo* activity



— 2°-Gen Amylinomimetic
— Leptin

Drug Delivery Technologies Under Evaluation

Non-Invasive Systems*



Once Daily Systems*



Once Weekly/Monthly*



Implantable Systems*



Drug delivery may improve

- > Safety and efficacy
- > Physicians' willingness to prescribe
- > Patients' willingness to fill
- > Patient's compliance
- > Patient's long-term adherence/persistence

**Pharmaceutical properties of candidate
are tailored to target product profile and
drug delivery modality**

* Photos are illustrative examples only



Discovery Research Conclusions

- > Broad, proprietary discovery platform supported by unique bioinformatics and technology
- > Drug candidates are derived from a combination of discovery, design and opportunistic licensing
- > Peptide therapeutics comprise a sustainable resource for long-term drug discovery and development in multiple chronic diseases



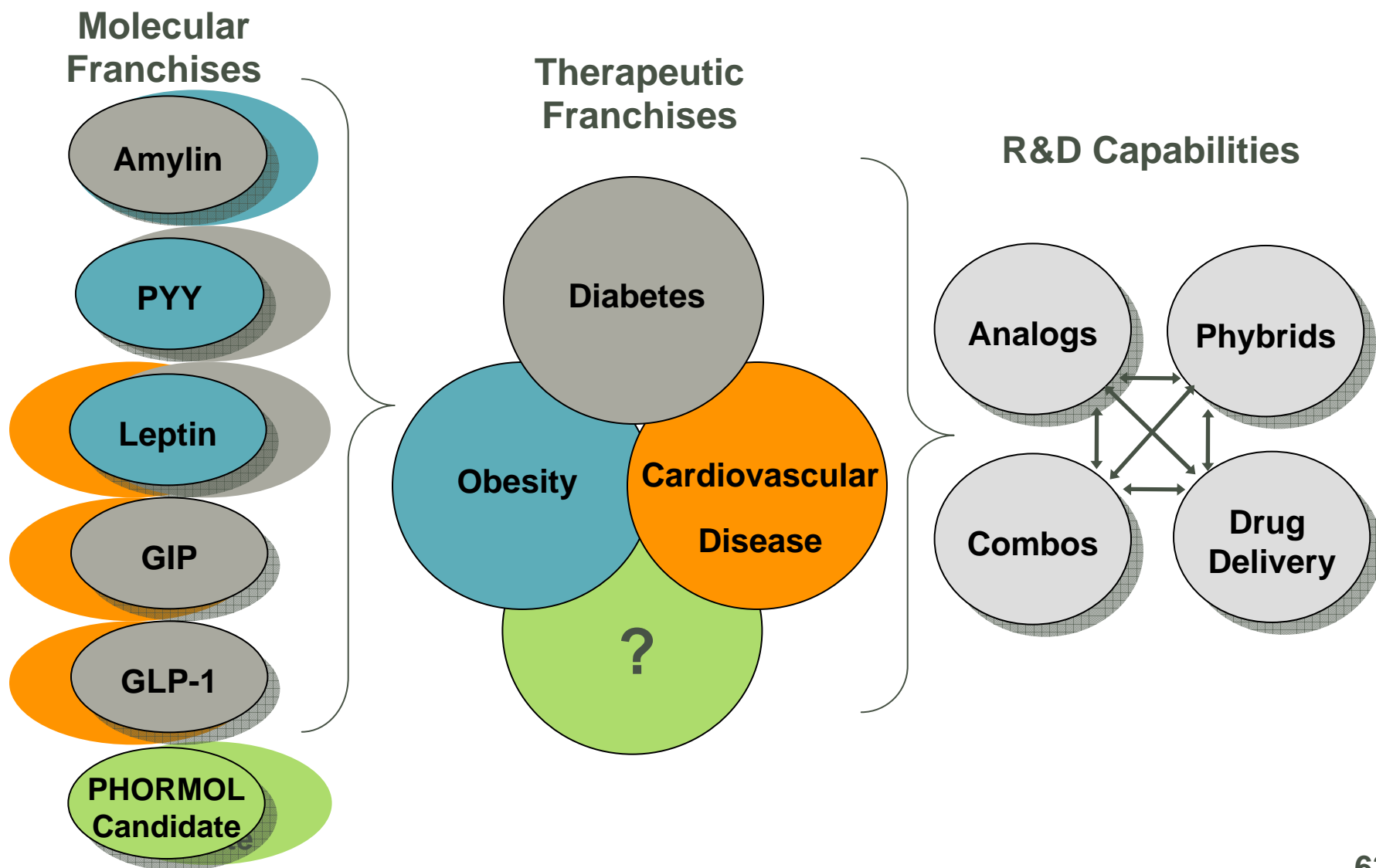
Closing Remarks

Dan Bradbury

President and Chief Operating Officer



Research Strategy: NOVEL THERAPIES FOR THE FUTURE





Challenging Science. Changing Lives.

- > Building sustainable growth for the future
- > Amylin has a large, broad discovery platform
 - > Supported by unique bioinformatics
- > Selected early-stage technology acquisition
- > Amylin's R&D approach is risk-advantaged
 - > Well-qualified drug candidates with favorable safety profiles
- > Amylin has a robust pipeline
 - > Promising candidates in several therapeutic areas



Panel Participants

- > **Soumitra Ghosh, PhD**
 - > *Executive Director, Research*
- > **David Maggs, MD**
 - > *Vice President, Medical Affairs*
- > **Lisa Porter, MD**
 - > *Vice President, Clinical Development*
- > **Chris Rhodes, PhD**
 - > *Executive Director, Pharmaceutical Sciences*
- > **Christian Weyer, MD, MAS**
 - > *Executive Director, Clinical Research*



Panel Q&A