Lilly Diabetes & Obesity

ADA Update

June 7, 2022

SAFE HARBOR PROVISION

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; the extent and duration of the effects of the COVID-19 pandemic; litigation and investigations; business development transactions; economic conditions; and changes in laws and regulations, including health care reform.

For additional information about the factors that affect the company's business, please see the company's latest Form 10-K and subsequent filings with the Securities and Exchange Commission.

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

Agenda

Introduction
Mike Mason, President, Lilly Diabetes

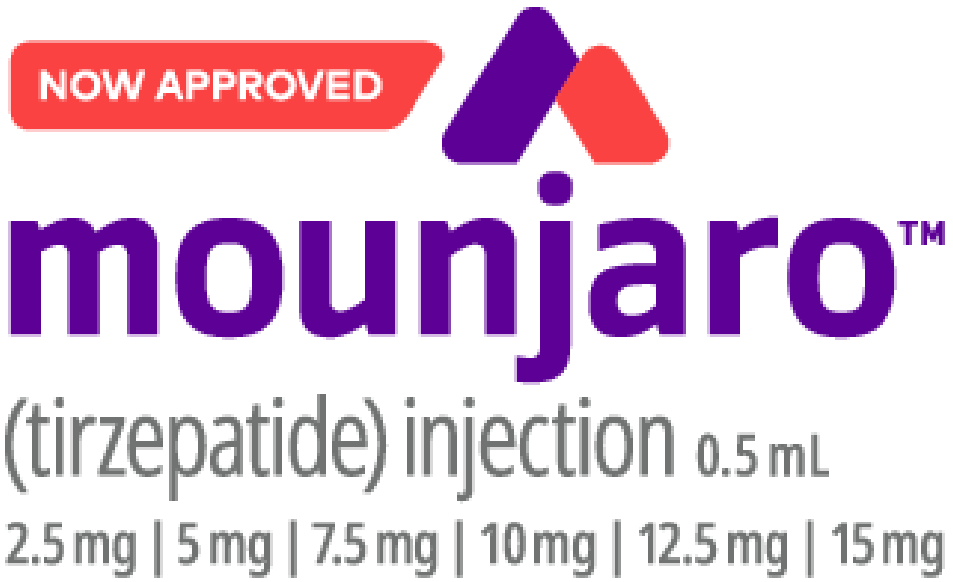
Tirzepatide SURMOUNT-1 Phase 3 Results & New Insights
Jeff Emmick, M.D., Ph.D., Vice President, Lilly Diabetes Product Development

Early Phase ADA Highlights & Portfolio Overview
Ruth Gimeno, Ph.D., Vice President, Lilly Diabetes and Metabolic Research

Q&A

MOUNJARO™ NOW APPROVED IN THE U.S. FOR T2D

FIRST AND ONLY GIP AND GLP-1 RECEPTOR AGONIST AVAILABLE FOR PATIENTS



- Delivered superior A1C reductions versus all comparators in Phase 3 SURPASS clinical trials
- Although not indicated for weight loss, led to significantly greater weight reductions versus comparators in a key secondary endpoint
- Shipments to wholesalers are underway and pharmacies will begin to see supply as prescriptions are written
- Enabling new patient starts through patient support programs as we work to build broad access:
  - 1 month sample (4 weeks) of starting 2.5 mg pens prior to HCP writing a 5 mg prescription
  - Copay program with out-of-pocket costs as little as $25 per month for eligible commercially insured patients

T2D=type 2 diabetes; HCP=healthcare professional

Not for promotional use

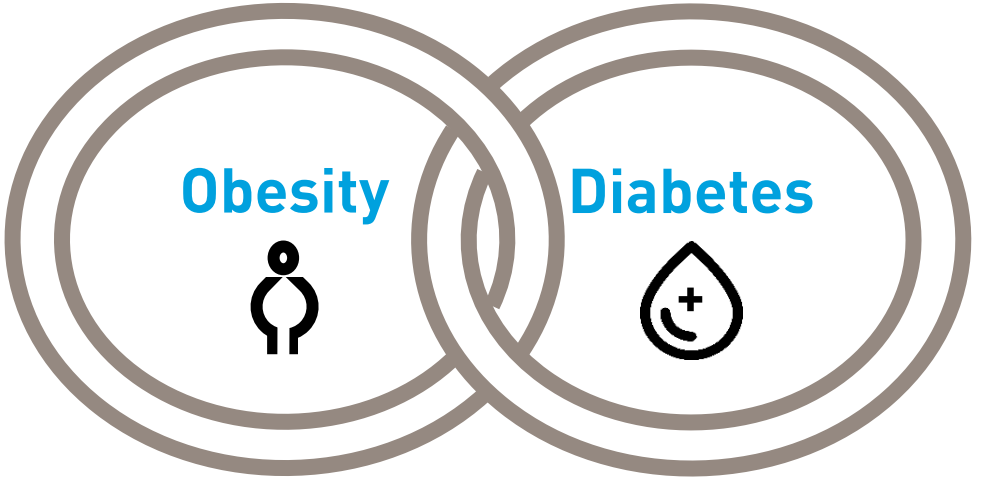
INNOVATION DRIVES EXPANDED STRATEGIC FOCUS

DIABETES AND OBESITY

OUR FOUNDATION

Improving and simplifying glycemic control

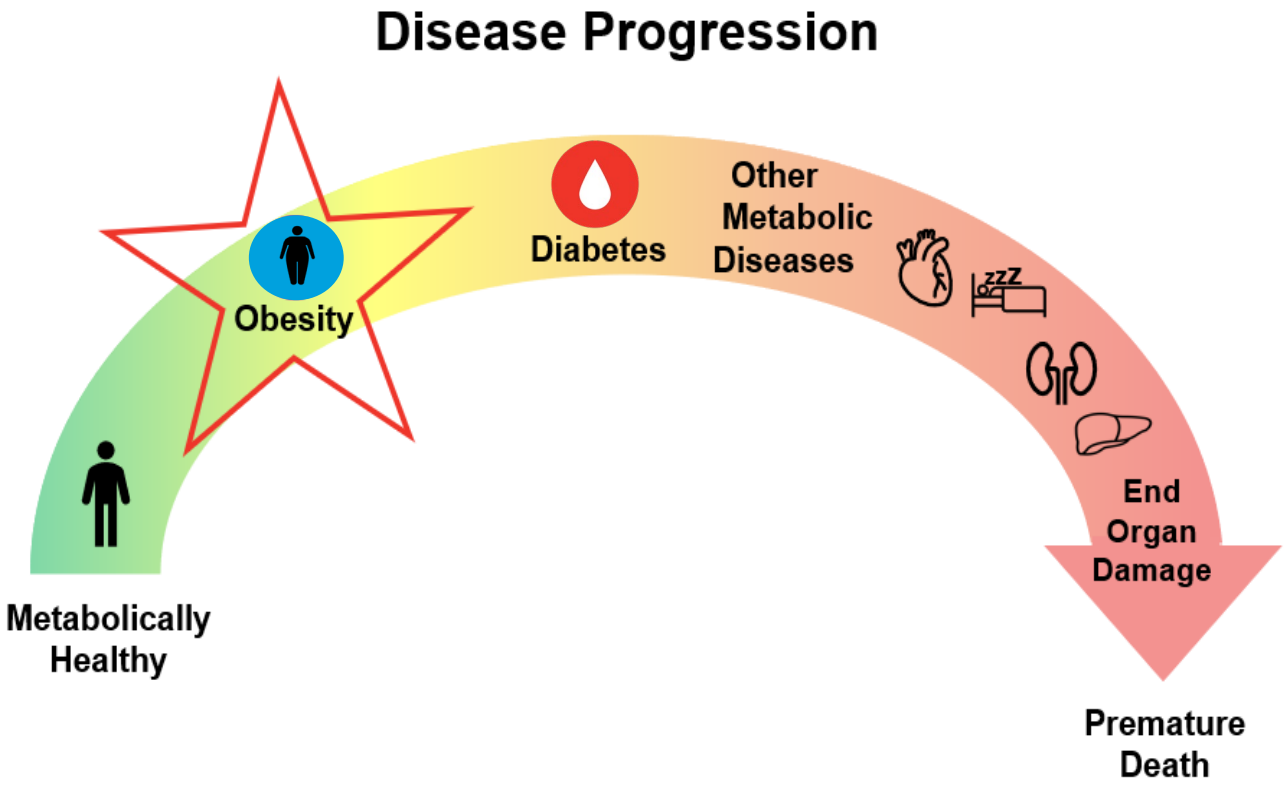
OUR EXPANDED FOCUS



Disrupting disease progression in Diabetes & Obesity to improve outcomes

DELIVERING BREAKTHROUGH OBESITY OUTCOMES

LOOKING AHEAD TO DISRUPT DISEASE PROGRESSION



We aim to revolutionize obesity care and change the lives of people living with obesity—a **chronic disease**—by raising the bar for treatment and setting a new standard of care through:

- Driving quality patient-centric obesity care
- Improving morbidity and mortality outcomes
- Advancing obesity access

UNMET NEEDS

CURRENT PATIENT OUTCOMES ARE NOT ACCEPTABLE

Over **40% of the U.S. population** is living with obesity and **minority group members are disproportionally impacted**

In the US, **fewer than 3%** of people with obesity are pharmacologically treated for obesity. The economic impact associated with obesity is over **$1 trillion dollars.**

Obesity is the **leading risk factor for type 2 diabetes** and other metabolic diseases

One out of two people with diabetes does not meet treatment goals for glucose lowering (HbA1c)

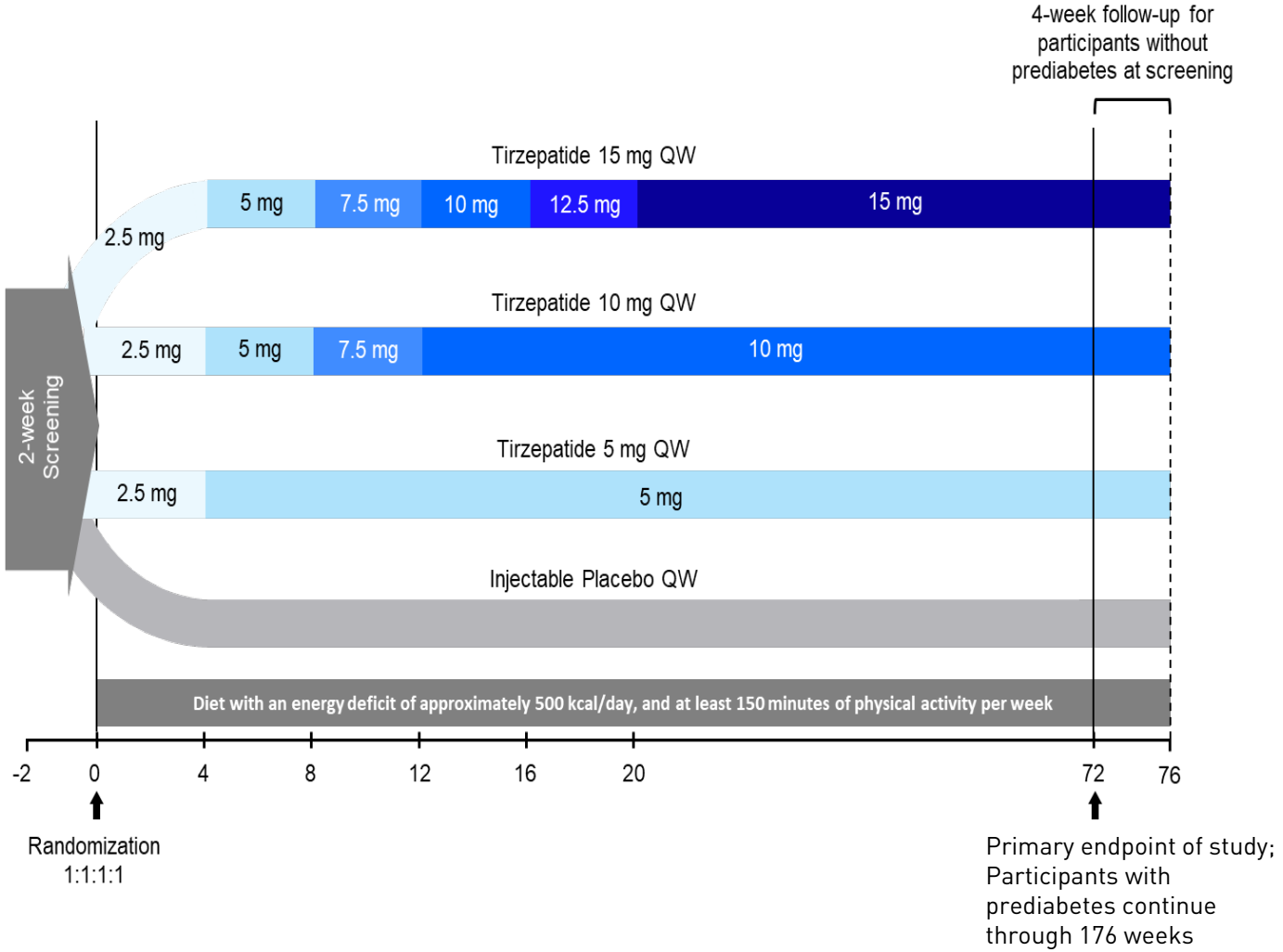
One person dies from diabetes and its complications **every eight seconds and obesity is a cause for nearly 1 out of 5 adult deaths**

Tirzepatide

SURMOUNT-1 Phase 3 Results

SURMOUNT-1: TRIAL DESIGN

EVALUATING WEIGHT MANAGEMENT IN PARTICIPANTS WITH OBESITY/OVERWEIGHT



- 2,539 participants randomized
- Primary Objective: tirzepatide 10 mg and/or 15 mg is superior to placebo at 72 weeks for
  - percent change in body weight, and
  - percentage of participants with ≥5% body weight reduction
- Key Secondary Objectives: evaluation of weight reduction targets, 5 mg dose, change in lipids, blood pressure, waist circumference, and physical functioning
- Continues through 176 weeks to evaluate onset of T2D in participants who had pre-diabetes upon entering the study and impact on body weight reduction over time

QW=once weekly; T2D=type 2 diabetes; Key inclusion criteria includes 18 years or older and BMI greater than or equal to 30 kg/m or greater than or equal to 27 kg/m with at least one of the following previously diagnosed conditions: hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease

SURMOUNT-1: BASELINE CHARACTERISTICS

DEMOGRAPHICS WELL BALANCED ACROSS TREATMENT GROUPS

Demographic Parameters (mean ± SD, unless otherwise specified)	Placebo (N=643)	TZP 5 mg (N=630)	TZP 10 mg (N=636)	TZP 15 mg (N=630)	Total (N=2539)
Age (y)	44.4 ± 12.5	45.6 ± 12.7	44.7 ± 12.4	44.9 ± 12.3	44.9 ± 12.5
Female, n (%)	436 (67.8)	426 (67.1)	427 (67.1)	425 (67.5)	1714 (67.5)
Race, n (%)					
American Indian or Alaska Native	58 (9.0)	56 (8.9)	58 (9.1)	59 (9.4)	231 (9.1)
Asian	71 (11.0)	68 (10.8)	71 (11.2)	66 (10.5)	276 (10.9)
Black or African American	55 (8.6)	48 (7.6)	47 (7.4)	51 (8.1)	201 (7.9)
White	450 (70.0)	447 (71.0)	452 (71.1)	443 (70.3)	1792 (70.6)
Native Hawaiian or Other Pacific Islander	2 (0.3)	2 (0.3)	2 (0.3)	3 (0.5)	9 (0.4)
Multiple	7 (1.1)	9 (1.4)	6 (0.9)	8 (1.3)	30 (1.2)
Ethnicity, n (%)					
Hispanic or Latino	310 (48.2)	308 (48.9)	297 (46.7)	299 (47.5)	1214 (47.8)
Not Hispanic or Latino	281 (43.7)	276 (43.8)	286 (45.0)	280 (44.4)	1123 (44.2)
Not Reported	52 (8.1)	46 (7.3)	53 (8.3)	51 (8.1)	202 (8.0)

TZP=tirzepatide; SD=standard deviation

SURMOUNT-1: BASELINE CHARACTERISTICS

CLINICAL CHARACTERISTICS WELL BALANCED ACROSS TREATMENT GROUPS

Clinical Characteristics (mean ± SD, unless otherwise specified)	Placebo (N=643)	TZP 5 mg (N=630)	TZP 10 mg (N=636)	TZP 15 mg (N=630)	Total (N=2539)
Weight (kg)	104.8 ± 21.37	102.9 ± 20.71	105.8 ± 23.32	105.6 ± 22.92	104.8 ± 22.12
BMI (kg/m^2)	38.2 ± 6.89	37.4 ± 6.63	38.2 ± 7.01	38.1 ± 6.69	38.0 ± 6.81
Waist circumference (cm)	114.0 ± 14.92	113.2 ± 14.25	114.8 ± 15.80	114.4 ± 15.59	114.1 ± 15.16
Prediabetes, n (%)	270 (42.0)	247 (39.2)	262 (41.2)	253 (40.2)	1032 (40.6)
Systolic blood pressure (mmHg)	122.9 ± 12.77	123.6 ± 12.45	123.8 ± 12.77	123.0 ± 12.94	123.3 ± 12.73
eGFR (CKD-EPI, ml/min/1.73 m^2)	98.1 ± 18.28	97.6 ± 17.87	98.3 ± 18.26	98.2 ± 17.67	98.1 ± 18.02

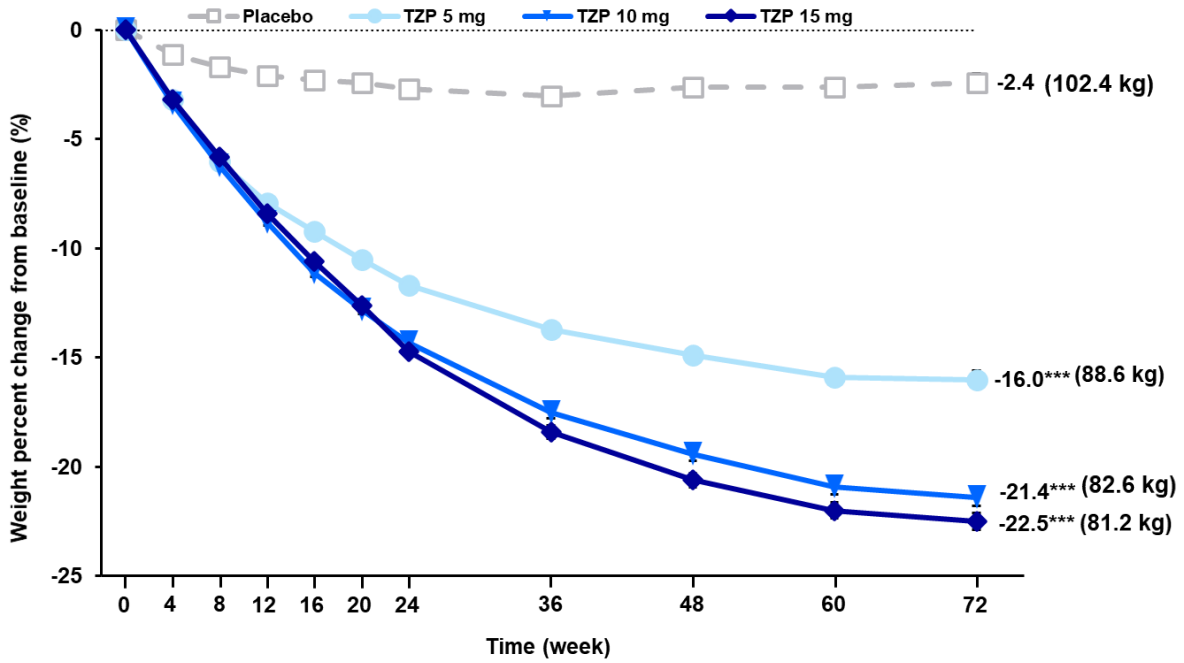
TZP=tirzepatide; SD=standard deviation; eGFR=estimated glomerular filtration rate

SURMOUNT-1: EFFICACY DATA

PARTICIPANTS ON HIGHEST DOSE ACHIEVED 22.5% WEIGHT REDUCTION ON AVERAGE

MEAN BODY WEIGHT CHANGE AT 72 WEEKS

Efficacy Estimand



Overall mean weight at baseline = 104.8 kg (BMI = 38.0 kg/m^2)

KEY EFFICACY RESULTS

- All tirzepatide treatment arms demonstrated statistically superior and clinically meaningful weight reduction compared to placebo
- In the 15 mg treatment arm, mean weight reduction was 24 kg (52 lb) at 72 weeks
- In pooled data from the 10 and 15 mg treatment arms, participants achieved over 13 kg weight reduction (29 lb) at 20 weeks
- Full 3-year study results will evaluate longer term impact of tirzepatide on weight reduction in people with prediabetes
- Tirzepatide improved all prespecified cardiometabolic key secondary endpoints

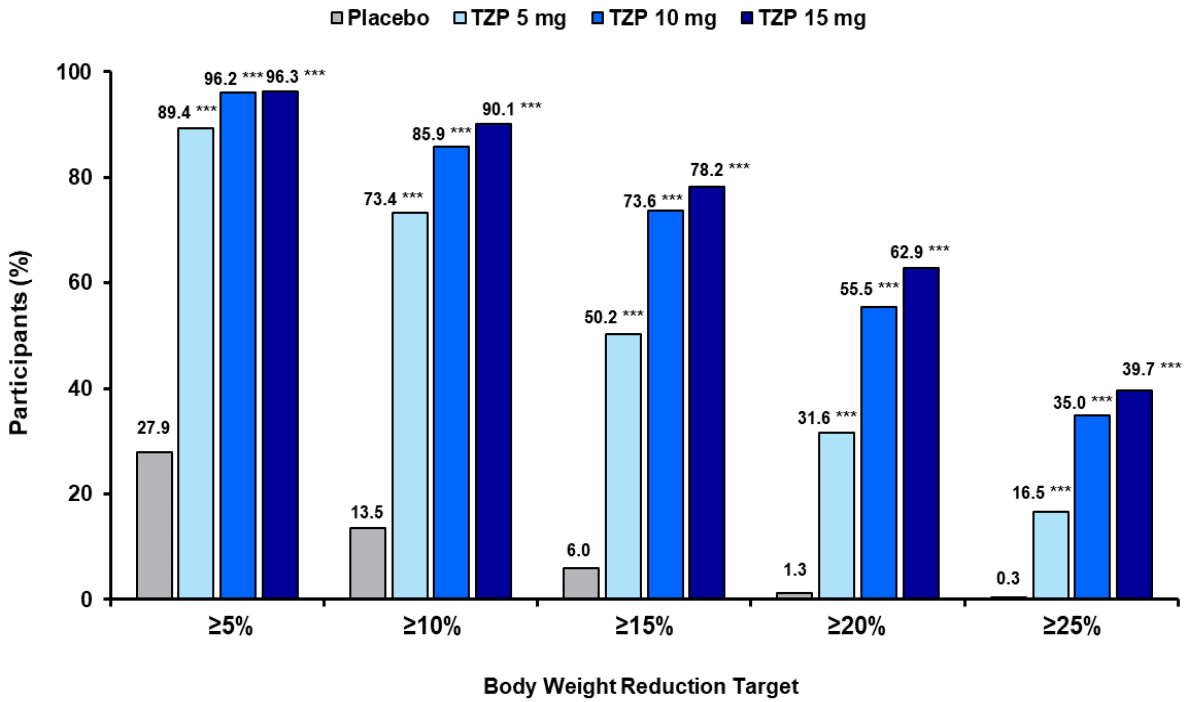
TZP=tirzepatide; T2D=type 2 diabetes; MMRM analysis, mITT population (efficacy analysis set). Data presented over time are LS means ± standard errors. Numbers in parentheses are LS means for actual values. TZP vs. placebo at 72 weeks: ***p<0.001; For the treatment-regimen estimand: ANCOVA analysis, mITT population (full analysis set). MMRM analysis, mITT population (efficacy analysis set). TZP vs. placebo at 72 weeks: p<0.001

SURMOUNT-1: EFFICACY DATA

MET CO-PRIMARY ENDPOINT OF ACHIEVING AT LEAST 5% BODY WEIGHT REDUCTION FOR 10 & 15 MG DOSES

PERCENTAGE OF PARTICIPANTS ACHIEVING WEIGHT REDUCTION (%) TARGET

Efficacy Estimand



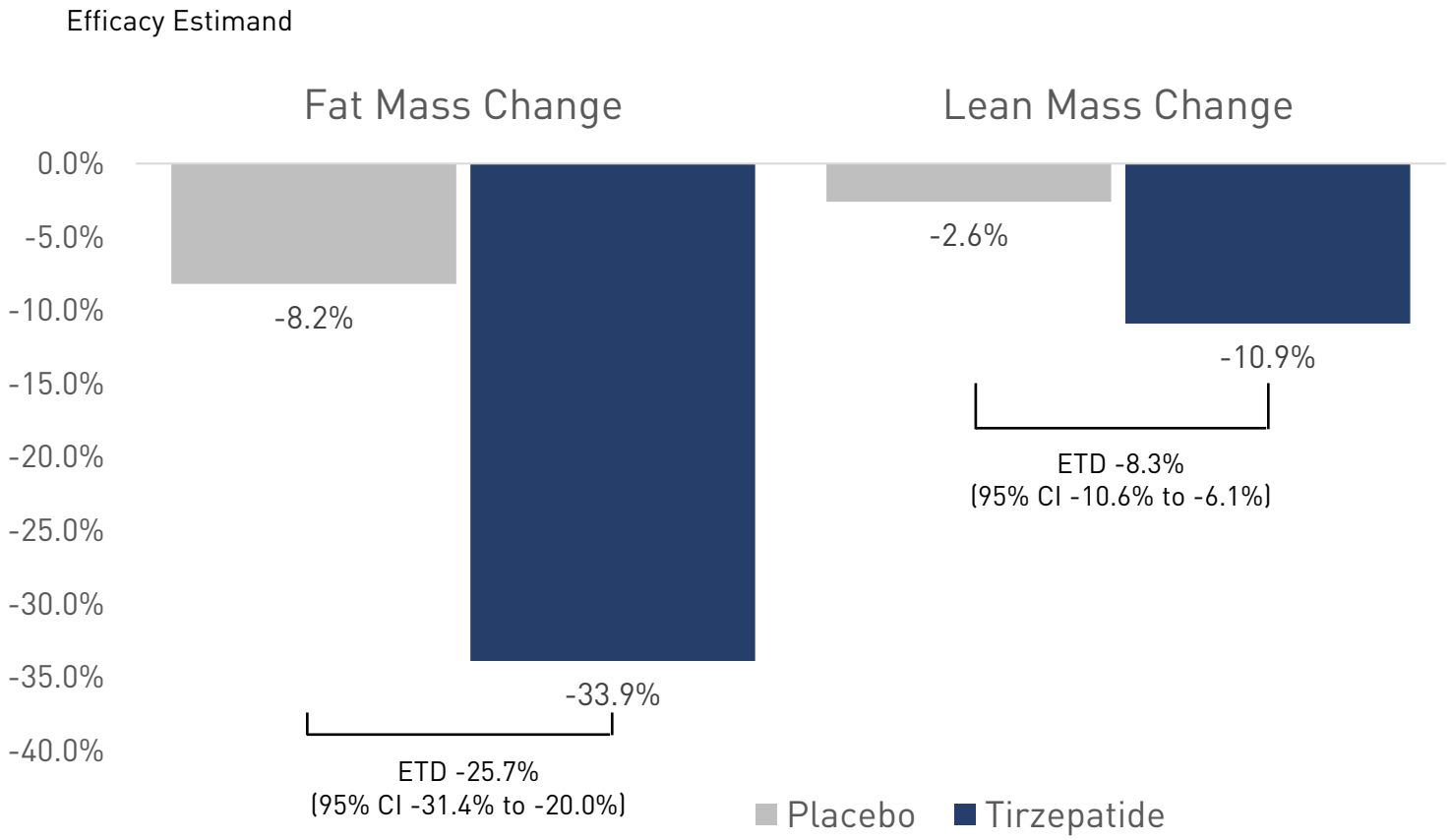
KEY EFFICACY RESULTS

- Percent of participants who achieved body weight reduction targets on the 15 mg treatment arm:
  - 63% achieved ≥ 20%
  - 40% achieved ≥ 25% (exploratory endpoint)
- In the placebo arm, 1% of participants achieved ≥ 20% weight reduction and 0.3% of participants achieved ≥ 25% weight reduction
- Physical functioning assessment improved while on tirzepatide compared to placebo, based an increase in the SF-36v2 score

TZP=tirzepatide; Logistic Regression, mITT population (efficacy analysis set). TZP vs. placebo at 72 weeks: ***p<0.001; Percentage of participants achieving greater than or equal to 25% weight reduction is an exploratory endpoint; For the treatment-regimen estimand: Logistic regression analysis, mITT population (full analysis set). TZP vs. placebo at 72 weeks: p<0.001.

SURMOUNT-1: EFFICACY DATA

BODY COMPOSITION AT 72 WEEKS SHOWS MEAN PERCENT CHANGE FROM BASELINE



- Ratio of total fat mass to total lean mass decreased more with tirzepatide from 0.93 at baseline to 0.70 at week 72, versus 0.95 to 0.88 with placebo
- Larger percentage reduction in fat mass resulted in an overall improvement in body composition, comparable to that reported with lifestyle-based and surgical treatments for obesity

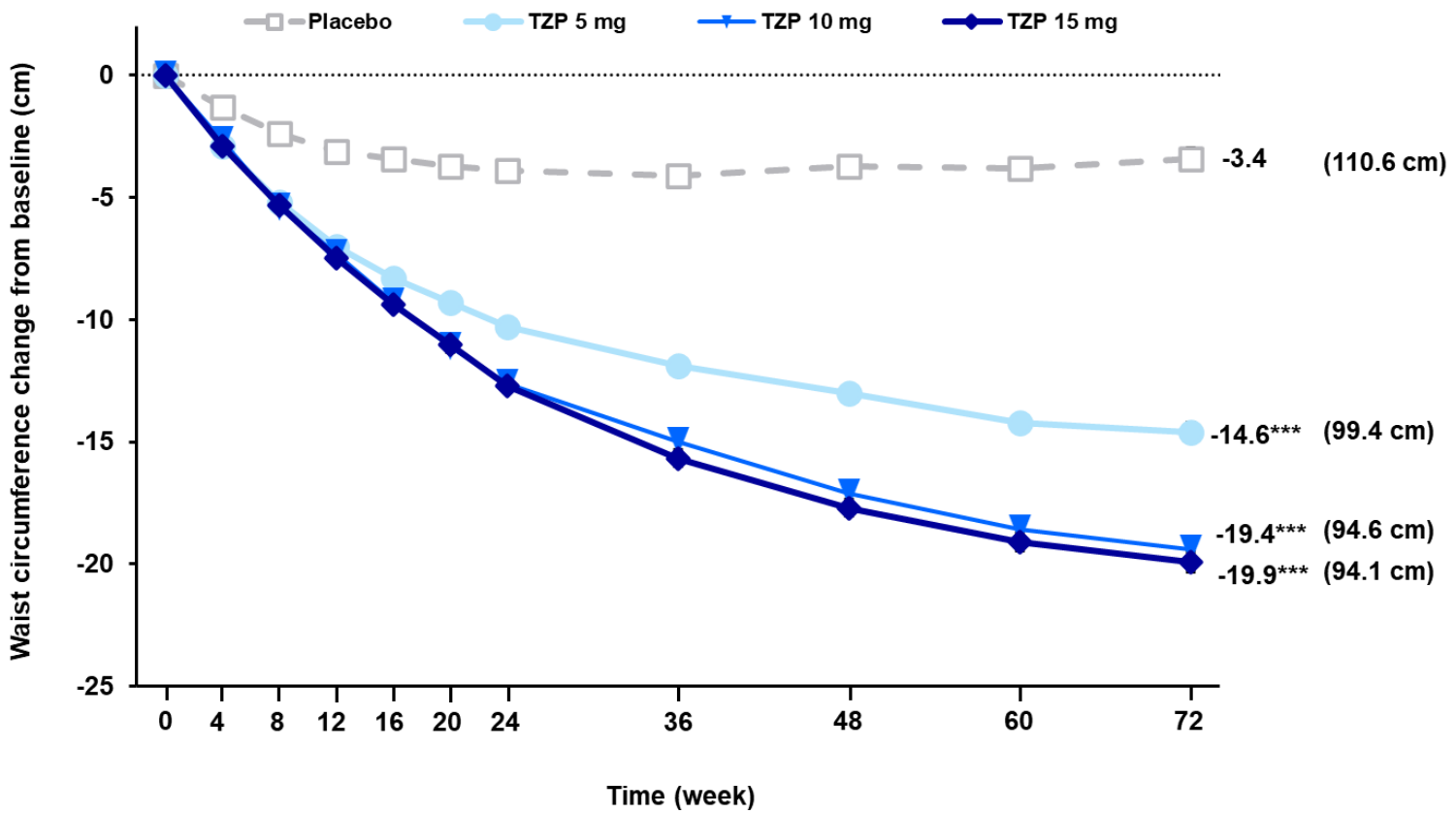
Participants on tirzepatide had ~3x greater percent reduction in fat mass (-33.9%) than lean mass (-10.9%).

DXA subpopulation for efficacy estimand : n=160; Tirzepatide: pooled 5 mg, 10 mg and 15 mg groups. Efficacy Estimand: ANCOVA analysis, Data presented are LS means; ETD=estimated treatment difference relative to placebo

SURMOUNT-1: KEY SECONDARY ENDPOINTS

MET WAIST CIRCUMFERENCE ENDPOINTS AT 72 WEEKS

Efficacy Estimand



Overall waist circumference at baseline = 114.1 cm

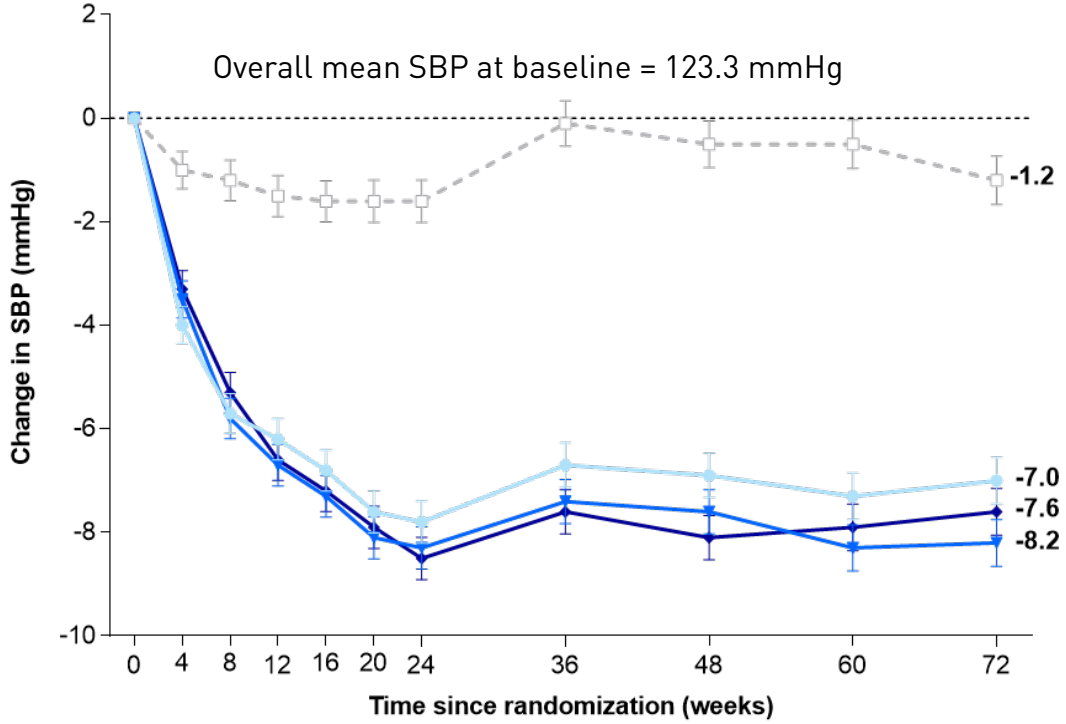
Waist circumference was reduced in all treatment arms, and 10 and 15 mg dose showed reduction of 19.4 cm (7.6 in) and 19.9 cm (7.8 in), respectively.

MMRM analysis, mITT population (efficacy analysis set). Data presented over time are LS means ± standard errors. Numbers in parentheses are LS means for actual values.
TZP vs. placebo at 72 weeks: ***p<0.001; TZP=tirzepatide

SURMOUNT-1: KEY SECONDARY ENDPOINTS

MET BLOOD PRESSURE AND LIPIDS ENDPOINTS AT 72 WEEKS

SYSTOLIC BLOOD PRESSURE



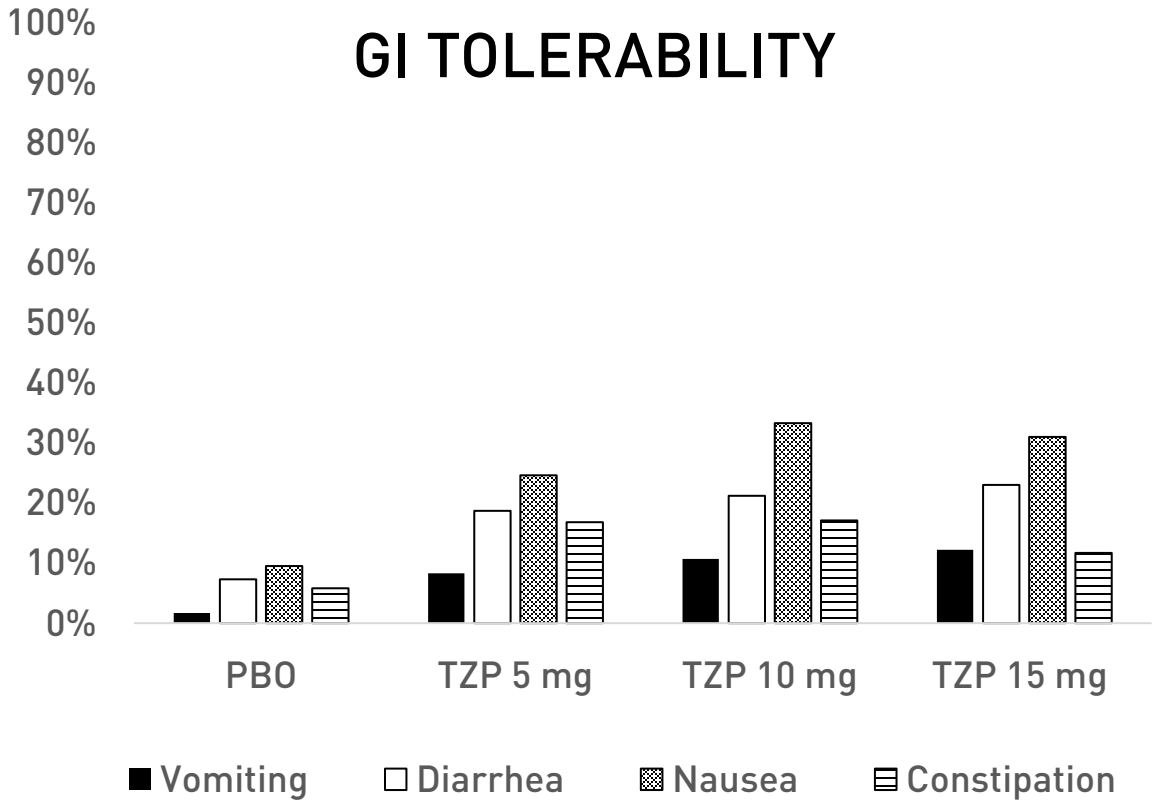
KEY TAKEAWAYS

- Showed clinically meaningful reduction in systolic blood pressure. Significant decreases in diastolic blood pressure were also seen
- Led to significant improvements in lipid parameters with reductions in triglycerides and non-HDL cholesterol and increases in HDL cholesterol
- Potential impact of the improvements in cardiometabolic parameters will be further assessed in our SURMOUNT-MMO study

MMRM analysis, mITT population (safety analysis set). Data presented are LS means ± standard errors; SBL=systolic blood pressure

SURMOUNT-1: SAFETY AND TOLERABILITY DATA

OVERALL SAFETY PROFILE SIMILAR TO INCRETIN-BASED THERAPIES APPROVED FOR OBESITY



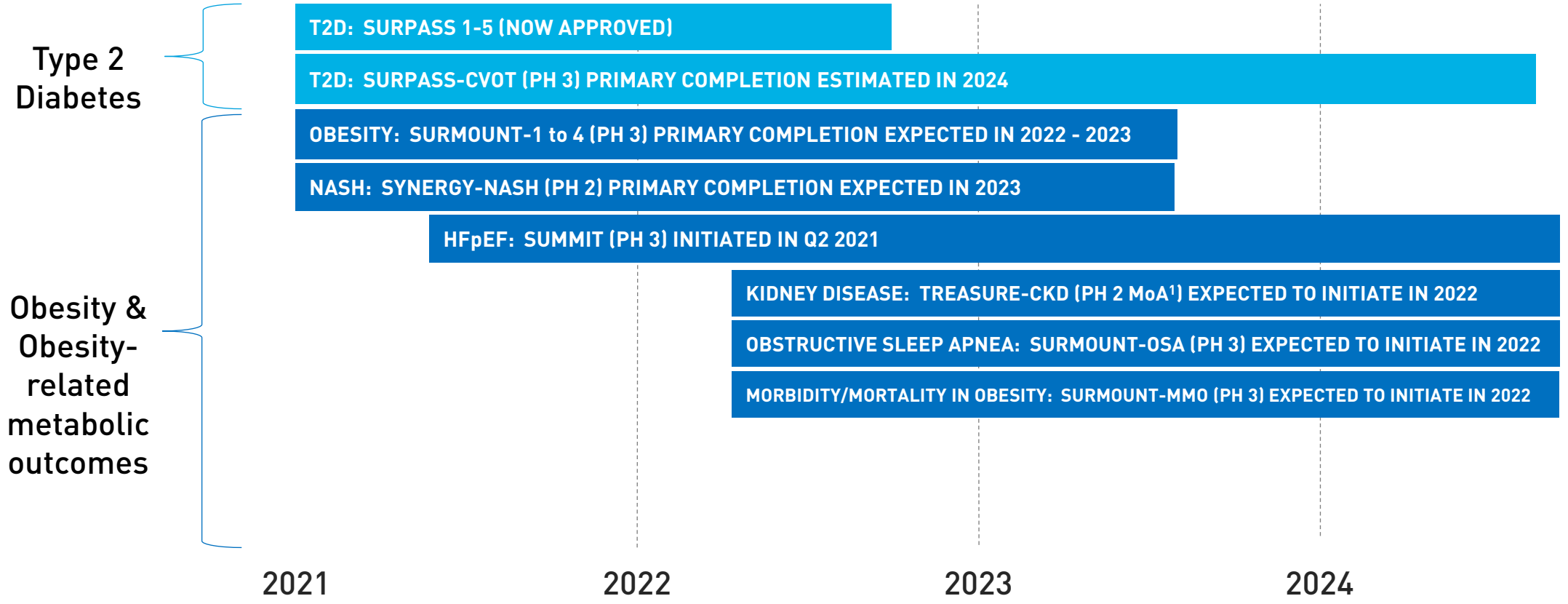
- Most frequent adverse events were GI-related, mild-to-moderate in intensity, and generally occurred during the dose escalation period
- Study drug discontinuation due to GI adverse events was reported in less than 5% of participants on tirzepatide
- Serious adverse events were balanced between participants on tirzepatide and placebo
- Treatment discontinuation due to adverse events was between 4.3% and 7.1% for each tirzepatide treatment arm compared to 2.6% for placebo

Overall treatment discontinuation rates ranged from ~14% to 16% in the tirzepatide treatment arms compared to over 26% for placebo.

GI=gastrointestinal; TZP=tirzepatide; PBO= placebo

TIRZEPATIDE CLINICAL DEVELOPMENT PROGRAM

EVALUATING TIRZEPATIDE EFFECTS TO EXPAND ITS POTENTIAL BENEFITS FOR PATIENTS



Robust development program is planned to demonstrate how treating obesity can improve patient outcomes across a wide range of diseases.

[1] Not an outcomes study; T2D=type 2 diabetes; CVOT=cardiovascular outcomes trial; NASH=non-alcoholic steatohepatitis; HFpEF=heart failure with preserved ejection fraction; CKD/DKD=chronic kidney disease/diabetic kidney disease; MoA=mechanism of action; OSA=obstructive sleep apnea

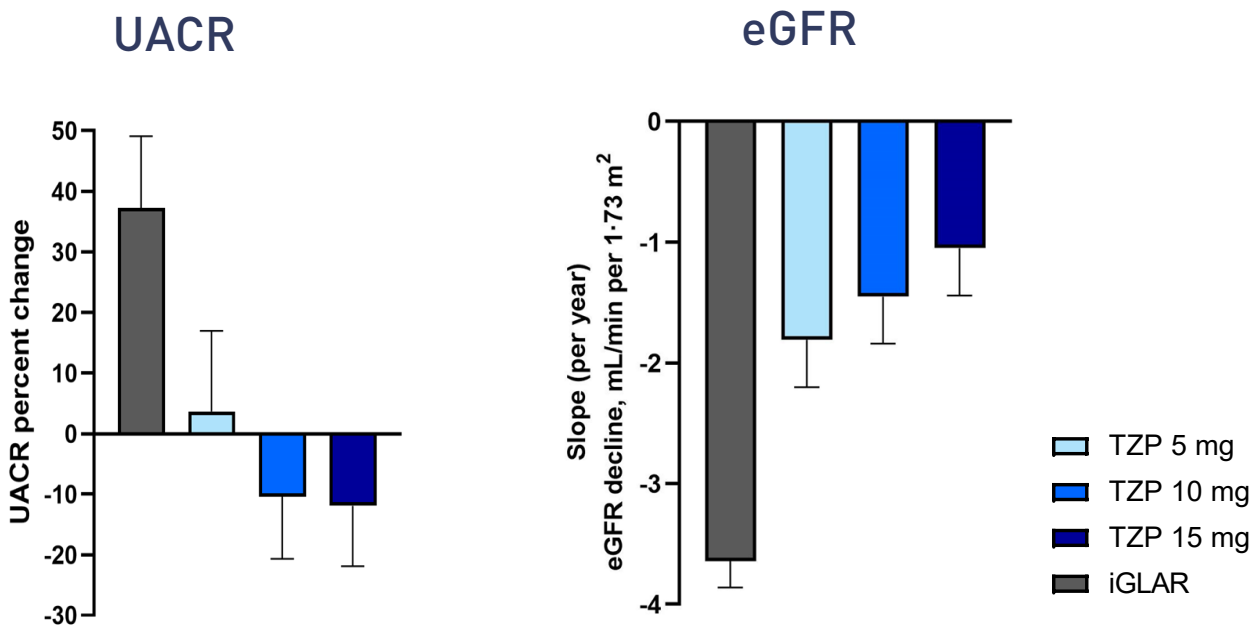
Tirzepatide

New Insights from SURPASS and MoA Studies

TIRZEPATIDE MAY CONFER KIDNEY PROTECTION

SURPASS-4 EXPLORATORY ENDPOINT SHOWED IMPROVEMENT IN UACR AND KIDNEY FUNCTION

SURPASS-4 KIDNEY DATA



Effects of tirzepatide versus insulin glargine on UACR and rate of eGFR decline in participants with type 2 diabetes and high cardiovascular risk

KEY TAKEAWAYS

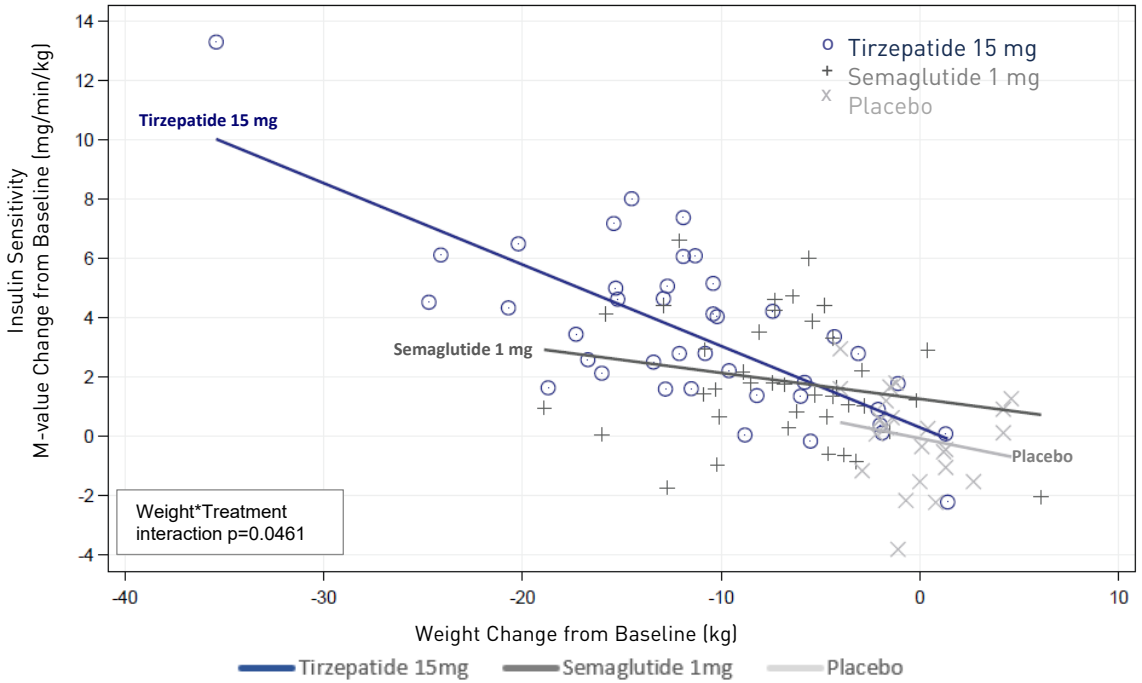
- Tirzepatide reduced the risk of renal disease (HR=0.58) as measured with a composite endpoint of kidney function (macroalbuminuria, 40% eGFR decline, ESKD, renal death).
- Tirzepatide reduced UACR and slowed the decline of eGFR
- Effect appeared to be independent of SGLT2 use

TZP=tirzepatide; eGFR=estimated glomerular filtration rate; UACR=urine albumin-to-creatinine ratio; iGLAR=insulin glargine; HR=heart rate; ESKD=end-stage kidney disease

TIRZEPATIDE IMPROVED INSULIN SENSITIVITY MORE THAN SEMAGLUTIDE

EVIDENCE FOR WEIGHT-INDEPENDENT INSULIN SENSITIZATION

INSULIN SENSITIVITY AS A FUNCTION OF WEIGHT CHANGE



Assessment of insulin sensitivity in patients with type 2 diabetes treated for 26 weeks[1]

KEY TAKEAWAYS

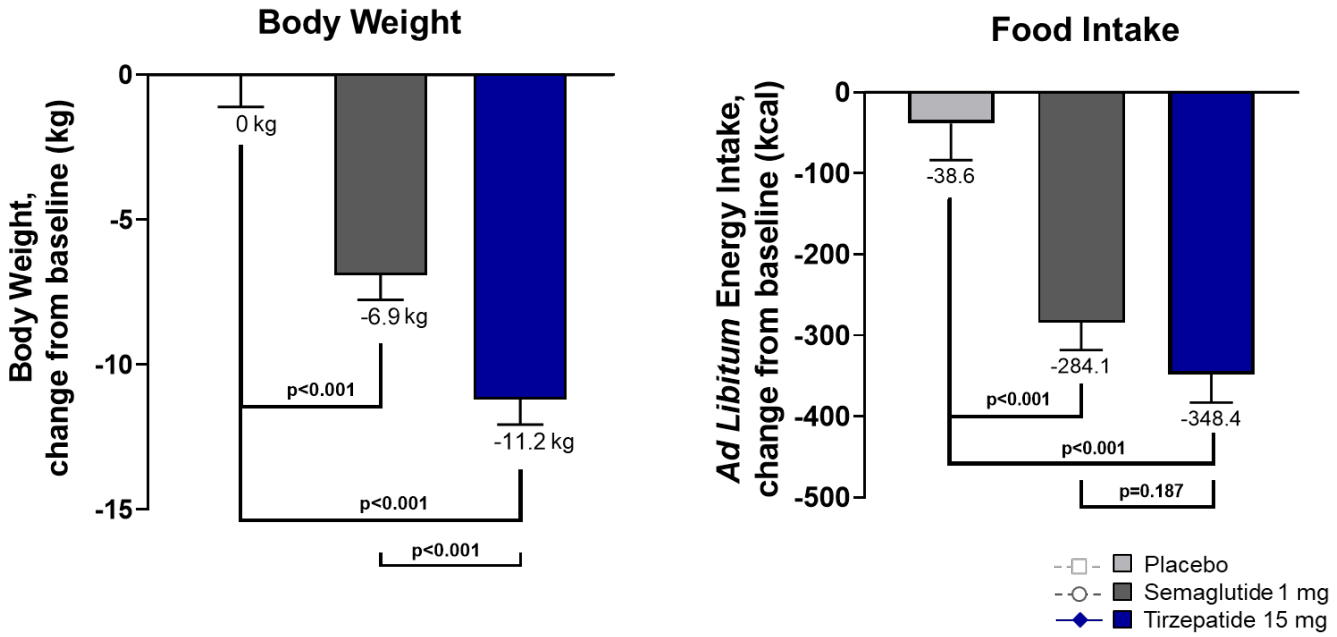
- Tirzepatide 15 mg achieved 63% improvement in insulin sensitivity over baseline while semaglutide 1.0 mg achieved 35%[1]
- Per unit weight loss, the insulin sensitivity increase was more pronounced for tirzepatide
- Tirzepatide finding is consistent with preclinical data that shows weight independent insulin sensitization conferred by GIP alone[2]
- The enhanced insulin sensitivity conferred by tirzepatide may contribute to the durable glycemic control shown in SURPASS-4

New analysis of MoA study=NCT03951753; 1=Heise, et al (2022) *Lancet Diabetes Endocrinol* 10:418; 2=GIPR agonism mediates weight-independent insulin sensitization by tirzepatide in obese mice, described in Samms, et al (2021) *The Journal of Clinical Investigation* 15:131(12)

TIRZEPATIDE DECREASES FOOD INTAKE

FINDINGS FROM FIRST MOA STUDY TO CONTINUE IN FURTHER DEDICATED STUDIES

MECHANISM OF ACTION STUDY



Effects of tirzepatide 15 mg versus placebo or semaglutide 1 mg on body weight and food intake (ad libitum meal) after 28 weeks in type 2 diabetes[1]

KEY TAKEAWAYS

- Tirzepatide decreased food intake and appetite
- In preclinical models, tirzepatide protected against decreased energy expenditure after weight loss, unlike selective GLP-1 receptor agonists
- Two dedicated MoA studies in individuals with obesity but without diabetes are ongoing to investigate the effects of tirzepatide on food preference and energy expenditure (NCT04311411, NTC04081337)

Data from MoA study=NCT03951753; 1=Heise, et al (2022) *Lancet Diabetes Endocrinol* 10:418; TZP=tirzepatide; MoA=mechanism of action

Early Phase ADA Highlights

Oral GLP-1, GGG, Oxyntomodulin, BIF

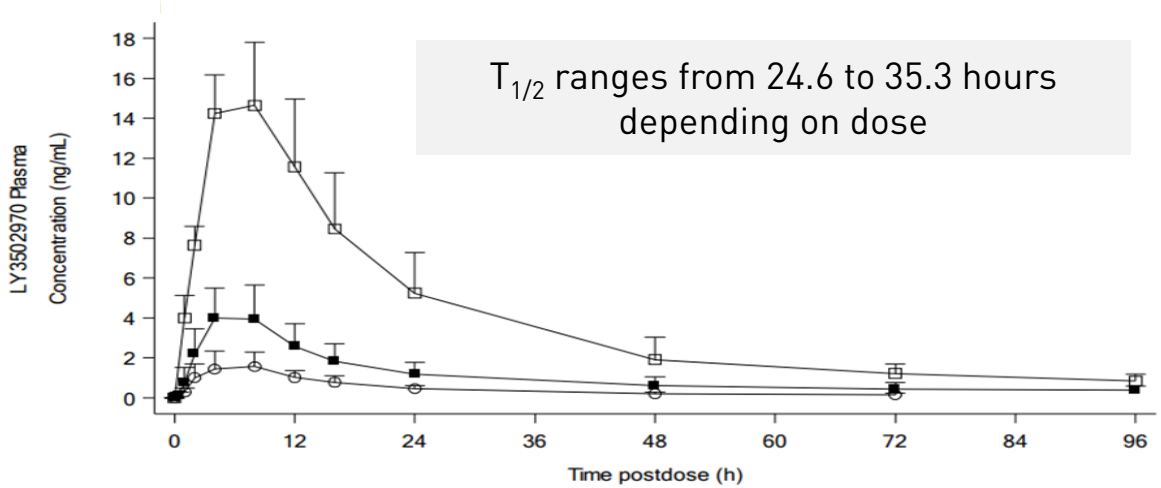
ORAL GLP-1R NPA (LY3502970)

POTENTIAL TO EXPAND THE REACH OF GLP-1 MECHANISM THROUGH CONVENIENT ORAL OPTION

GLP-1R NPA (LY3502970)

- A 12-week proof-of-concept study in T2D showed potential to match high-dose subcutaneous GLP-1 receptor agonists:
  - Mean change in A1C from baseline: -1.77%
  - Mean change in weight from baseline: 4.71 kg
- Goal is once-daily dosing with no food or water restrictions and additional benefits versus orally delivered peptides
- Phase 2 studies in T2D and obesity initiated in Q3 2021

PK DATA (SINGLE DOSE)



$T_{1/2}$ ranges from 24.6 to 35.3 hours depending on dose

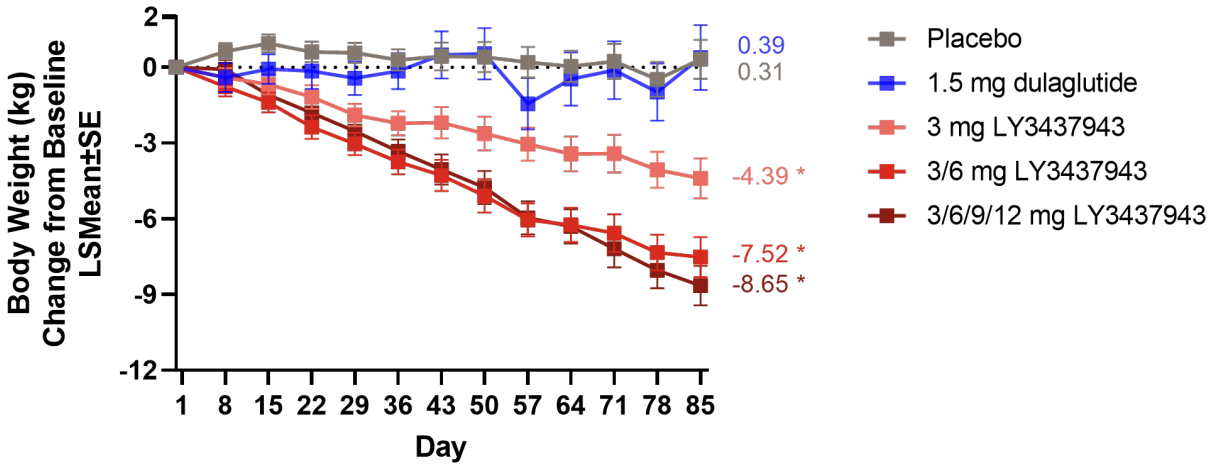
- Low PK variability, dose-proportional exposure and long half-life enable QD dosing
- A low peak-to-trough ratio (~2) may result in tolerability comparable to the best injectable GLP-1R agonists

Note: GLP-1R NPA (LY3502970) is licensed from Chugai; GLP-1R NPA=GLP-1 receptor non-peptidic agonist; T2D=type 2 diabetes; POC=proof-of-concept; $T_{1/2}$,=half-life; QD=once per day

GIP, GLP-1 AND GLUCAGON TRIPLE RECEPTOR AGONIST (GGG LY3437943)

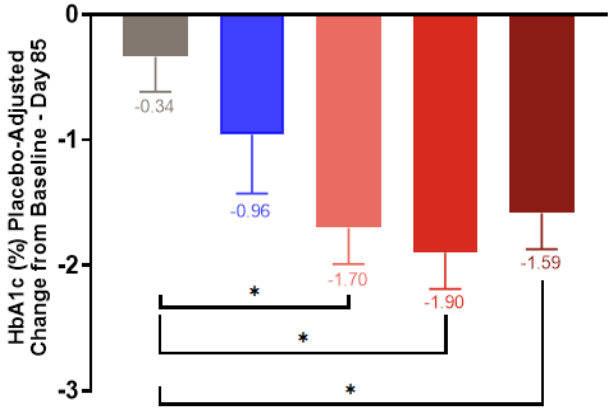
PHASE 1 12-WEEK MULTIPLE ASCENDING DOSE DATA IN T2D

WEIGHT REDUCTION



- Dose-dependent weight reduction of up to 8.65 kg (10.1% change from baseline) within a 12-week study
- Visual analog scoring suggests decreased appetite comparable to dulaglutide 1.5 mg

HBA1C



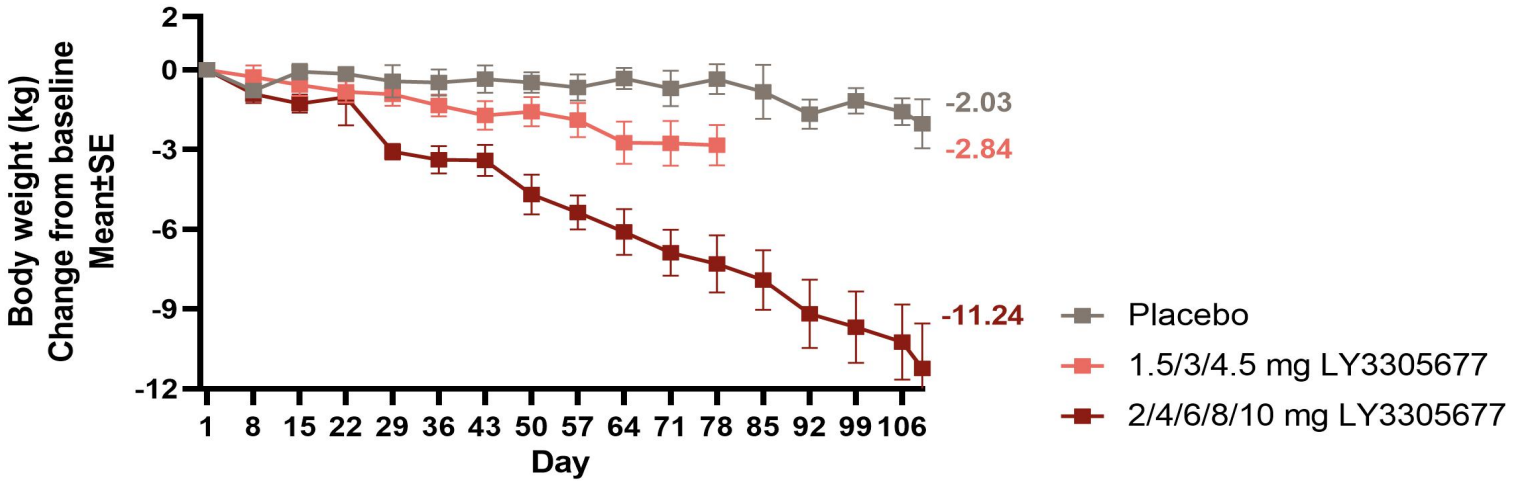
- Significantly decreased mean HbA1c up to 1.90% from baseline at dose levels of ≥3 mg
- Consistent with incretin effect, notable augmentation of insulin response following OGTT resulting in profound decrease in post-prandial glucose load

Not all arms are shown in the graph above; T2D=type 2 diabetes; OGTT=oral glucose tolerance test

OXYNTOMODULIN (MAZDUTIDE LY3305677)

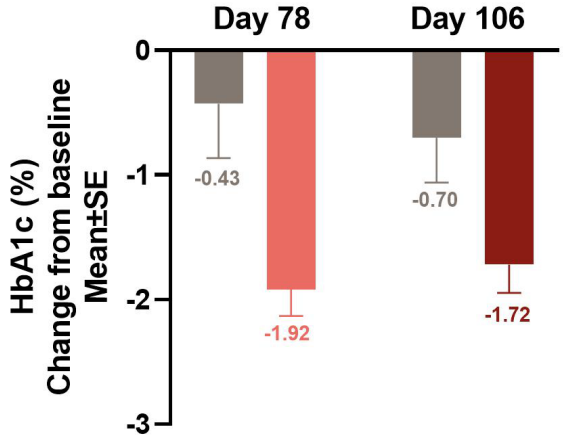
PHASE 1 16-WEEK MULTIPLE ASCENDING DOSE DATA IN T2D

WEIGHT REDUCTION



- Weight reduction of up to 11.2 kg (12.7% change from baseline) at 16 weeks
- Mazdutide improved markers of insulin sensitivity, has favorable effects on lipid markers and decrease waist circumference.

HBA1C



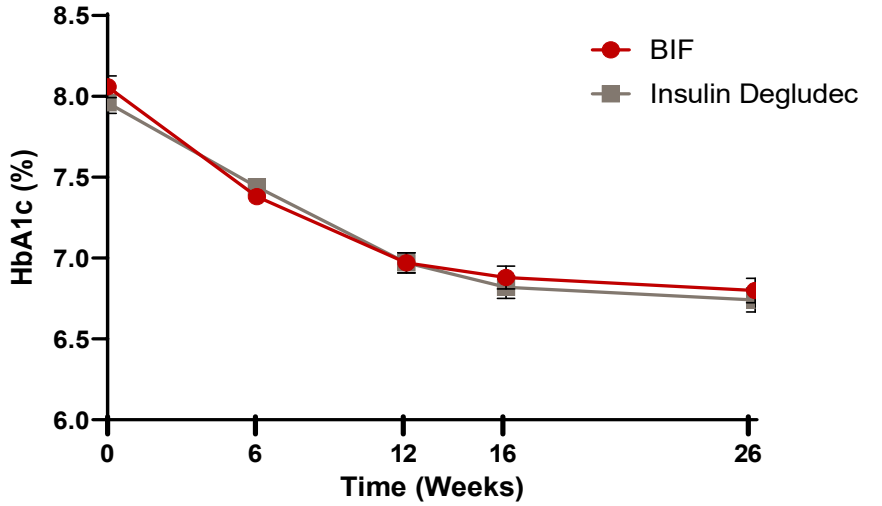
- In subjects with T2D, mean HbA1c changes from baseline were -1.92% and -1.72% at weeks 12 (low dose) and week 16 (high dose), respectively
- Mazdutide showed a safety profile similar to selective GLP-1 receptor agonists

T2D=type 2 diabetes

WEEKLY BASAL INSULIN FC (BIF LY3209590)

INSULIN NAÏVE T2D - PHASE 2 EFFICACY AND SAFETY PROFILE SIMILAR TO DEGLUDEC

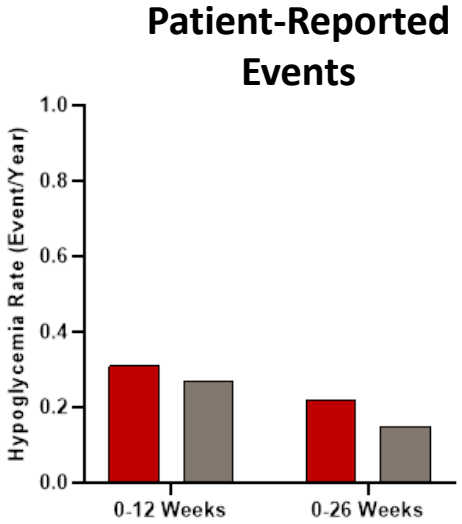
GLUCOSE CONTROL

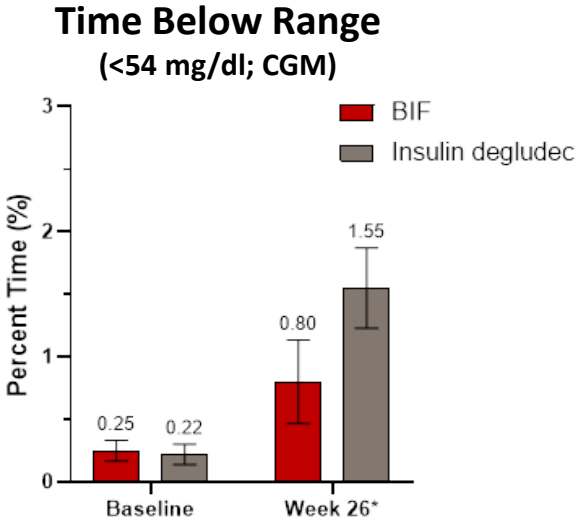


- Once weekly BIF was noninferior to daily insulin degludec for glycemic control as measured by change in HbA1c after 26 weeks
- Both treatment groups showed significant improvement from baseline at Week 26 (p<0.001), achieving a mean HbA1c <7%

BIF and Degludec were titrated to a target fasting glucose of ≤100 mg/dL; T2D = type 2 diabetes

HYPOGLYCEMIA (<54 MG/DL)





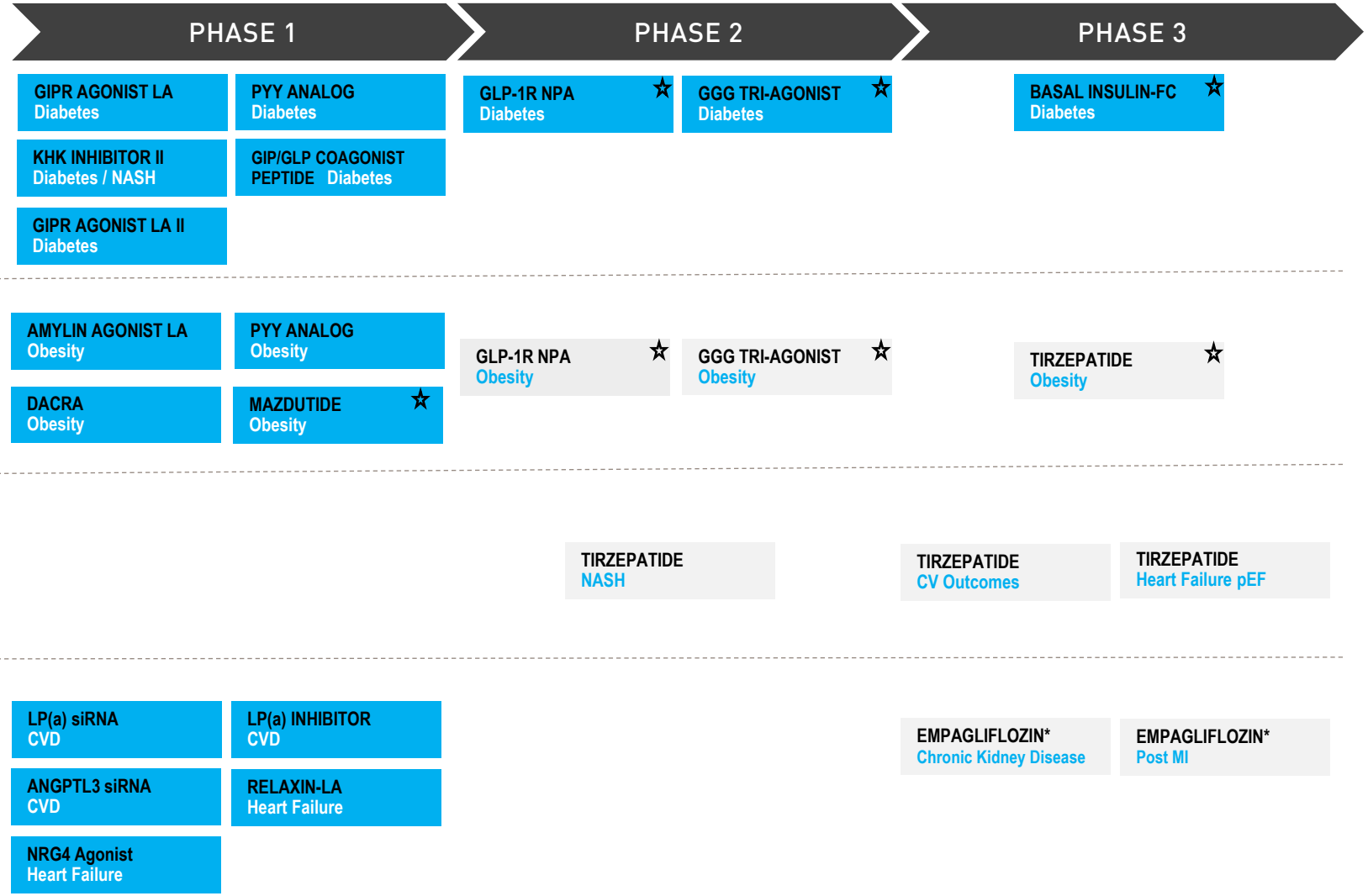
- Time spent below range, or in hypoglycemia, was similar for BIF compared to insulin degludec
- No severe hypoglycemia was reported and no serious adverse events were related to study drug

CGM=continuous glucose monitoring; assessed at baseline and week 26 for ~60% of study participants

Portfolio Overview

LILLY SELECT NME AND NILEX PIPELINE

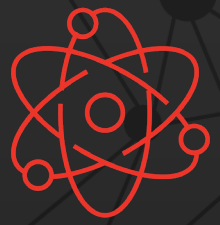
MULTIPLE OPPORTUNITIES ACROSS DIABETES, OBESITY AND RELATED INDICATIONS



Summary

The **approval of Mounjaro** is the first of 5 potential near-term launch opportunities that we expect could **fuel our already strong growth trajectory** led by Trulicity, Jardiance, Taltz and Verzenio as we work to find more effective treatment options for patients.

As we move earlier in the disease cascade, we are aiming to **disrupt disease progression** by revolutionizing obesity care and improving patient outcomes with potential new medicines like tirzepatide.



We are looking to **further raise the bar and provide new potential treatment options** for people with type 2 diabetes and obesity with potential new medicines like oral GLP-1 NPA, GGG, oxyntomodulin and BIF.


Lilly