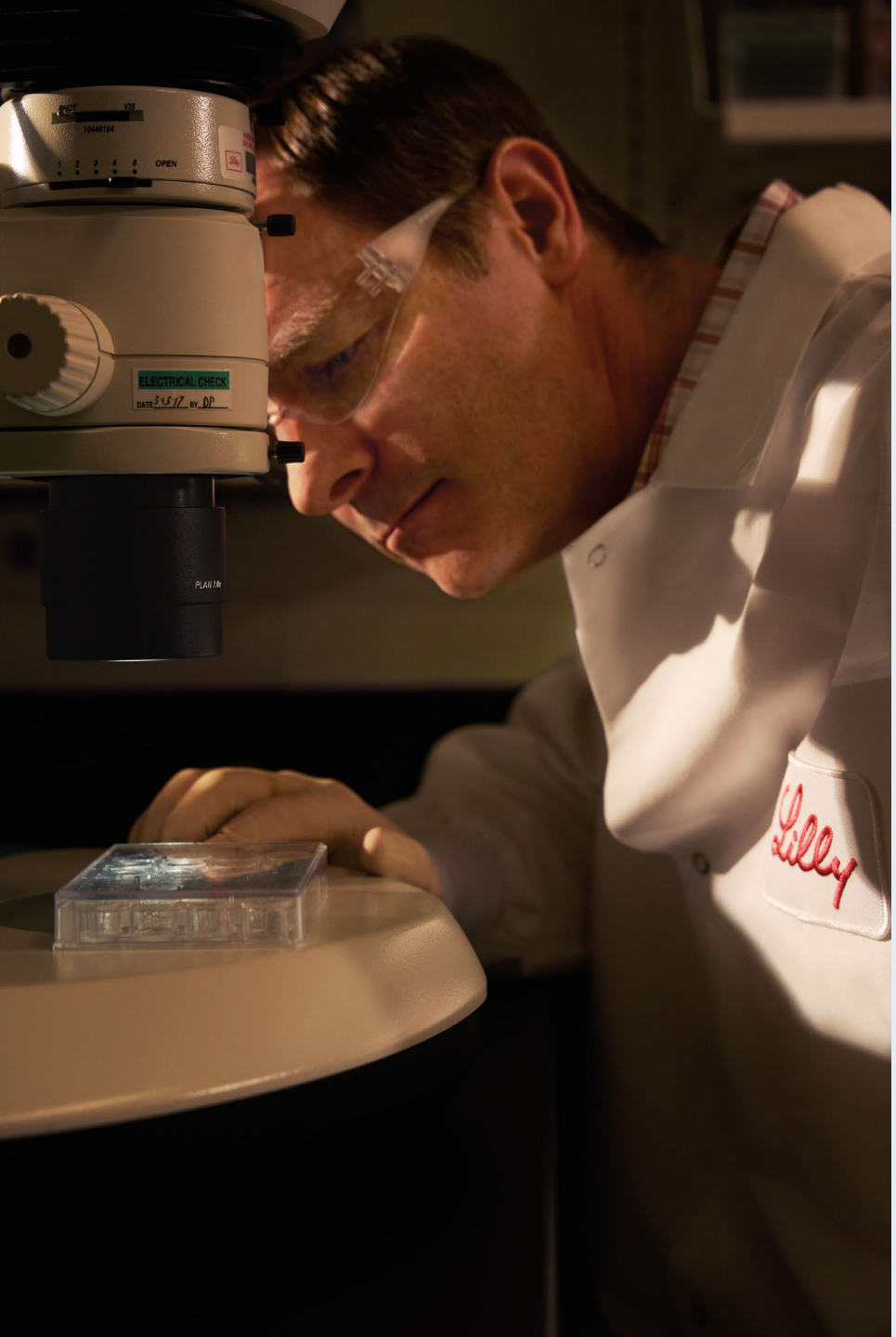
A MEDICINE COMPANY


ELI LILLY AND COMPANY
2025 LILLY ADA INVESTOR EVENT
Lilly



Agenda

Introduction
Kenneth Custer, Ph.D., President, Cardiometabolic Health

ACHIEVE-1 Data and 2025 Key Events
Jeff Emmick, M.D., Ph.D., Sr. Vice President, Cardiometabolic Health Product Development

Early Phase Update
Ruth Gimeno, Ph.D., Group Vice President, Diabetes & Metabolic Research

Question & Answer Session

Safe Harbor Provision and Other Information

This presentation contains forward-looking statements that are based on management's current expectations, but actual results may differ materially due to various factors. The company's results may be affected by factors including, but not limited to, the risks and uncertainties in pharmaceutical research and development; competitive developments; regulatory actions; litigation and investigations; business development transactions; economic conditions; and changes in laws and regulations, including healthcare reform.

For additional information about the factors that affect the company's business, please see the company's latest Form 10-K and subsequent Forms 10-Q and 8-K filed with the Securities and Exchange Commission. These materials are not intended to promote the products referenced herein or otherwise influence healthcare prescribing decisions. The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval or become commercially available for the uses being investigated.

The company undertakes no duty to update forward-looking statements except as required by applicable law.

Cardiometabolic Health Strategy

Our Purpose

Lilly unites caring with discovery to make life better for people around the world

Our Pursuit

We deliver life-changing medicines that address the most significant global health challenges

- Provide freedom from **Diabetes**
- Eliminate serious health issues caused by **Obesity**
- Reduce **Cardiovascular deaths**

Incretin-Based Therapies Not an Overnight Success

1996

Dr. John Eng licenses **exendin-4** to Amylin

2002

Lilly-Amylin alliance for **exenatide** signed

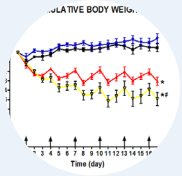
2005

Approval of **Byetta**

2010

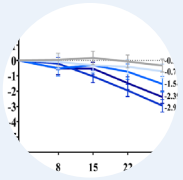
AWARD-1 Phase 3 study of **dulaglutide** in T2D begins

Proof of concept in mice of weight loss from GIP+GLP-1



2014

FDA approval for **Trulicity**



2017

First in human data of **tirzepatide** showing weight loss

Tirzepatide Phase 2 trial in T2D begins

2019

Trulicity REWIND CV outcomes study positive readout

2022

Mounjaro launches for T2D

SURMOUNT-MMO outcomes study in obesity begins

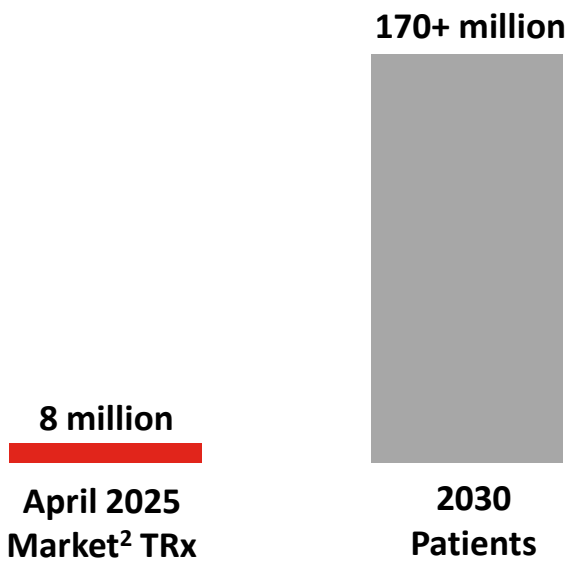
2023

Zepbound approved by FDA for chronic weight management

T2D=type 2 diabetes; CV=cardiovascular

Significant Addressable Market: Estimated 170M+ by 2030[1]

U.S. Market Penetration vs Projected Market Size



Current penetration is 5% of addressable 2030 market

OUS addressable market expected to be ~1 billion

Obesity market will segment based on patient needs

- Route of Administration
- Dosing Frequency
- Additional Metabolic Benefits
- Tolerability
- Depth of Weight Loss
- Quality of Weight Loss
- Depth of Glycemic Control
- Others

[1]Market: Patients who have obesity or overweight with an obesity-related co-morbidity: hypertension, dyslipidemia, obstructive sleep apnea, nonalcoholic fatty liver disease, heart failure, chronic kidney disease, prediabetes; and patients with Type 2 Diabetes

[2]US Incretin Analog Market: IQVIA weekly NPA total prescriptions for injectable GLP-1s, oral GLP-1s and GLP-1/GIP dual agonists

Cardiometabolic Health Select Development Program

DATA AT ADA

A Leading Portfolio for Obesity & Related Conditions

GLP-1/GIP Dual Agonist TIRZEPATIDE	GLP-1 Small Molecule ORFORGLIPRON
GLP-1, GIP, Glucagon Agonist RETATRUTIDE	Activin Receptor BIMAGRUMAB
Amylin ELORALINTIDE	Oxyntomodulin MAZDUTIDE
GLP-1 Small Molecule NAPERIGLIPRON	GIP Agonist GIPR AGONIST LA
GLP-1/GIP Dual Agonist GLP-1/GIP COAGONIST III	GIP Agonist MACUPATIDE
Peptide YY Analog Agonist NISOTIROSTIDE	GLP-1, GIP, Glucagon Agonist ORAL GGG PEPTIDE
PNPLA3 siRNA	SCAP siRNA

Cardiometabolic Related Outcomes

- siRNA Lp(a) Inhibitor
LEPODISIRAN
- Oral Lp(a) Inhibitor
MUVALAPLIN
- siRNA ANGPTL3
SOLBINSIRAN
- INTEGRIN α5β1
- LA ANP

Non-Incretin Diabetes

- Once-Weekly Basal Insulin
INSULIN EFSITORA ALFA
- Glucose Sensing Insulin
GS INSULIN RECEPTOR AGONIST

Incretins Beyond Cardiometabolic Health

Substance Use Disorder	Inflammation
Brain Health	Pain

[1]China development with Innovent for Obesity (regulatory review) and Type 2 Diabetes (Phase 3)

Orforglipron Has Potential to Make Significant Impact on Public Health

Broad Development Plan

- **Obesity** *2 Studies*
- **Type 2 Diabetes** *5 Studies*
- **Obstructive Sleep Apnea**
- **Hypertension**
- **Maintenance**
- **Other**

Scalable Supply

- **Separate Small Molecule Manufacturing Footprint**
- **Investment At-Risk to Support Global Launch**
- **No Cold-Chain Storage Requirement**

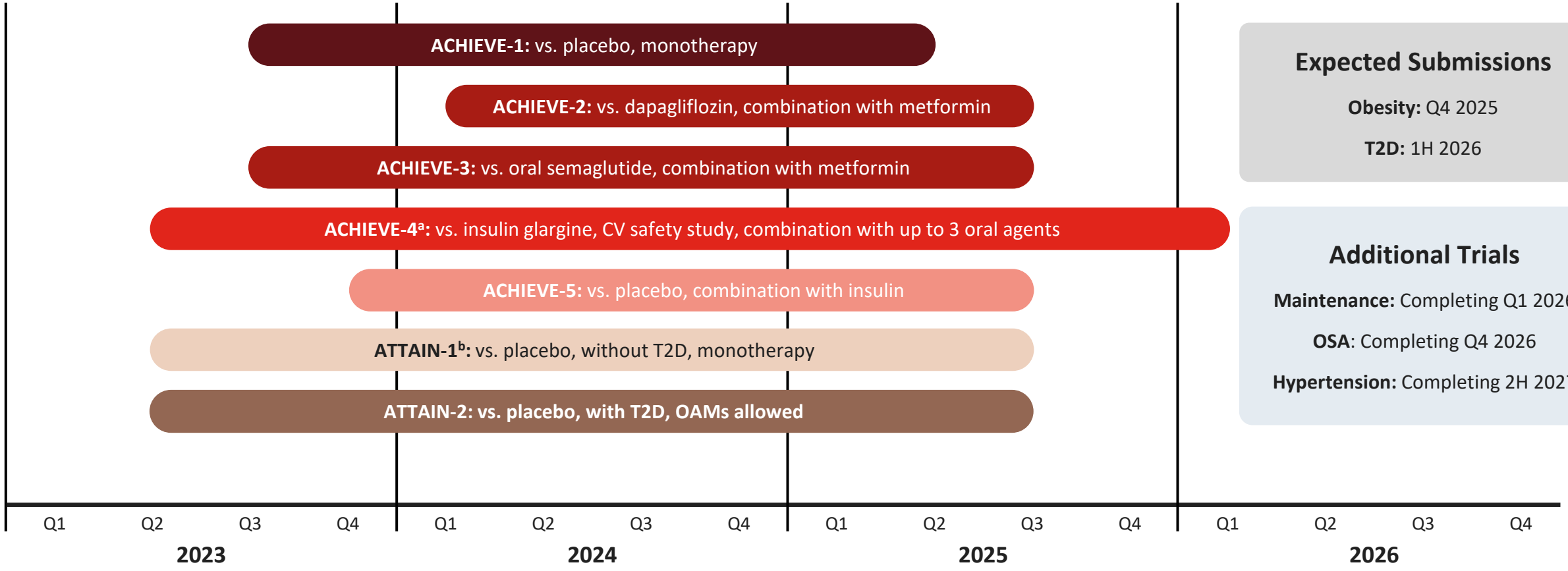
Commercial Potential

- **Once-Daily Pill**
- **No Food or Water Restrictions**
- **International Reach and Scale**

ORFORGLIPRON OVERVIEW & ACHIEVE-1

Orforglipron Global Development Program

ACHIEVE Type 2 Diabetes Program and ATTAIN Obesity Program



Expected Submissions

Obesity: Q4 2025

T2D: 1H 2026

Additional Trials

Maintenance: Completing Q1 2026

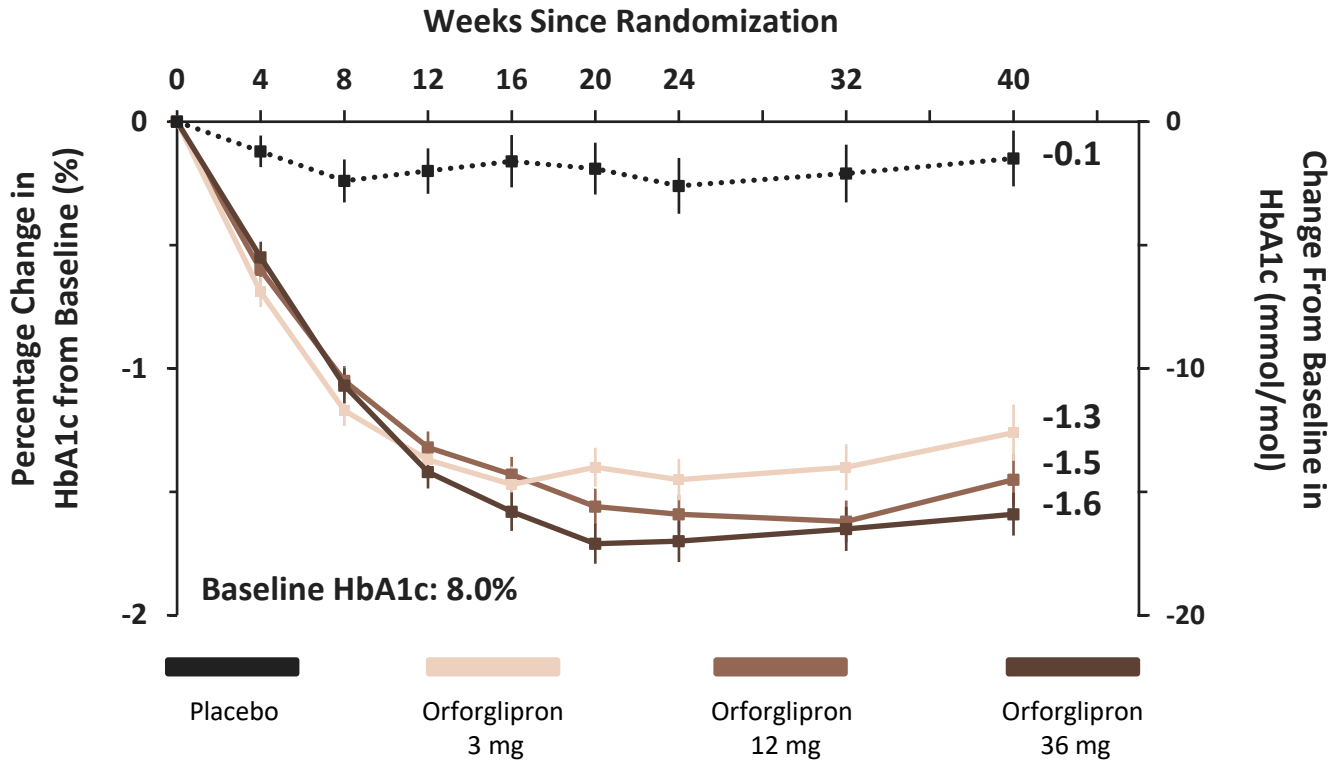
OSA: Completing Q4 2026

Hypertension: Completing 2H 2027

[a]Event-driven trial, minimum duration 104 weeks; [b]2-year extension for participants with prediabetes
CV=cardiovascular; OAM=oral anti-hyperglycemic medication; OSA=moderate-to-severe obstructive sleep apnea; T2D=type 2 diabetes

ACHIEVE-1: HbA1c Change Results

Efficacy Estimand[1] Change from Baseline HbA1c



[1]Efficacy estimand represents efficacy had all participants remained on study intervention (with possible dose interruptions) for 40 weeks without initiating additional antihyperglycemic medications (>14 days of use)

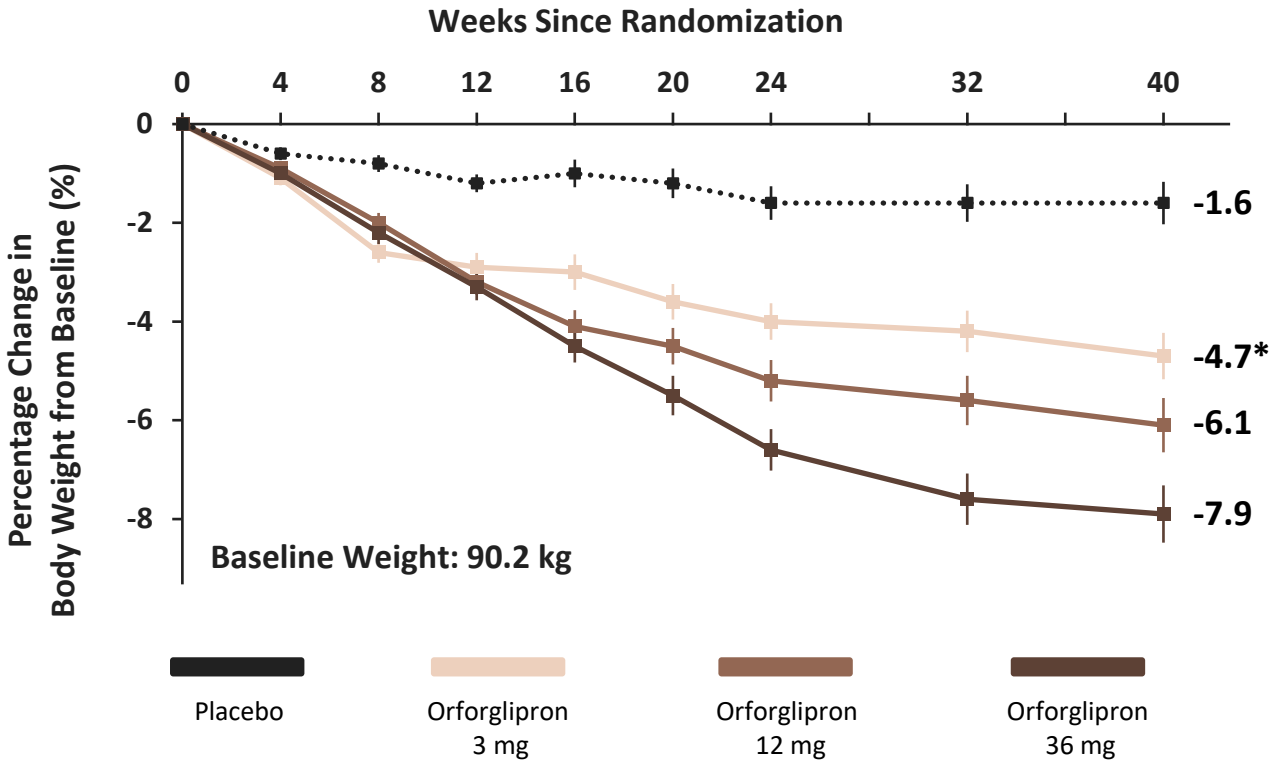
All 3 doses of orforglipron achieved superiority vs placebo

Significant reductions in HbA1c observed as early as 4 weeks

Approximately 3/4 of patients achieved ADA HbA1c target of <7%, and 2/3 reached HbA1c ≤6.5%

ACHIEVE-1: Body Weight Change Results

Efficacy Estimand[1] Change from Baseline Weight



[1]Efficacy estimand represents efficacy had all participants remained on study intervention (with possible dose interruptions) for 40 weeks without initiating additional antihyperglycemic medications (>14 days of use)
*3 mg weight endpoint was not controlled for Type 1 error

Dose-dependent reduction in body weight

Approximately 2/3 of patients achieved ≥5% weight reduction

Approximately 1/3 of patients achieved ≥10% weight reduction

ACHIEVE-1: Safety and Tolerability

Tolerability Profile

	Placebo	Orforglipron 3 mg	Orforglipron 12 mg	Orforglipron 36 mg
Discontinuations				
due to AEs (%)	1%	6%	4%	8%
due to GI AEs (%)	0%	3%	2%	6%
Adverse Events				
Nausea (%)	2%	13%	18%	16%
Vomiting (%)	1%	5%	7%	14%
Diarrhea (%)	9%	19%	21%	26%

Liver Safety

- **Patients had baseline ALT/AST values up to 5X ULN**
- **No patient with baseline ALT or AST ≥3X ULN shifted to a higher category**
- **No patients met the criteria for Hy's Law**
- **Post-baseline ALT or AST ≥3X ULN were balanced between placebo and treatment arms**

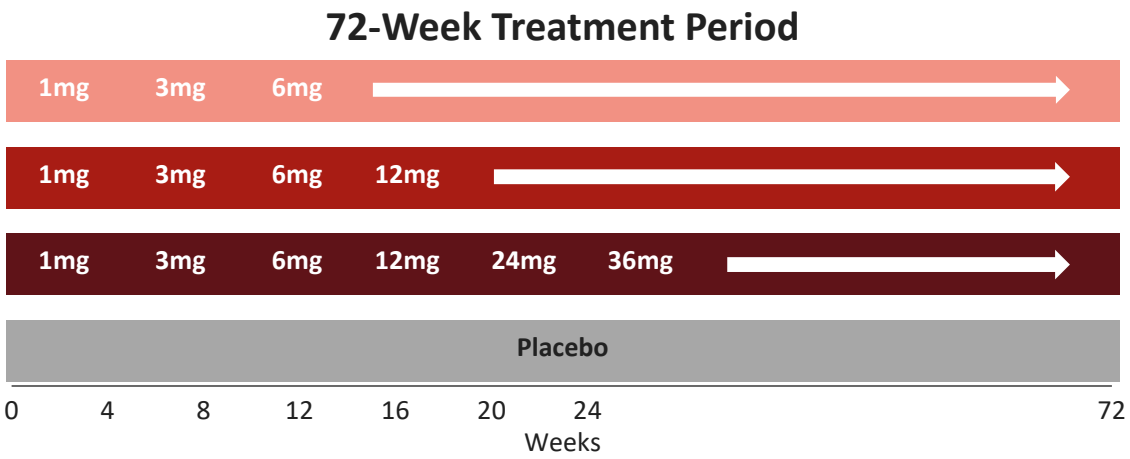
Orforglipron safety and tolerability profile in ACHIEVE-1 was consistent with injectable GLP-1 medicines

AE=adverse event; GI=Gastrointestinal; ALT=alanine aminotransferase; AST=aspartate aminotransferase;
ULN=upper limit of normal calculated based on reference range given for each patient at each measurement

ORFORGLIPRON
ATTAIN-1

ATTAIN-1: Orforglipron in Obesity

Trial Design



- Dose escalation every 4 weeks until reaching target dose of 6mg, 12 mg or 36 mg
- Topline results Q3 2025

Key Considerations

Baseline Characteristics

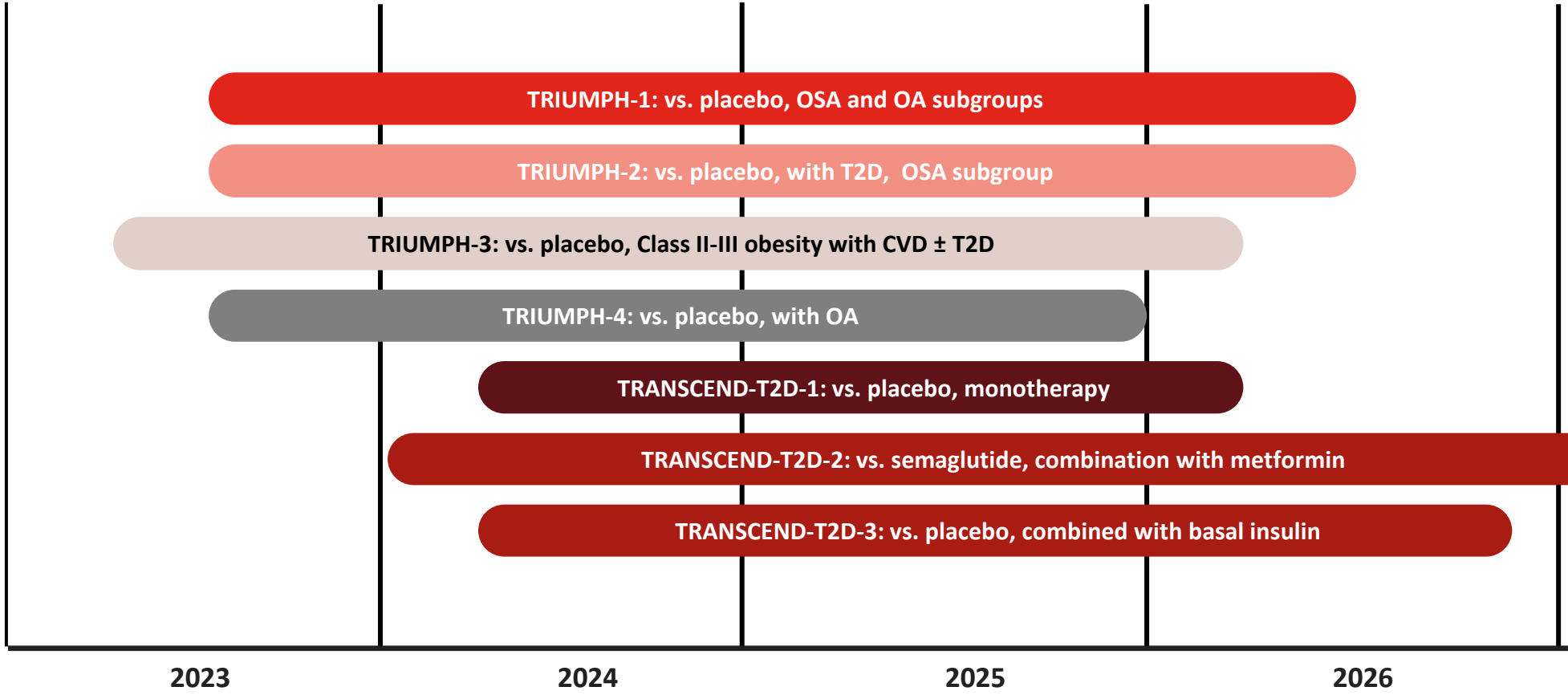
Weight (kg)	103.2
BMI (kg/m^2)	37.0
Age (years)	45.1
Female (%)	64.2%

- Orforglipron could provide an easy-to-use option leveraged across a range of care settings
- Potential to demonstrate efficacy and tolerability within the range of injectable GLP-1 medicines

RETATRUTIDE

Retatrutide Global Development Program

TRIUMPH[1] Obesity & Related Complications and TRANSCEND Type 2 Diabetes Program



Expected Submissions

Obesity, OA & OSA: 2H 2026

T2D: 1H 2027

Additional Trials

H2H vs TZP: Completing 2H 2026

Maintenance : Completing 1H 2028

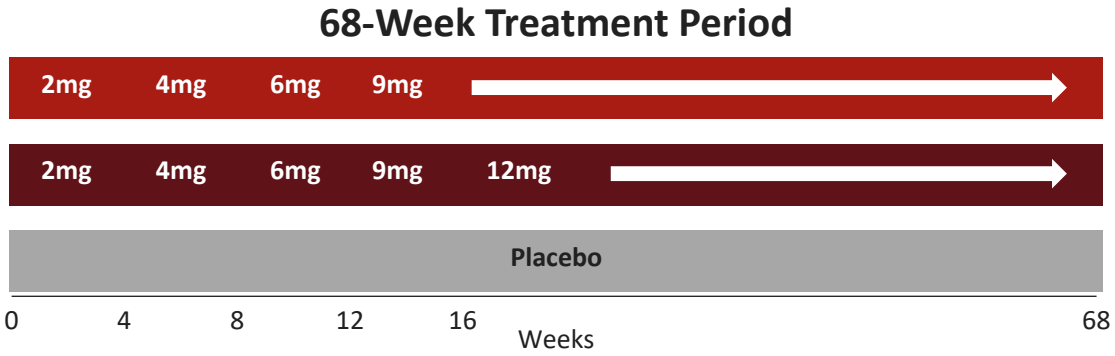
Outcomes: Completing 1H 2029

CLBP: Initiating 2H 2025

[1]TRIUMPH trials are in a population with obesity or overweight with at least obesity-related co-morbidity unless otherwise specified
OA=osteoarthritis; OSA=moderate-to-severe obstructive sleep apnea; CVD=cardiovascular disease; T2D=type 2 diabetes; H2H=head-to-head; TZP=tirzepatide; CLBP=chronic low back pain

TRIUMPH-4: Retatrutide in Knee OA Pain and Overweight or Obesity

TRIUMPH-4 Trial Design



- Evaluating changes in pain[1] and weight reduction in people with knee OA pain and overweight or obesity
- Dose escalation every 4 weeks until reaching target dose of 9 mg or 12 mg
- TRIUMPH-4 topline results expected Q4 2025

Key Considerations

Baseline[2] Characteristics

Weight (kg)	112.7
BMI (kg/m^2)	40.4
Age (years)	55.2
Female (%)	63.4

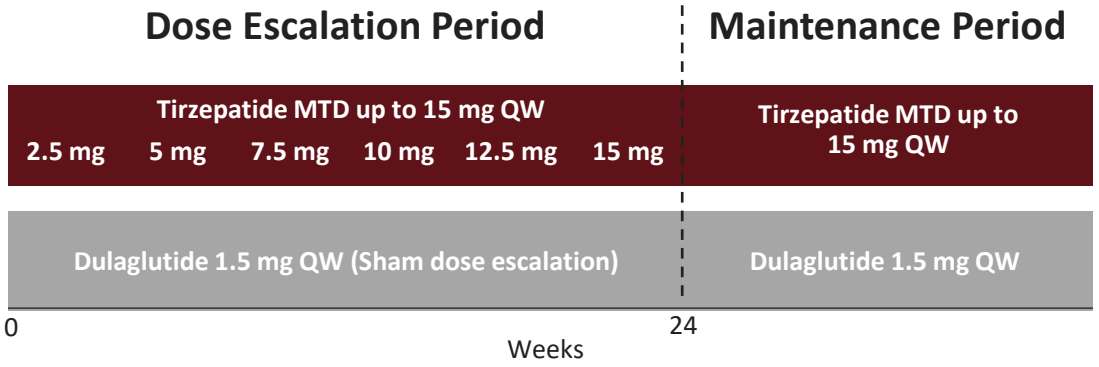
- TRIUMPH-4 is the shortest of four retatrutide obesity registration studies
- Expect smaller percentage weight loss than other TRIUMPH trials based on duration and study population
- TRIUMPH-1 has longer duration (80 weeks) and includes 4 mg, 9 mg, and 12 mg maintenance doses

[1]Based on WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain subscale score; [2]Preliminary baseline data
OA=Osteoarthritis

TIRZEPATIDE
SURPASS-CVOT

SURPASS-CVOT: Tirzepatide vs. Dulaglutide

SURPASS-CVOT Study Design

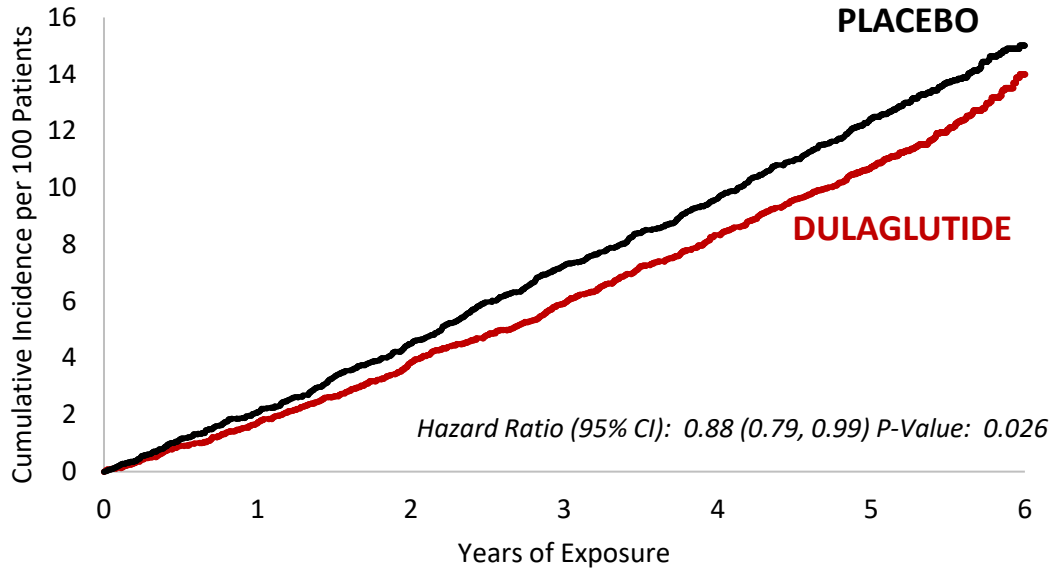


N=13,299; approximately 1,615 MACE-3 events

- **Primary endpoint MACE-3: CV death, myocardial infarction or stroke**
- **SURPASS-CVOT includes only patients with established cardiovascular disease**

Dulaglutide Reduced Risk of MACE-3 by 12% vs. Placebo

REWIND Top-Line Efficacy Results



Designed to evaluate tirzepatide against dulaglutide, which demonstrated CV risk reductions in patients with multiple risk factors or established CV disease

CVOT=cardiovascular outcomes trial; CV=cardiovascular; MTD=maximum tolerated dose; HR=hazard ratio

SURPASS-CVOT: Tirzepatide vs. Dulaglutide

Bar for Superiority

- Dulaglutide demonstrated CV benefit in both primary and secondary prevention population in REWIND
- Non-inferiority to dulaglutide constitutes superiority to putative placebo

Establishing CV Benefit

Upper Bound of ~95% Confidence Interval

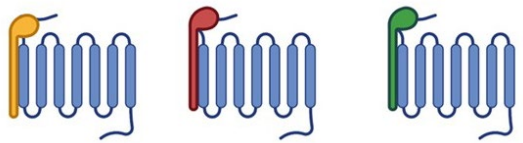
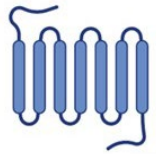
Non-inferiority vs. dulaglutide	<1.05
Superiority vs. dulaglutide	<1.0

Both non-inferiority and superiority support U.S. regulatory submission for CV benefit indication and demonstrate superiority to putative placebo

CVOT=cardiovascular outcomes trial; CV=cardiovascular

EARLY PHASE UPDATE

Eloralintide: A Selective Amylin Receptor Agonist

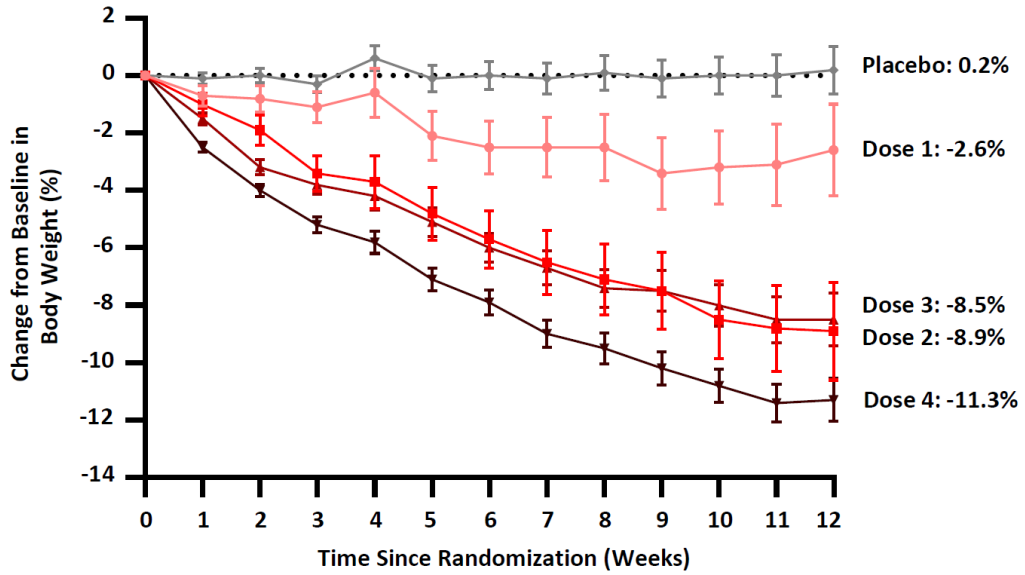
	Amylin	Calcitonin
	 Amylin 1R Amylin 2R Amylin 3R	 Calcitonin R
	Co-secreted with insulin in response to food	Secreted by the thyroid to regulate blood calcium
Central Actions	↓ Food Intake	↓ Food Intake ↑ Nausea & Vomiting
Peripheral Actions	↓ Gastric Emptying ↓ Glucagon Secretion	↓ Osteoclast Activity ↓ Calcium Reabsorption

Eloralintide

- Increased amylin selectivity versus calcitonin receptors
- Acylated molecule designed for once weekly dosing
- Encouraging preclinical weight loss and tolerability profile

Eloralintide: Efficacy and Tolerability at 12 Weeks

Eloralintide Phase 1 Efficacy



- Weight loss up to 11.3%
- Long half-life enables weekly dosing

Eloralintide Phase 1 Tolerability

% of participants with GI AEs	Placebo (N=27)	Eloralintide[1] Dose 2 (N=6)	Dose 3 (N=23)	Dose 4 (N=36)	Overall (N=73)
Decreased appetite	3.7%	16.7%	26.1%	19.4%	19.2%
Diarrhea	0%	16.7%	8.7%	11.1%	9.6%
Nausea	0%	0%	13.0%	8.3%	8.2%
Vomiting	0%	0%	0%	8.3%	4.1%

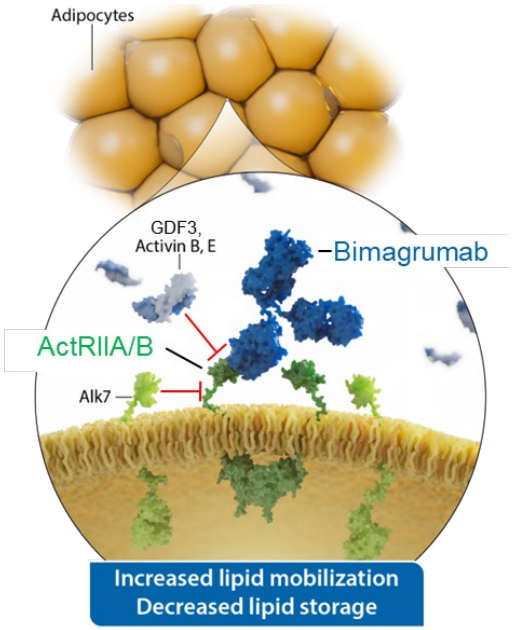
- Well-tolerated with <10% incidence of GI side effects
- No dose titration in Phase 1

Phase 2 monotherapy study completing 2H 2025; combination studies with tirzepatide in progress

[1]No GI AEs reported in Eloralintide Dose 1 (N=8)
GI=gastrointestinal; AE=adverse event

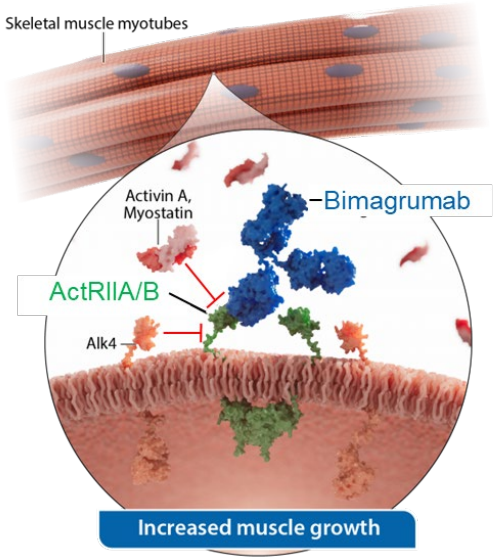
Bimagrumab: Targeting the Activin Pathway for Obesity

Adipose



Blocks activin E and GDF3 signaling with the goal of decreasing fat mass

Muscle



Blocks activin A and myostatin signaling with the goal of increasing muscle mass

Bimagrumab

- **Monoclonal antibody that blocks activin type II receptors**
- **BELIEVE Phase 2B study evaluated IV bimagrumab dosed quarterly ± semaglutide**
- **Additional Phase 2 trials evaluating SC bimagrumab dosed weekly ± tirzepatide**

IV=intravenous; SC=subcutaneous

Next Generation Efforts for Obesity

	Incretins	Amylins	Novel Targets
INNOVATION THEMES	Oral and long-acting multifunctional incretins	Different selectivity profiles[1]	New Benefits
PHASE 2	NAPERIGLIPRON (GLP-1R NPA II) MAZDUTIDE[2]	ELORALINTIDE	BIMAGRUMAB
PHASE 1	GIP/GLP-1 COAGONIST III GIPR AGONIST LA		NISOTIROSTIDE
	MACUPATIDE ORAL GGG PEPTIDE		

[1]KBP-336, a dual amylin-calcitonin receptor agonist, is being evaluated in Phase 2 by our partner Key Biosciences
[2]China development with Innovent for Obesity (regulatory review) and Type 2 Diabetes (Phase 3)

STRATEGY

Broad development strategy building on tirzepatide as foundational medicine

Developing next generation of medicines to meet needs of heterogeneous population

Industry-leading pipeline constructed through internal and external innovation and decades of experience

PIPELINE KEY EVENTS

Multiple Phase 3 data readouts in 2025 including tirzepatide, orforglipron and retatrutide

Plan to launch two new incretin therapies, orforglipron and retatrutide, by end of 2027

Key Phase 2 updates expected in 2025/2026, including eloralintide

OPPORTUNITY

More than 1 billion people worldwide could benefit from these innovative medicines

Potential to drive profound positive impact at population health level

Exciting time at Lilly as we advance industry-leading pipeline of new medicines to treat cardiometabolic disorders

Question and Answer Panel

Kenneth Custer, Ph.D.
Executive Vice President & President,
Lilly Cardiometabolic Health

Jeff Emmick
Sr. Vice President, Cardiometabolic
Health Product Development

Ruth Gimeno, Ph.D.
Group Vice President, Diabetes &
Metabolic Research

Mike Czapar
Sr. Vice President, Investor Relations


Lilly

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