ADA Scientific Sessions

June 6, 2026

The First Phase 3 Obesity Study of Retatrutide, a GIP, GLP-1, and Glucagon Receptor Agonist, in People with Obesity (TRIUMPH-1)

Ania M. Jastreboff, MD, PhD

Harvey & Kate Cushing Professor, Yale University School of Medicine
Internal Medicine, Endocrinology & Metabolism
Pediatrics, Pediatric Endocrinology
Director, Yale Obesity Research Center (Y-Weight)

Disclosures

RETATRUTIDE
OBESITY
TRIUMPH-1

RESEARCH SUPPORT:

- Amgen
- Boehringer Ingelheim
- Eli Lilly
- NIH/NIDDK
- Novo Nordisk
- Rhythm Pharmaceuticals

OPTIONS/SHARES:

- Intellihealth
- Metsera
- State 4 Tx – academic co-founder
- Syntis Bio

SCIENTIFIC ADVISORY BOARD:

- Amgen
- AstraZeneca
- Boehringer Ingelheim
- Biohaven
- Eli Lilly
- i2o
- Kailera
- Metsera
- Novo Nordisk
- Pfizer
- Regeneron
- Roche/Genentech
- Scholar Rock
- Structure Therapeutics
- Viking
- Wave
- WW (WeightWatchers)
- Zealand Pharmaceuticals

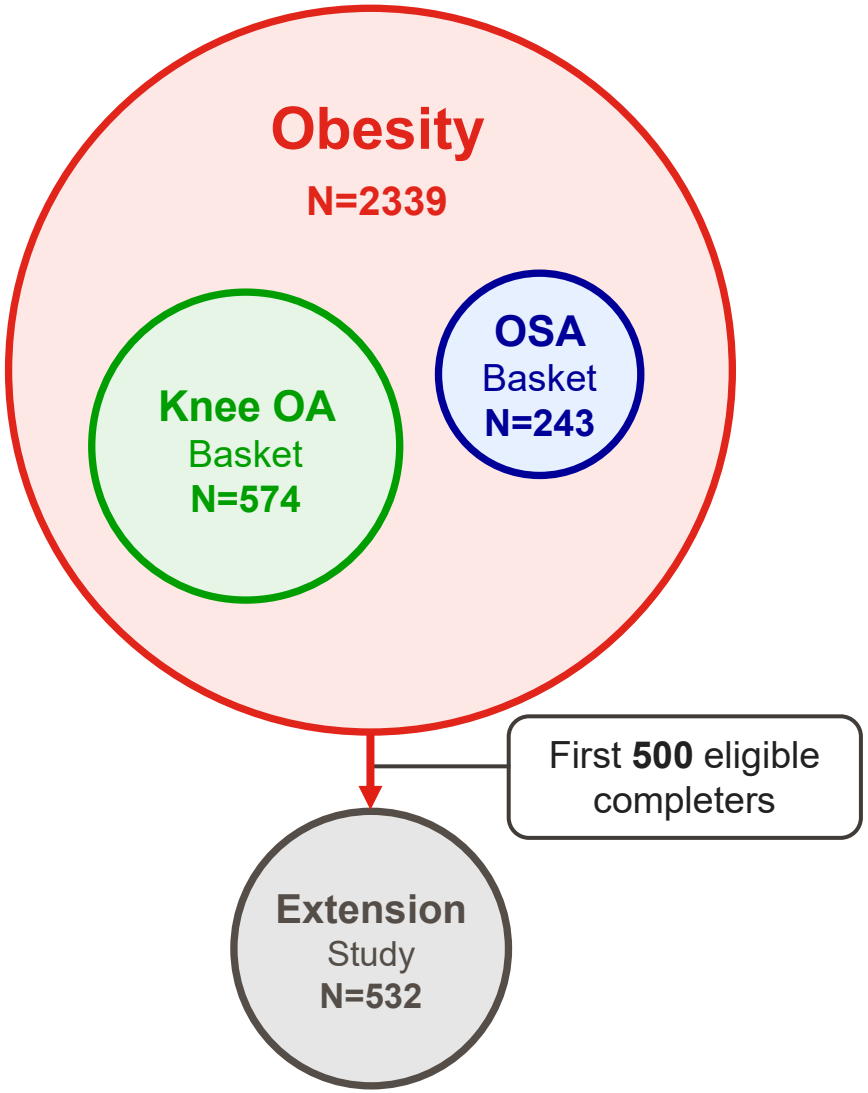
TRIUMPH-1

Study Design and Participant Disposition

TRIUMPH-1: Retatrutide Phase 3 Obesity Trial

Study Overview

RETATRUTIDE
OBESITY
TRIUMPH-1



Obesity
Primary Endpoint
Percent change in **Weight** at 80 weeks

Osteoarthritis
Primary Endpoint
Change in **Knee Pain**

OSA
Primary Endpoint
Change in **Apnea-Hypopnea Index**

Extension
Primary Objective
Percent change in **Weight** at 104 weeks

OSA=obstructive sleep apnea; OA=osteoarthritis.

TRIUMPH-1: Retatrutide Phase 3 Obesity Trial

Key Inclusion and Exclusion

RETATRUTIDE
OBESITY
TRIUMPH-1

TRIUMPH-1

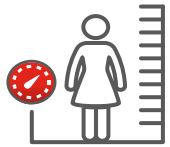
Participants (N=2339)

Key Inclusion Criteria

- **≥18** years of age
- **BMI ≥30 kg/m²** or **BMI ≥27 kg/m²** with **≥1 obesity-related disease**

Key Exclusion Criteria

- Any type of **diabetes** or a history of **ketoacidosis**, or **hyperosmolar state**
- **Stable weight** within 90 days prior to screening



- Goal **80% enrichment** BMI ≥35 kg/m²
- **70% cap** on female participants

Knee OA Basket

Participants (N=574)

Additional Inclusion Criteria

- **WOMAC Pain subscale score of 4-9** (on a 0-10 scale), and
- **Meets American College of Rheumatology criteria** (clinical and radiological) for knee OA

OSA Basket

Participants (N=243)

Additional Inclusion Criteria

- **Moderate-to-severe OSA** on screening PSG (AHI ≥15), and
- **On stable PAP therapy** or **unable/unwilling to use PAP**

Extension Study

Participants (N=532)

Key Inclusion Criteria

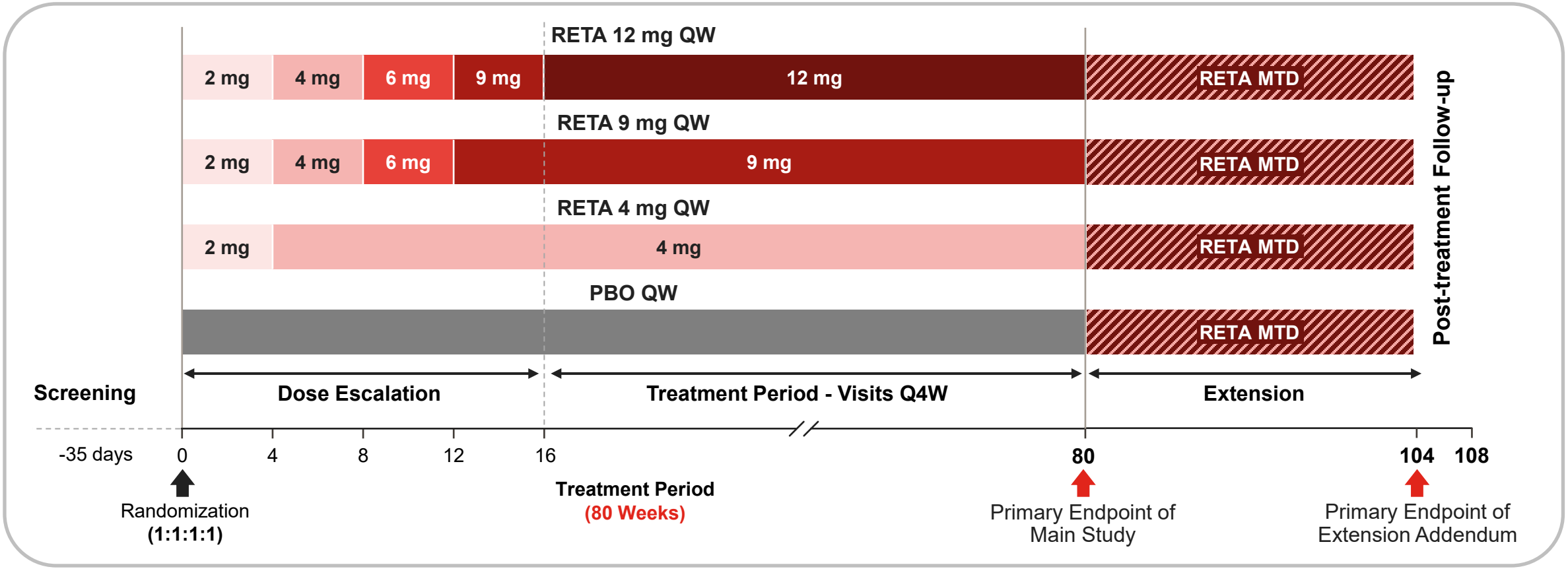
- Initial baseline **BMI ≥35 kg/m²**
- Completed the main study (Week 80)
- **On target dose** at Week 80

AHI=Apnea-Hypopnea Index; OA=osteoarthritis; OSA=obstructive sleep apnea; PAP=positive airway pressure; PSG=polysomnography; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

TRIUMPH-1: Study Design

RETATRUTIDE
OBESITY
TRIUMPH-1

Randomized, double-blind, Phase 3 trial of weekly retatrutide vs. placebo in participants with obesity, including subsets of participants with OSA or knee OA



Participants received individualized **lifestyle counselling** on **healthy diet** and **physical activity**

Giblin K, et al. Diabetes Obes Metab. 2026; https://clinicaltrials.gov/study

BMI=body mass index; MTD=maximum tolerated dose; OA=osteoarthritis; OSA=obstructive sleep apnea; PBO=placebo; RETA=retatrutide

Primary and Key Secondary Endpoints

TRIUMPH-1 Overall Study

Primary Endpoint

Percent change in weight at week 80 with retatrutide 9 mg or 12 mg

Key Secondary Endpoints

- Percent change in weight at week 80 with **retatrutide 4 mg**
- Percentage of participants reaching **weight reduction thresholds** of **≥5%, ≥10%, ≥15%, ≥20%, ≥25%, ≥30%,** and **≥35%**
- Change in:
  - **systolic blood pressure**
  - **triglycerides** and **non-HDL cholesterol**
  - **hsCRP**
  - **physical function** and **psychosocial** quality of life measures

HDL=high-density lipoprotein; hsCRP=high-sensitivity C-reactive protein.

TRIUMPH-1

Participant Characteristics

Baseline Demographics

Overall Study and Baskets

Characteristic	TRIUMPH-1 Total (N=2339)	Knee OA Basket (N=574)	OSA Basket (N=243)
Age, years	**48.6** (12.2)	**56.1** (9.1)	**47.6** (10.5)
Female, n (%)	1533 (**65.5**)	435 (**75.8**)	89 (**36.6**)
Race, n (%)			
White	1723 (**73.7**)	421 (**73.3**)	129 (**53.1**)
Black or African American	172 (**7.4**)	55 (**9.6**)	19 (**7.8**)
Asian	185 (**7.9**)	7 (**1.2**)	3 (**1.2**)
American Indian or Alaska Native	169 (**7.2**)	71 (**12.4**)	70 (**28.8**)
Native Hawaiian or other Pacific Islander	7 (**0.3**)	3 (**0.5**)	0
Multiple	43 (**1.8**)	2 (**0.3**)	8 (**3.3**)
Ethnicity, n (%)			
Hispanic or Latino	577 (**24.7**)	130 (**22.6**)	195 (**80.2**)

OA basket: Participants were older and included more female participants

OSA basket: More Hispanic participants and more male participants

OA=osteoarthritis; OSA=obstructive sleep apnea.

Anthropometric Measures

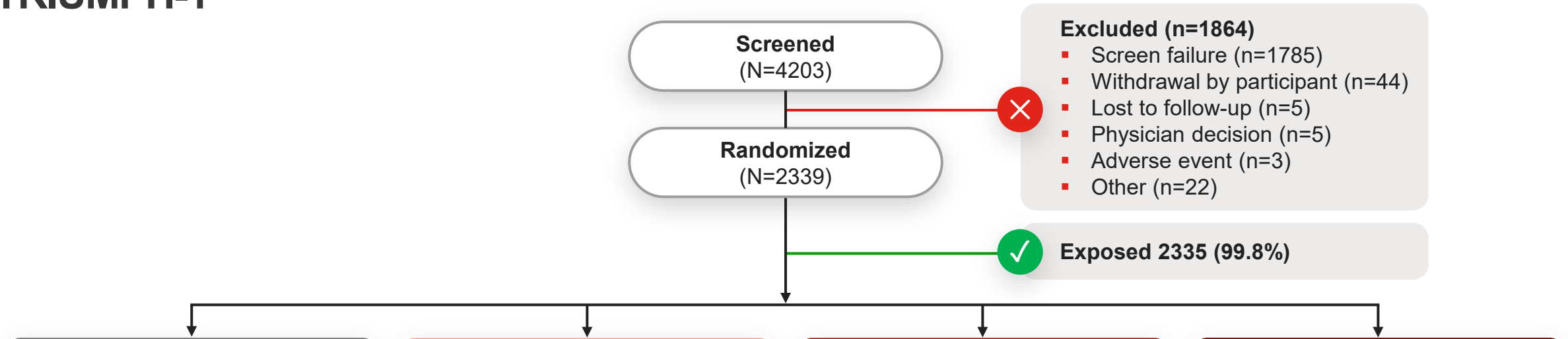
TRIUMPH-1 Overall Study

Characteristic	PBO (N=587)	RETA 4 mg (N=584)	RETA 9 mg (N=584)	RETA 12 mg (N=584)	Total (N=2339)
Waist circumference, cm	118.2 (16.0)	118.4 (16.2)	118.0 (15.7)	118.8 (15.5)	**118.3** (15.8)
Waist-to-height ratio	0.7 (0.1)	0.7 (0.1)	0.7 (0.1)	0.7 (0.1)	**0.7** (0.1)
Body Weight, kg	112.3 (24.7)	113.3 (26.2)	112.2 (24.1)	113.0 (23.9)	**112.7** (24.7)
BMI, kg/m^2	39.8 (6.9)	40.3 (7.3)	40.0 (7.2)	40.0 (6.8)	**40.0** (7.0)
BMI category, n (%)					
Overweight: 27-<30 kg/m^2	12 (2.0)	12 (2.1)	13 (2.2)	9 (1.5)	46 (**2.0**)
Class 1 Obesity: ≥30 to <35 kg/m^2	127 (21.6)	110 (18.8)	120 (20.5)	126 (21.6)	483 (**20.6**)
Class 2 Obesity: ≥35 to <40 kg/m^2	213 (36.3)	208 (35.6)	207 (35.4)	196 (33.6)	824 (**35.2**)
Class 3 Obesity: ≥40 kg/m^2	235 (40.0)	254 (43.4)	244 (41.8)	253 (43.3)	986 (**42.1**)
Participants with BMI ≥35 kg/m^2, n (%)	448 (76.3)	462 (79.1)	451 (77.2)	449 (76.9)	1810 (**77.4**)

Average baseline BMI = class 3 obesity (BMI ≥40 kg/m^2)

Data are shown as mean (SD) unless stated otherwise
BMI=body mass index; PBO=placebo; RETA=retatrutide; SD=standard deviation

Participant Disposition
TRIUMPH-1



PBO (N=587)	RETA 4 mg (N=584)	RETA 9 mg (N=584)	RETA 12 mg (N=584)
375 (63.9%) completed on-treatment at week 80	508 (87.0%) completed on-treatment at week 80	481 (82.4%) completed on-treatment at week 80	440 (75.3%) completed on-treatment at week 80
440 (75.0%) completed treatment period	534 (91.4%) completed treatment period	531 (90.9%) completed treatment period	523 (89.6%) completed treatment period

PBO: 75% completed the study, with ~64% completing on treatment

RETA: ~89%-91% completed the study, with ~75%-87% completing on treatment

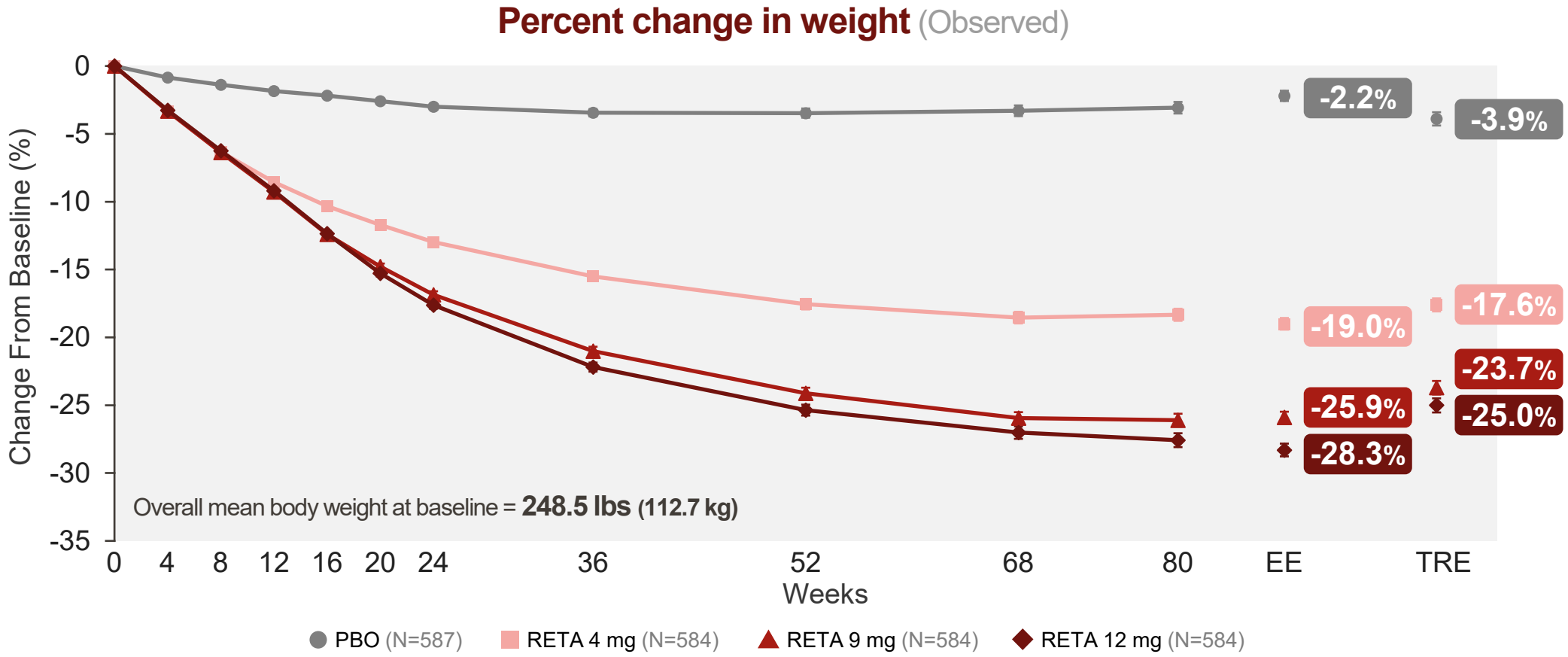
PBO=placebo; RETA=retatrutide

TRIUMPH-1

Primary and Secondary Outcomes

Weight Reduction Over 80 Weeks With Retatrutide

TRIUMPH-1 Primary Outcome



With RETA 4 mg, a dose which had only one up-titration step, weight reduction was an average of 19% at 80 weeks

With RETA 12 mg, weight reduction was an average of 28.3% at 80 weeks

All groups p<0.001 vs. PBO.
PBO=placebo; RETA=retatrutide; EE=Efficacy Estimand; TRE=Treatment Regimen Estimand.All groups

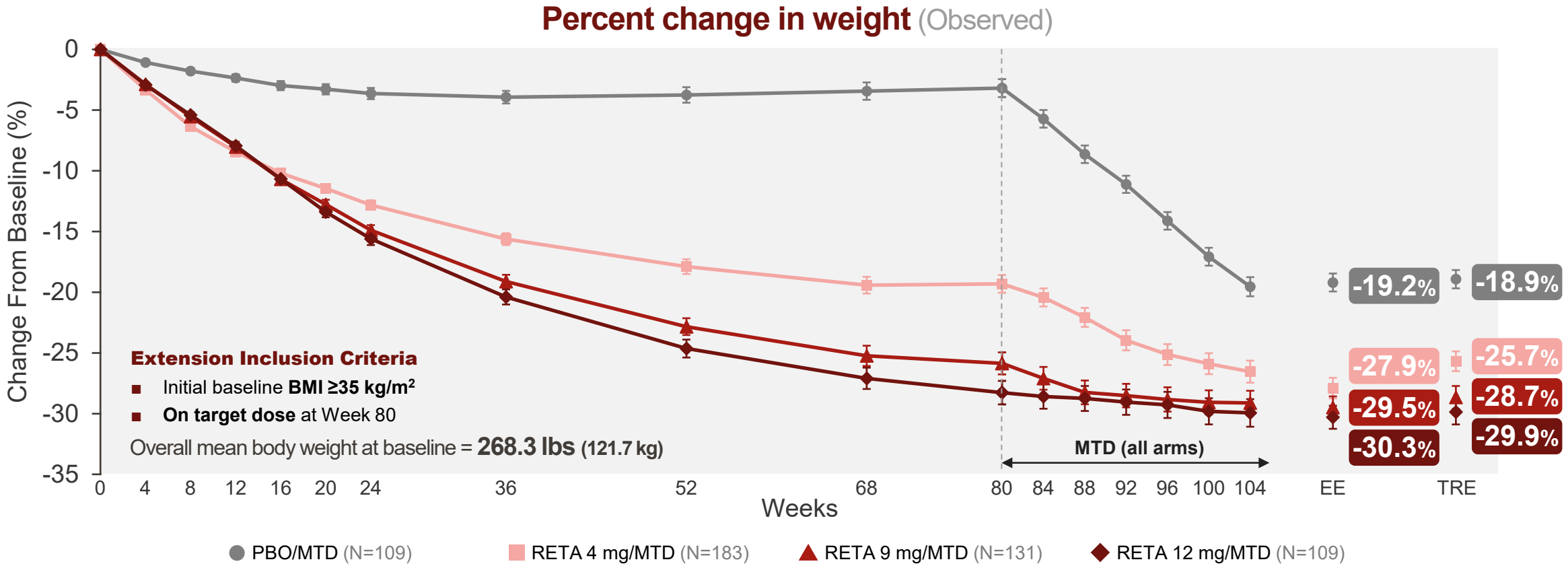
Weight Reduction Over 104 Weeks With Retatrutide

RETATRUTIDE
OBESITY
TRIUMPH-1

TRIUMPH-1 Extension

All Addendum Participants

N=532 total



Participants in the extension lost up to an average of 30% of their initial weight at 104 weeks

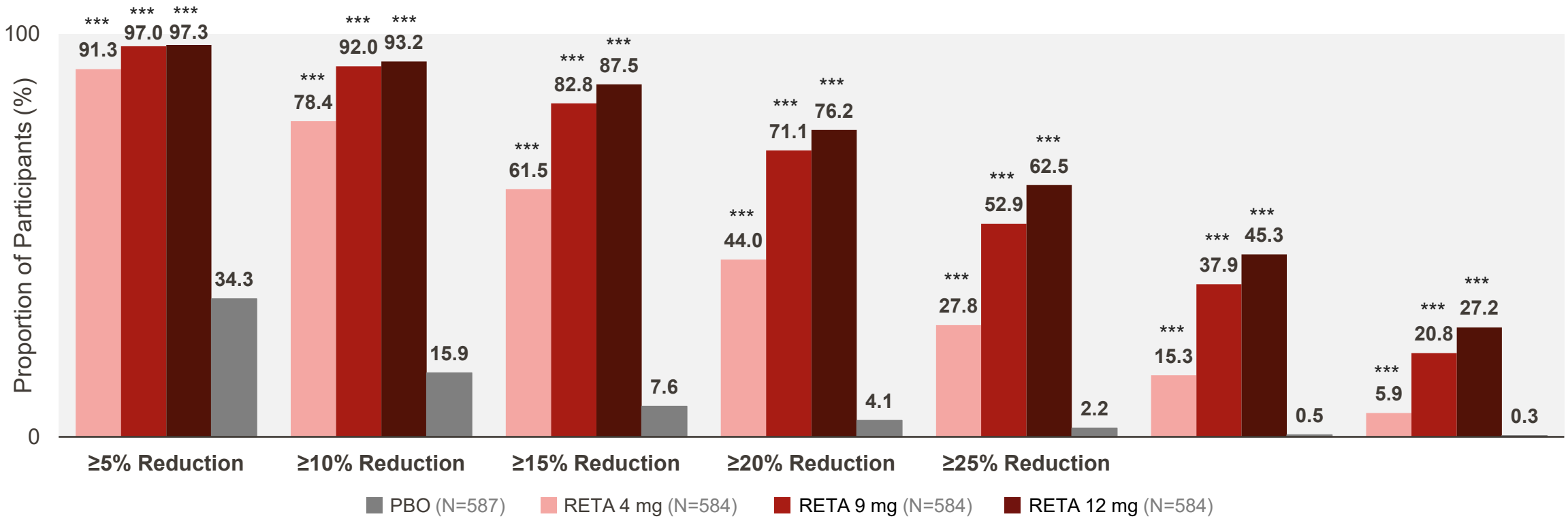
All groupp<0.001 vs. PBO.

BMI=body mass index; EE=Efficacy Estimand; MTD=maximum tolerated dose; PBO=placebo; RETA=retatrutide; TRE=Treatment Regimen Estimand.

Percent of Participants Reaching
Weight Reduction Thresholds with Retatrutide at Week 80

RETATRUTIDE
OBESITY
TRIUMPH-1

Efficacy Estimand



Clinically meaningful weight reduction in nearly all participants treated with RETA, including reaching higher weight reduction thresholds of ≥30% and ≥35%

***p<0.001 vs. PBO.
PBO=placebo; RETA=retatrutide.

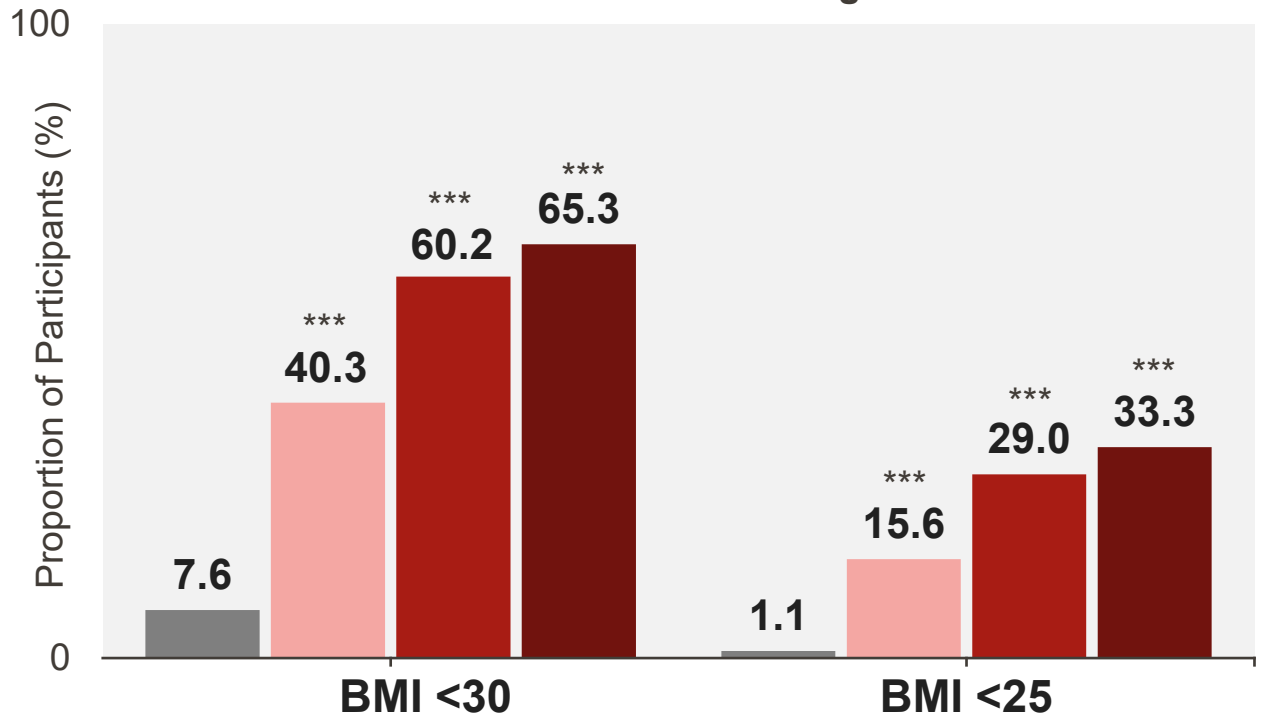
Percentage of Participants Reaching
BMI and WtHR Targets with Retatrutide at Week 80

RETATRUTIDE OBESITY TRIUMPH-1

Efficacy Estimand

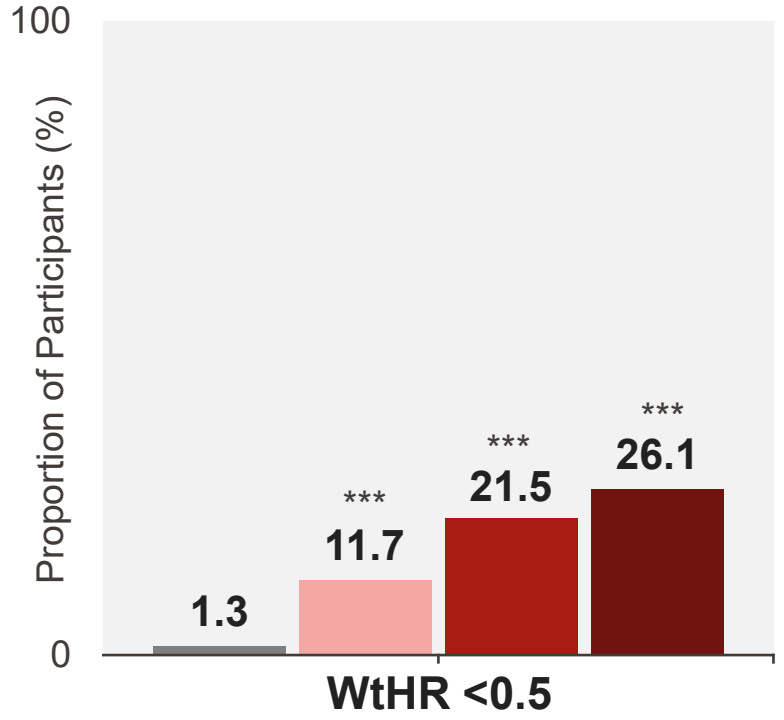
Body Mass Index

Mean baseline BMI = **40 kg/m²**



Waist-to-Height Ratio (WtHR)

Mean baseline WtHR = **0.7**



PBO (N=587) RETA 4 mg (N=584) RETA 9 mg (N=584) RETA 12 mg (N=584)

The efficacy observed with RETA potentially allows for a treat-to-target approach rather than relative change in weight approach, though data are needed to demonstrate health benefits with targets

***p<0.001 vs. PBO.

BMI=body mass index; PBO=placebo; RETA=retatrutide; WtHR=waist-to-height ratio.

TRIUMPH-1

Primary Outcomes of the Knee OA and OSA Baskets

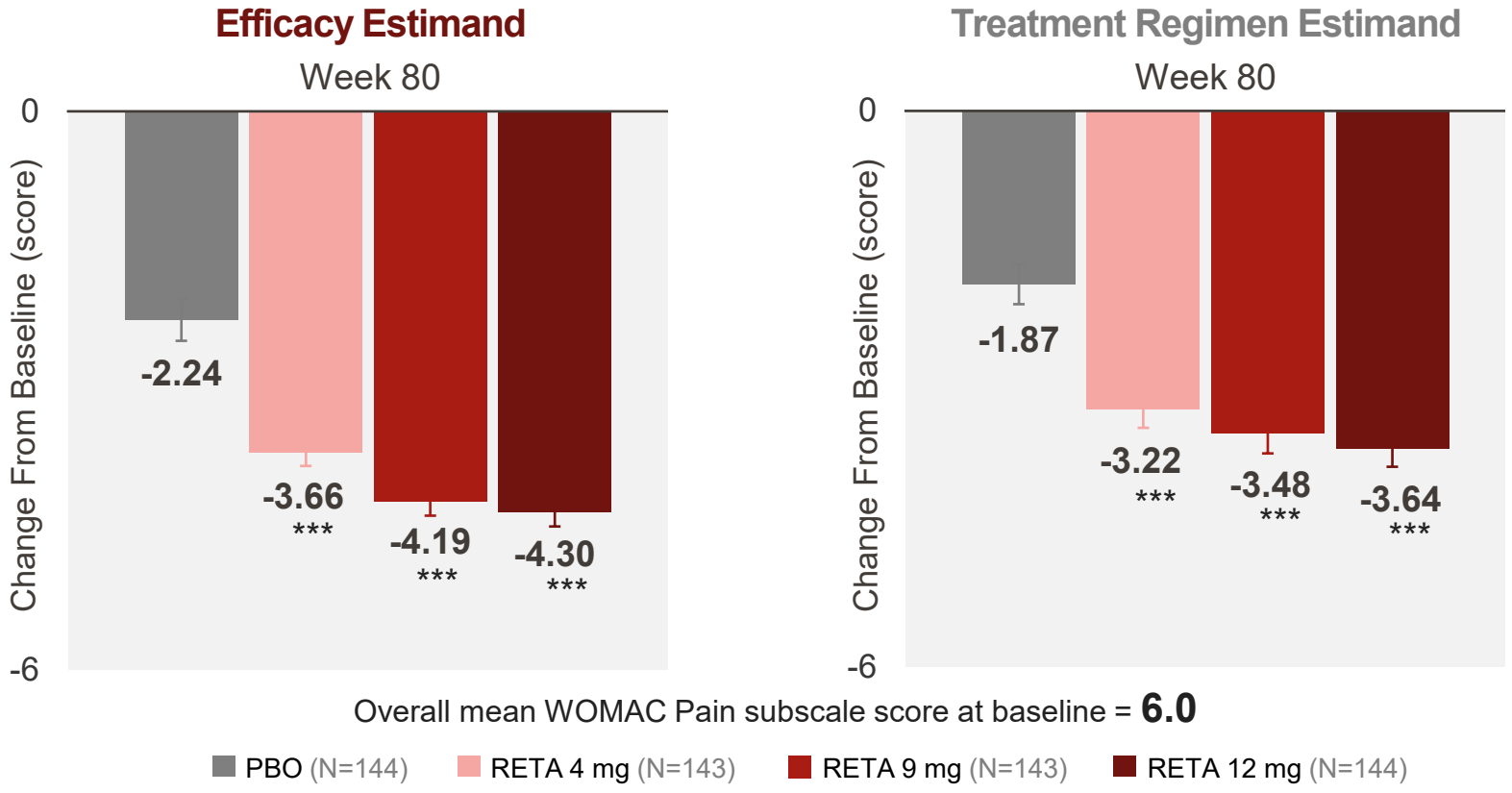
TRIUMPH-1- OA Basket

Knee Osteoarthritis

RETATRUTIDE
OA
TRIUMPH-1

N=574
total

Absolute Change in
WOMAC Pain Subscale Score



Overall mean WOMAC Pain subscale score at baseline = **6.0**

PBO (N=144) RETA 4 mg (N=143) RETA 9 mg (N=143) RETA 12 mg (N=144)

RETA resulted in a WOMAC pain score reduction more than the clinically significant threshold of 4 points

Which translates to up to more than a 70% decrease in pain with RETA

***p<0.001 vs. PBO.

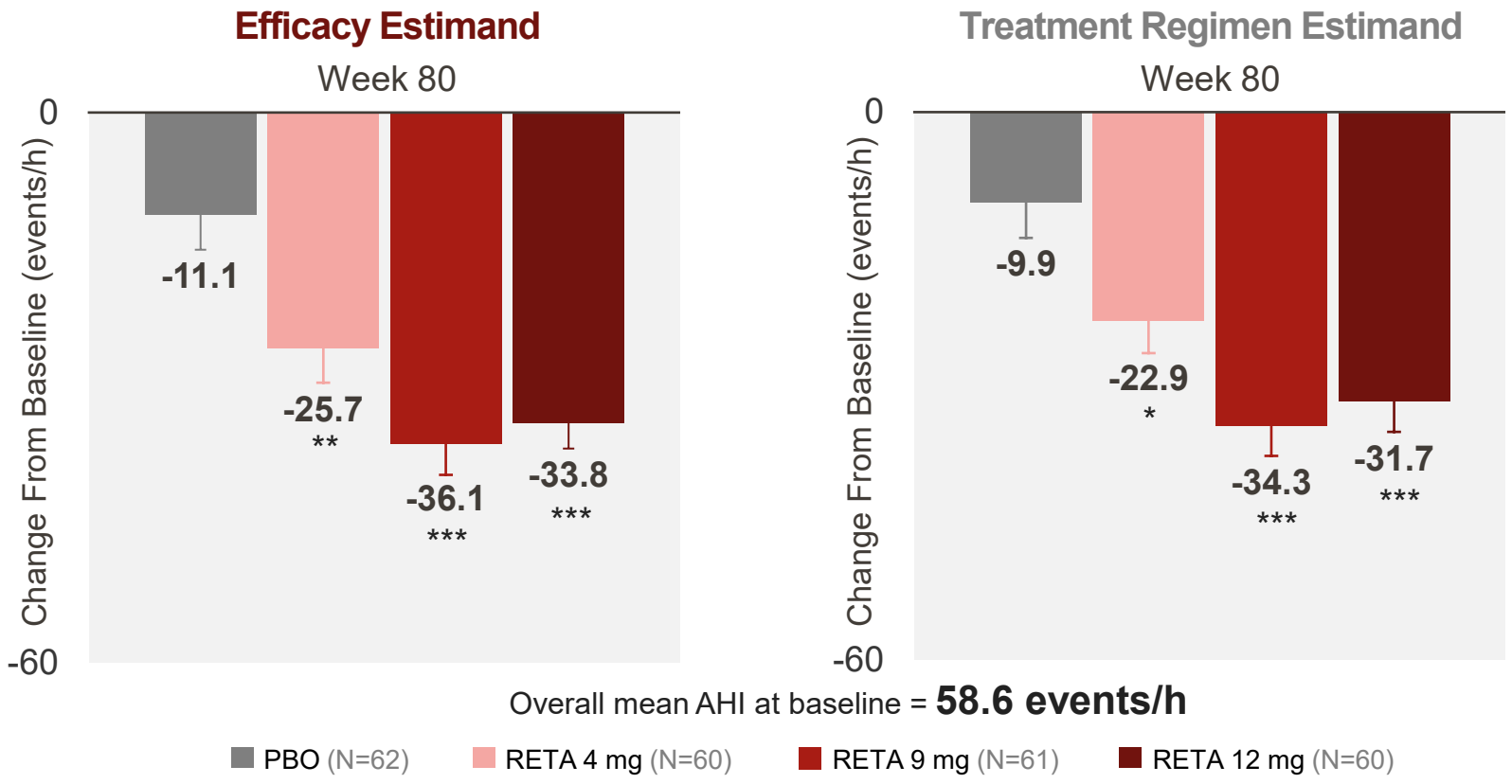
BMI=body mass index; OA=osteoarthritis; PBO=placebo; RETA=retatrutide; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

TRIUMPH-1 OSA Basket

Obstructive Sleep Apnea

N=243 total

Absolute Change in Apnea Hypopnea Index (AHI)



RETA resulted in an AHI reduction more than the clinically significant threshold of 15 events per hr

Which translates to up to more than a 60% decrease in AHI with RETA

*p<0.05, **p<0.01, ***p<0.001 vs PBO.
AHI=Apnea-Hypopnea Index; BMI=body mass index; OSA=obstructive sleep apnea; PBO=placebo; RETA=retatrutide.

TRIUMPH-1

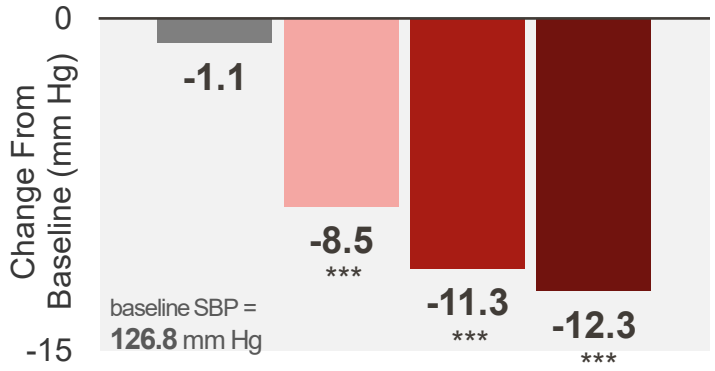
Cardiometabolic Measures and Patient-Reported Outcomes

Cardiometabolic Measures at 80 weeks with Retatrutide

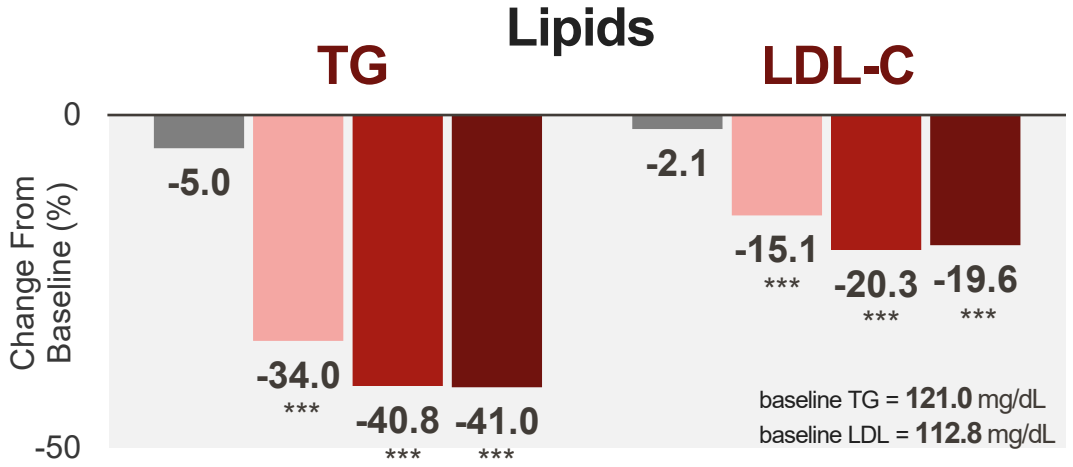
RETATRUTIDE OBESITY TRIUMPH-1

Efficacy Estimand

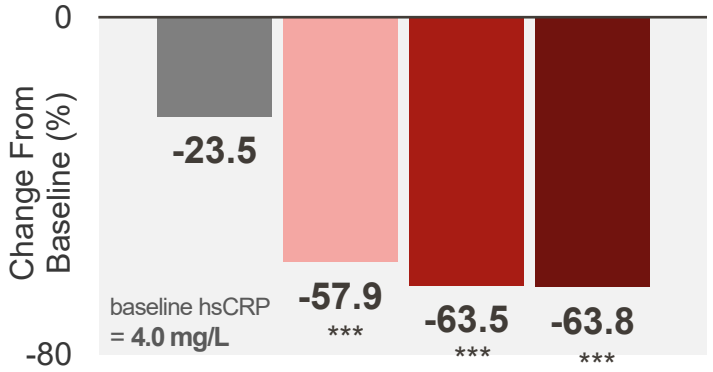
Systolic BP



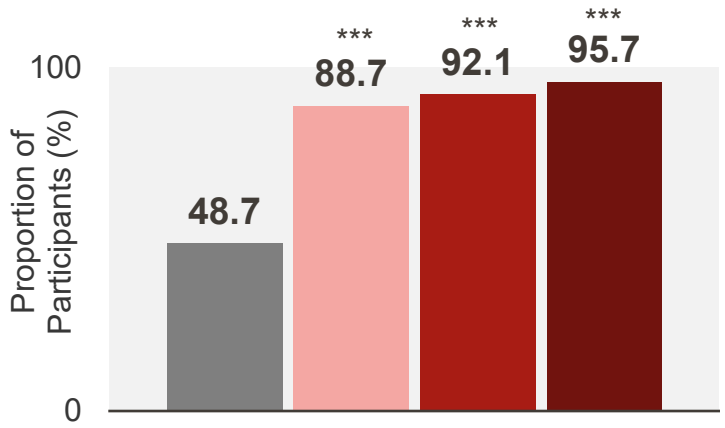
Lipids



hsCRP



Reversion to normoglycemia



Participants with prediabetes at baseline: **36.1%**

PBO RETA 4 mg RETA 9 mg RETA 12 mg

Greater improvements in blood pressure, lipids, hsCRP, and glycemia in all RETA arms than with PBO

***p<0.001 vs PBO

BP=blood pressure; hsCRP=high-sensitivity C-reactive protein; LDL-C=low-density lipoprotein cholesterol; PBO=placebo; RETA=retatrutide; SBP=systolic blood pressure;TG=triglycerides.

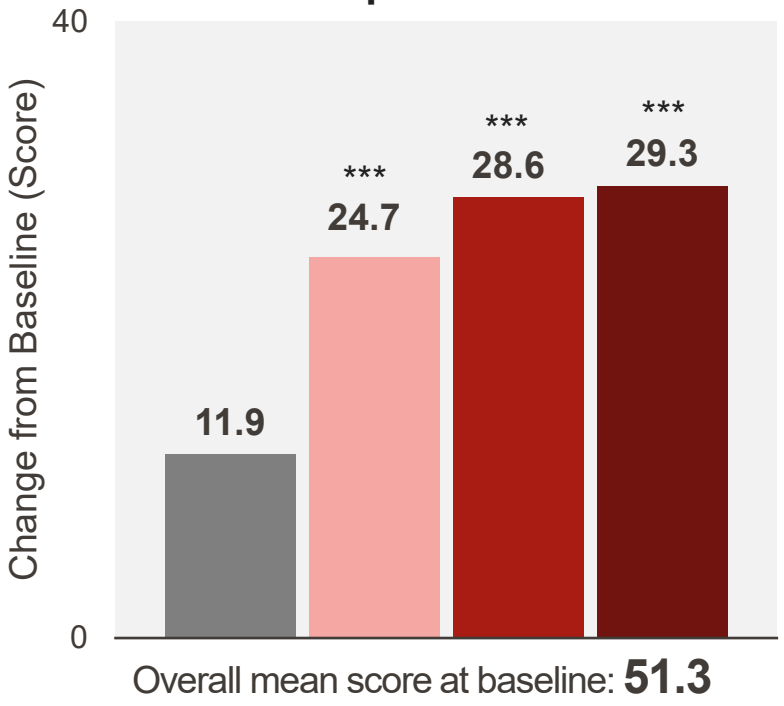
Patient-Reported Outcomes at Week 80 with Retatrutide

RETATRUTIDE OBESITY TRIUMPH-1

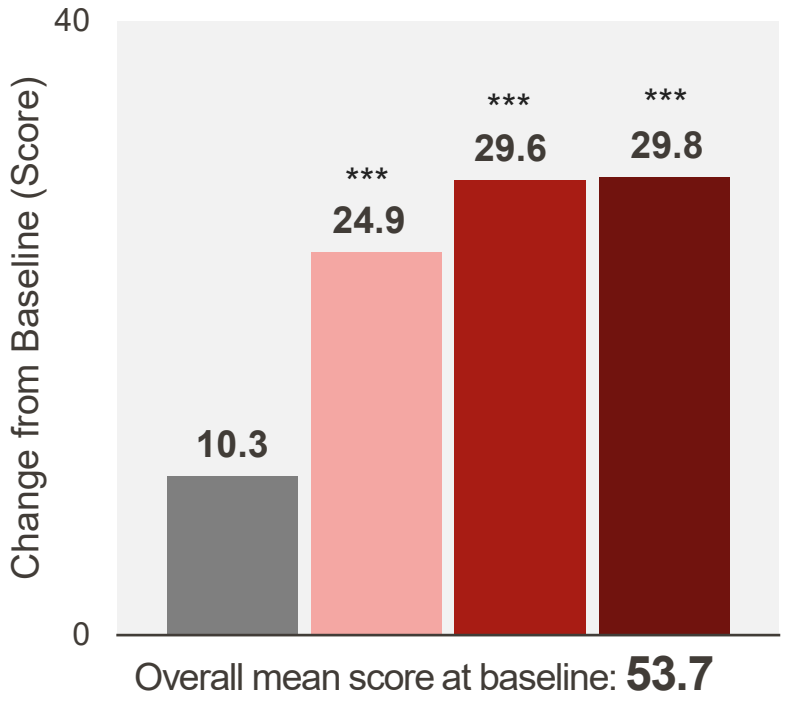
Efficacy Estimand

Impact of Weight on Quality of Life (IWQOL)

Physical Function
Composite Score



Psychosocial
Composite Score



PBO (N=587) RETA 4 mg (N=584) RETA 9 mg (N=584) RETA 12 mg (N=584)

Greater improvements in physical function and psychosocial quality of life measures with RETA than with PBO

.

***p<0.001 vs. PBO.

IWQOL-Lite-CT=Impact of Weight on Quality of Life–Lite Clinical Trials; PBO=placebo; RETA=retatrutide.

TRIUMPH-1

Safety and Tolerability

Overview of Adverse Events

Participants with AEs, n (%)	PBO (N=586)	RETA 4 mg (N=584)	RETA 9 mg (N=583)	RETA 12 mg (N=582)
Participants with ≥1 AE during treatment period	473 (80.7)	508 (87.0)	519 (89.0)	519 (89.2)
Participants with ≥1 serious AE	32 (5.5)	45 (7.7)	45 (7.7)	61 (10.5)
Death[a]	2 (0.3)	0	3 (0.5)	1 (0.2)

Treatment-emergent adverse events were reported in 80.7% of the participants in the PBO group and 87%-89.2% of participants in the RETA groups

Serious adverse events were reported in 5.5% of the participants in the PBO group and 7.7%-10.5% of participants in the RETA groups

[a]All deaths were adjudicated by an external committee of physicians as to whether the death was a cardiovascular-related death or not.
AE=adverse event; PBO=placebo; RETA=retatrutide.

Adverse Events Occurring in ≥5% of Participants

RETATRUTIDE
OBESITY
TRIUMPH-1

Participants with AEs by PT, n (%)	PBO (N=586)	RETA 4 mg (N=584)	RETA 9 mg (N=583)	RETA 12 mg (N=582)
Nausea	87 (14.8)	167 (28.6)	224 (38.4)	247 (42.4)
Diarrhea	79 (13.5)	147 (25.2)	199 (34.1)	186 (32.0)
Constipation	64 (10.9)	139 (23.8)	151 (25.9)	152 (26.1)
Vomiting	28 (4.8)	62 (10.6)	133 (22.8)	147 (25.3)
Upper respiratory tract infection	68 (11.6)	83 (14.2)	71 (12.2)	76 (13.1)
Decreased appetite	34 (5.8)	75 (12.8)	78 (13.4)	96 (16.5)
Headache	45 (7.7)	46 (7.9)	51 (8.7)	51 (8.8)
Fatigue	21 (3.6)	43 (7.4)	62 (10.6)	59 (10.1)
COVID-19	35 (6.0)	44 (7.5)	58 (9.9)	48 (8.2)
Dyspepsia	22 (3.8)	46 (7.9)	52 (8.9)	63 (10.8)
Dizziness	18 (3.1)	29 (5.0)	52 (8.9)	70 (12.0)
Nasopharyngitis	46 (7.8)	51 (8.7)	40 (6.9)	32 (5.5)
Urinary tract infection	28 (4.8)	40 (6.8)	47 (8.1)	47 (8.1)
Gastroesophageal reflux disease	18 (3.1)	40 (6.8)	52 (8.9)	49 (8.4)
Back pain	46 (7.8)	35 (6.0)	35 (6.0)	41 (7.0)
Arthralgia	44 (7.5)	38 (6.5)	42 (7.2)	32 (5.5)
Abdominal pain	11 (1.9)	41 (7.0)	34 (5.8)	60 (10.3)
Eructation	12 (2.0)	40 (6.8)	42 (7.2)	46 (7.9)
Influenza	35 (6.0)	43 (7.4)	29 (5.0)	28 (4.8)

UTIs were reported in 6.8%-8.1% of participants in RETA arms, and 4.8% with PBO, mostly mild to moderate in severity, resolved on treatment, and did not lead to discontinuation; 92% were in female participants

AE=adverse event; COVID-19=coronavirus disease 2019; PBO=placebo; RETA=retatrutide UTI=urinary tract infection.

AEs Leading to Treatment Discontinuation

RETATRUTIDE
OBESITY
TRIUMPH-1

AEs Leading to Treatment Discontinuation by PT, n (%)	PBO (N=586)	RETA 4 mg (N=584)	RETA 9 mg (N=583)	RETA 12 mg (N=582)
Participants with ≥1 AE leading to treatment discontinuation	29 (4.9)	24 (4.1)	40 (6.9)	66 (11.3)
Discontinuation from treatment due to GI AEs	7 (1.2)	13 (2.2)	22 (3.8)	27 (4.6)
Nausea	2 (0.3)	3 (0.5)	8 (1.4)	10 (1.7)
Diarrhea	0	1 (0.2)	3 (0.5)	4 (0.7)
Vomiting	0	1 (0.2)	3 (0.5)	3 (0.5)
Asthenia	0	0	1 (0.2)	3 (0.5)
Pulmonary embolism	1 (0.2)	0	0	2 (0.3)
Sensitive skin	0	1 (0.2)	0	2 (0.3)
Constipation	0	1 (0.2)	2 (0.3)	1 (0.2)
Pancreatitis acute	2 (0.3)	1 (0.2)	2 (0.3)	1 (0.2)
Abdominal pain	0	2 (0.3)	1 (0.2)	1 (0.2)
Fatigue	1 (0.2)	0	1 (0.2)	1 (0.2)
Gastroesophageal reflux disease	0	2 (0.3)	0	1 (0.2)
Malignant melanoma	0	2 (0.3)	0	1 (0.2)
Rash	1 (0.2)	1 (0.2)	1 (0.2)	0

Discontinuation due to adverse event occurred in 4%-11% of participants who received RETA and 5% of those who received PBO

Gastrointestinal adverse events were the most common reason for treatment discontinuation; 2.2-4.6% in the RETA arms and 1.2% in the PBO arm

AE=adverse event; PBO=placebo; PT=preferred term; RETA=retatrutide.

Adverse Event of Special Interest

RETATRUTIDE
OBESITY
TRIUMPH-1

Adverse event of special interest, n (%)	PBO (N=586)	RETA 4 mg (N=584)	RETA 9 mg (N=583)	RETA 12 mg (N=582)
Dysesthesia (skin burning sensation and related)	5 (0.9)	30 (5.1)	72 (12.3)	73 (12.5)
Injection site reactions	22 (3.8)	32 (5.5)	52 (8.9)	71 (12.2)
GI adverse events (severe or serious)	8 (1.4)	15 (2.6)	35 (6.0)	30 (5.2)
Hypotension, orthostatic hypotension, and **blood pressure decreased**	5 (0.9)	16 (2.7)	31 (5.3)	51 (8.8)
Malignancies	6 (1.0)	12 (2.1)	5 (0.9)	11 (1.9)
Arrhythmias & cardiac conduction disorders (severe or serious)	5 (0.9)	1 (0.2)	4 (0.7)	5 (0.9)
Pancreatitis (adjudication-confirmed)	2 (0.3)	1 (0.2)	3 (0.5)	4 (0.7)
Gallbladder / biliary tract disorders (severe or serious)	4 (0.7)	10 (1.7)	5 (0.9)	4 (0.7)
MACE (adjudication-confirmed)	1 (0.2)	1 (0.2)	5 (0.9)	3 (0.5)
Ketoacidosis due to inadequate nutritional intake & other types of **metabolic acidosis / ketosis** (severe or serious)	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.3)
Depression / suicidal ideation / behavior (severe or serious)	1 (0.2)	0	0	1 (0.2)

Most prevalent AESI were dysesthesia, injection site reactions, GI AEs, and reported hypotension, with the latter being more common in participants taking anti-hypertensive medications

AESI=adverse event of special interest; GI=gastrointestinal; MACE=major adverse cardiovascular event; PBO=placebo; RETA=retatrutide.

TRIUMPH-1

Summary

TRIUMPH-1: Summary of Phase 3 Obesity Trial With Retatrutide

RETATRUTIDE OBESITY TRIUMPH-1

Retatrutide, a **once-weekly triple hormone receptor agonist**, was generally well-tolerated and provided substantial reductions in weight as well as clinically meaningful improvements in health outcomes for patients with obesity, OSA, and knee OA

80 weeks (20 months) 12 mg

28.3% body weight

average weight reduction **70.3** lbs (31.9 kg)

Participants in Extension lost up to on average **30% (85 lbs)** at **104 weeks**

Weight Reduction Thresholds

- Nearly **all** lost ≥5%
- Over **85%** lost ≥15%
- More than **1 in 4** lost ≥35%

Anthropometric Treat-to-target

- BMI <30: 2/3
- BMI <25: 1/3
- WtHR <0.5: 1/4

80 weeks 4 mg

19% body weight reduction

1 titration step

Health Outcomes

- **Knee OA**: >**70%** reduction in the **WOMAC pain subscale**
- **OSA**: >**60%** reduction in **AHI**

Prediabetes reverted to **normoglycemia in >95% of participants**

- TG **41.0%**
- LDL **19.6%**
- SBP **12.3** mmHg

Most common side effects with retatrutide were **gastrointestinal** in nature, more frequent with **RETA 9 and 12 mg**

Reported hypotension was more common with **RETA** in participants taking **antihypertensive medication**

UTIs were more common in treatment with RETA and **occurred mostly** in **female participants**

We express our appreciation to the participants of the study, and the investigators and study coordinators who cared for them and the study sponsor, Eli Lilly.

Thank You