LILLY DIABETES

ADA Update

July 1, 2021

Lilly

Introduction
Mike Mason, President, Lilly Diabetes

SURPASS Overview
Jeff Emmick, M.D., Ph.D., Vice President, Lilly Diabetes Product Development

Early Phase Diabetes
Ruth Gimeno, Ph.D., Vice President, Lilly Diabetes and Metabolic Research

Q&A

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 may affect the company's business and could cause actual results to differ materially, please see the company's latest Form 10-K, subsequent 10-Q, and 8-K filed with the Securities and Exchange Commission.

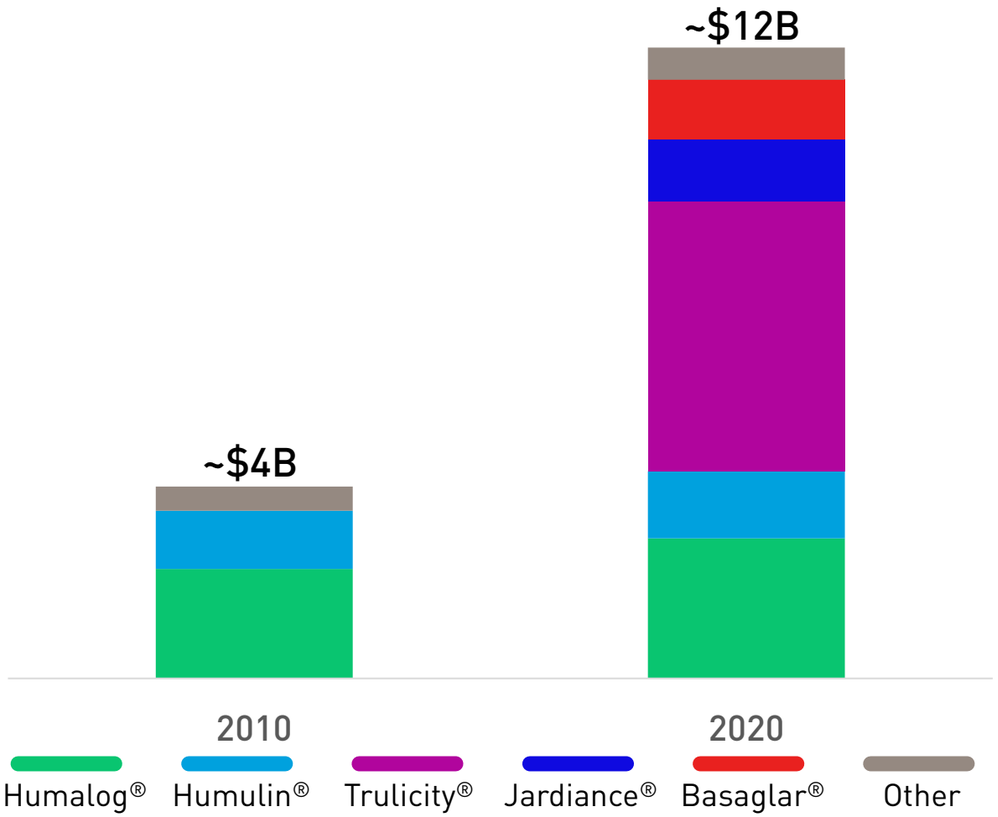
The company undertakes no duty to update forward-looking statements

MOMENTUM IN DIABETES BUSINESS

SIGNIFICANT GROWTH IN THE PAST DECADE WITH DIVERSE OPPORTUNITIES IN THE FUTURE

2010-2020
GROWTH BEYOND INSULIN

DIABETES WORLDWIDE REVENUE HAS MORE THAN TRIPLED



2020-2030
DIABETES & RELATED METABOLIC DISORDERS

- **Trulicity**: Additional doses and cardiovascular outcomes reinforce market leadership and are catalysts for continued class growth
- **Jardiance**: Continued market leadership in growing SGLT-2 inhibitor class with potential NILEX opportunities in HFrEF, HFpEF and CKD
- **Insulin**: Connected care potential to improve patient outcomes
- **Tirzepatide**: Potential paradigm changing treatment in type 2 diabetes with expanding NILEX opportunities in obesity and other metabolic disorders
- **Early-stage pipeline**: Opportunities across classes including basal insulin FC, GGG and oral incretins

Note: Jardiance and Basaglar are part of the Boehringer Ingelheim (BI) and Lilly Alliance and BI holds the marketing authorization for Jardiance; NILEX = line extension; HFrEF = heart failure with reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; CKD = chronic kidney disease; GGG = GIP, GLP-1 and Glucagon triple receptor agonist

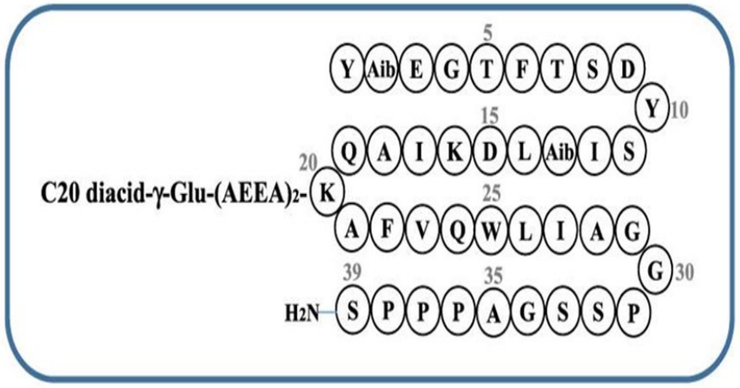
TIRZEPATIDE SURPASS PROGAM OVERVIEW & NEXT STEPS

TIRZEPATIDE DEVELOPMENT

AN EVOLUTION IN INCRETIN INNOVATION THAT MAY PROVIDE EARLY CONTROL OF GLUCOSE & BODY WEIGHT

TIRZEPATIDE OVERVIEW

- Multi-functional peptide based on the native GIP peptide sequence, modified to bind to both GIP and GLP-1 receptors
- GIP may enhance GLP-1's effect on food intake and increase energy expenditure, resulting in body weight reduction
- Mean half-life of ~5 days enabling once-weekly dosing; same user-friendly autoinjector as Trulicity

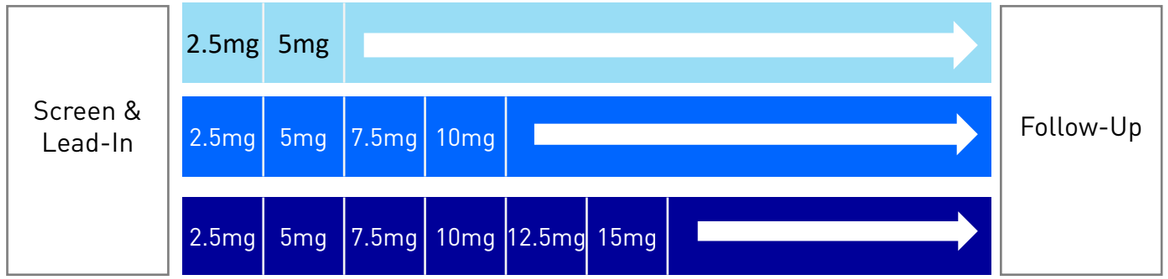


Coskun et al. *Mol Metab.* 2018. 18;3-14.

SURPASS PHASE 3 DESIGN

- Goal to replicate efficacy in HbA1c and weight loss shown in Phase 2b trial
- Optimized dose escalation scheme with low starting dose implemented to improve tolerability profile

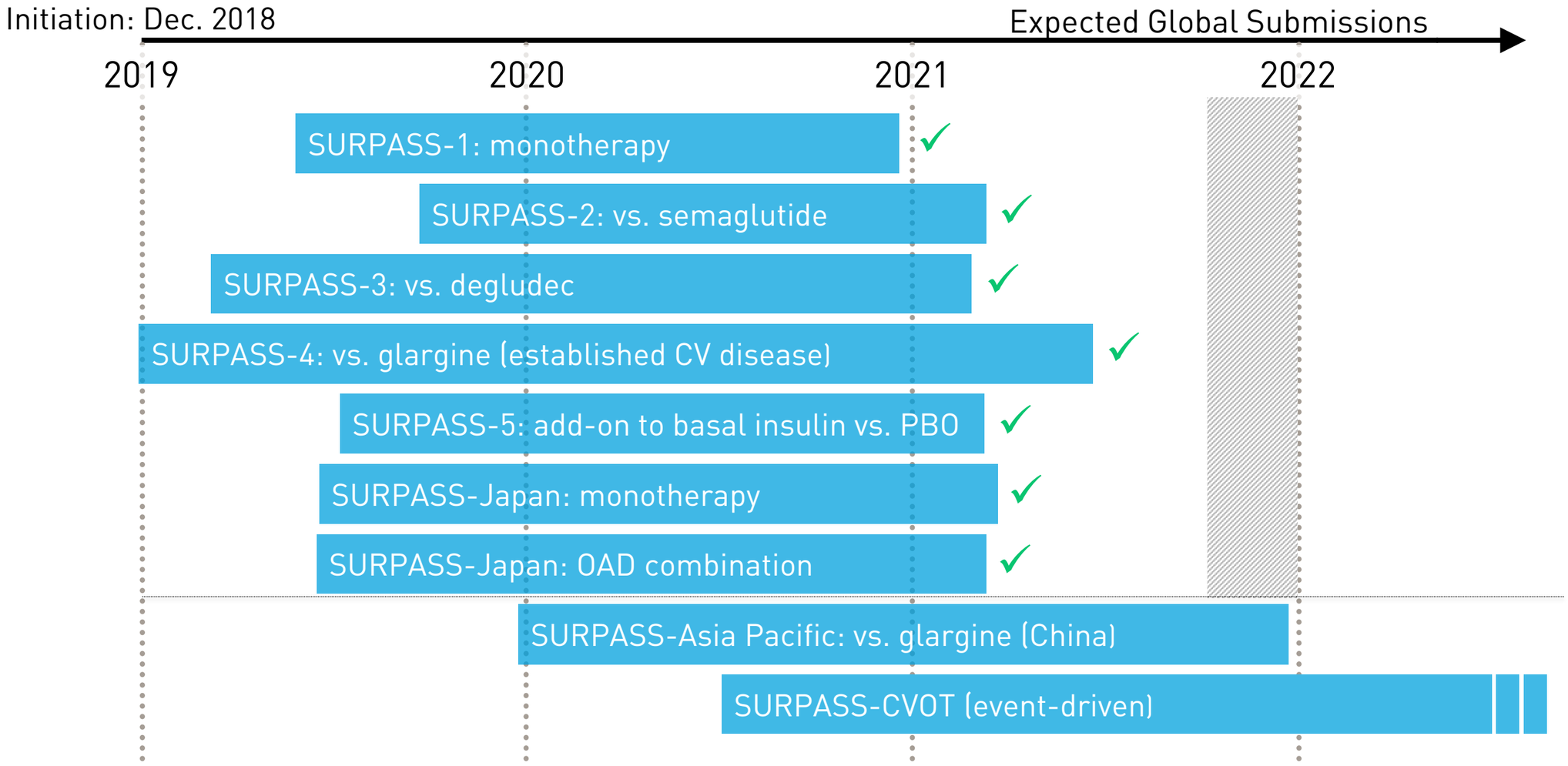
Dose Escalation Over 40-104 Week Treatment Period



Tirzepatide patients began on 2.5mg dose, increasing every 4 weeks until reaching target dose

SURPASS GLOBAL REGISTRATION PROGRAM

DESIGNED TO DELIVER ROBUST DATASET IN TYPE 2 DIABETES WITH MULTIPLE HEAD-TO-HEAD TRIALS



CV=cardiovascular; CVOT=cardiovascular outcomes trial; OAD=oral antidiabetic drug
Primary completion for SURPASS-CVOT is estimated for 2024 (event driven)

SURPASS KEY BASELINE CHARACTERISTICS

TIRZEPATIDE EVALUATED ACROSS A BROAD PATIENT POPULATION

	SURPASS-1 vs. placebo (no background therapy)	SURPASS-2 vs. semaglutide 1mg (metformin required)	SURPASS-3 vs. insulin degludec (metformin required +/- SGLT-2i)	SURPASS-4 vs. insulin glargine in patients with increased CV Risk (any combo metformin, SGLT-2i & SUs)	SURPASS-5 Add-on to insulin glargine (metformin allowed)
MEAN HBA1C (%)	7.9	8.3	8.2	8.5	8.3
MEAN WEIGHT (KG)	85.9	93.7	94.3	90.3	95.2
MEAN DURATION OF DIABETES (YEARS)	4.7	8.6	8.4	11.8	13.3
BACKGROUND OAM	N/A	✓	✓	✓	✓

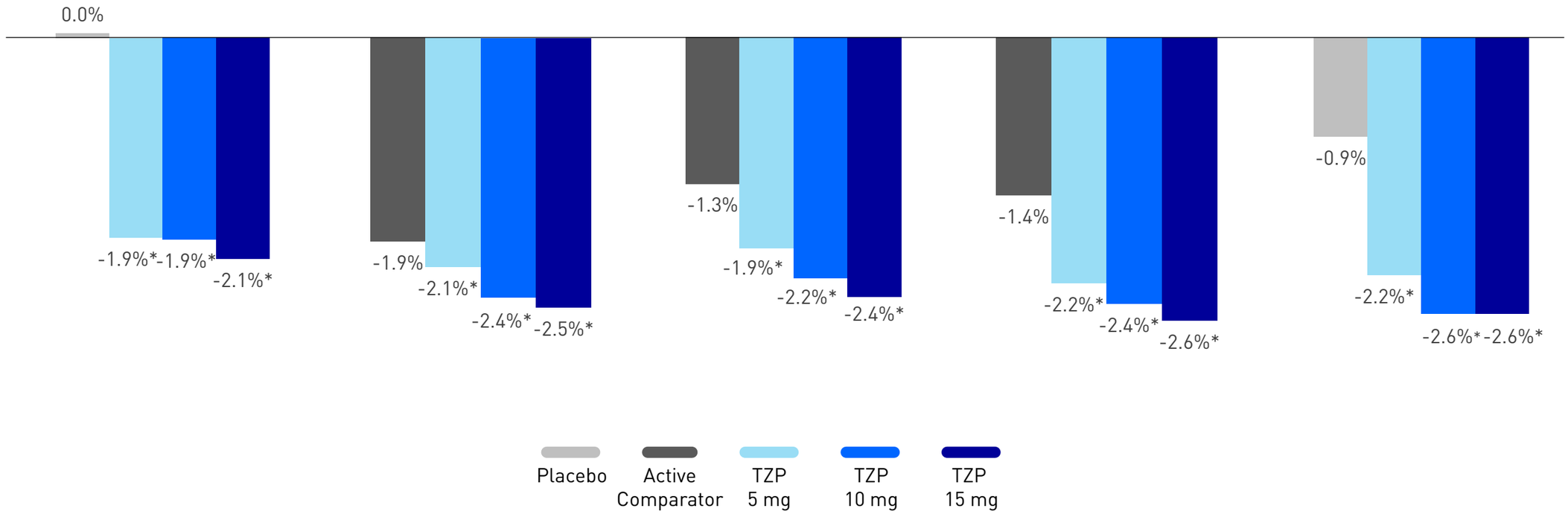
SU = Sulphonylureas; SGLT2i = Sodium-glucose Cotransporter-2 inhibitors; OAM = Oral Antidiabetic Medication

CONSISTENT HBA1C IMPROVEMENT ACROSS SURPASS TRIALS

TIRZEPATIDE WAS STATISTICALLY SIGNIFICANT IN HBA1C REDUCTION VERSUS ALL COMPARATORS STUDIED

	SURPASS-1 vs. placebo (40 weeks)	SURPASS-2 vs. semaglutide 1mg (40 weeks)	SURPASS-3 vs. insulin degludec (52 weeks)	SURPASS-4 vs. insulin glargine (52 weeks)	SURPASS-5 add on to insulin glargine (40 weeks)
Baseline HbA1c (%)	7.9	8.3	8.2	8.5	8.3

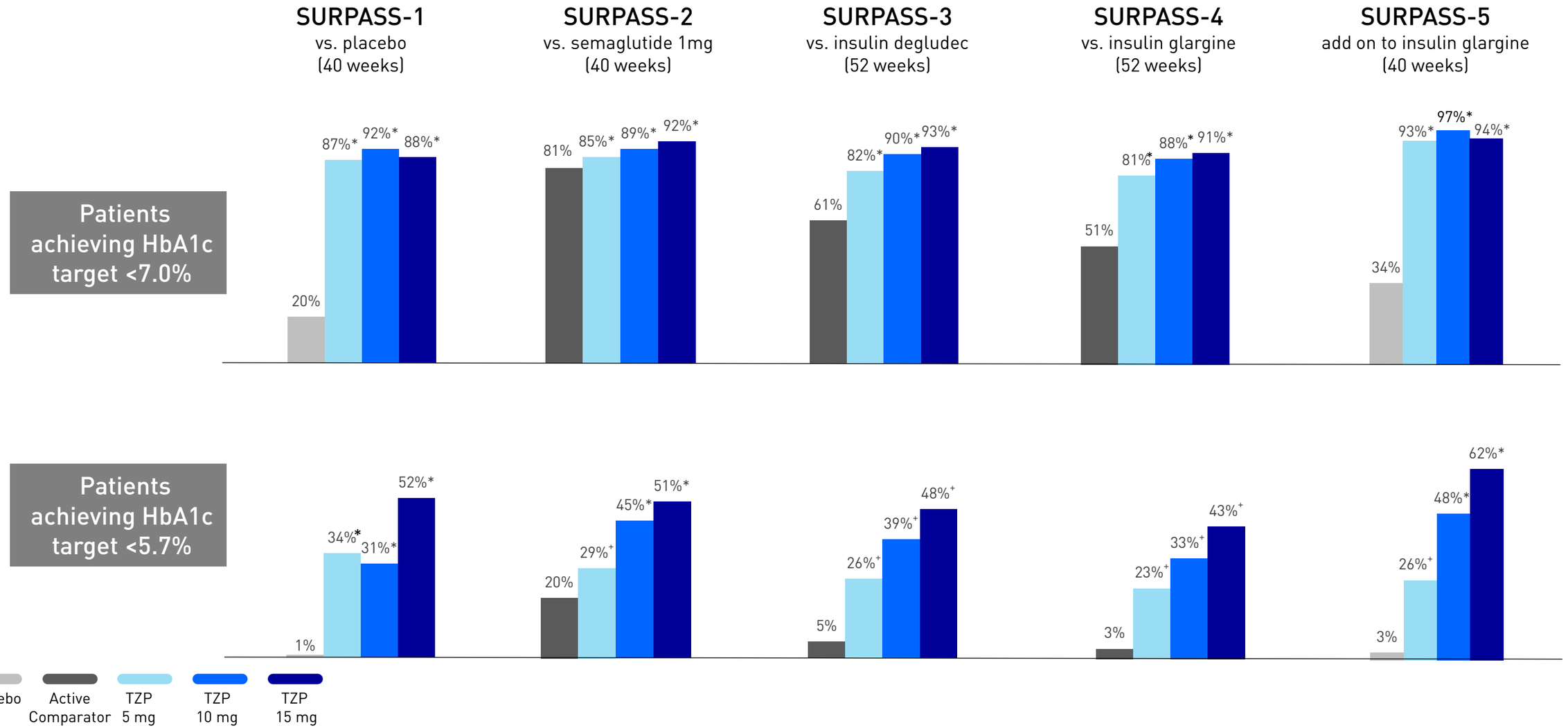
HbA1c reduction



*denotes statistical significance to comparator
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

SURPASS ACHIEVEMENT OF HBA1C TARGETS ACROSS TRIALS

TIRZEPATIDE HELPED UP TO 97% AND 62% OF PATIENTS REACH HBA1C BELOW 7.0% AND 5.7%, RESPECTIVELY



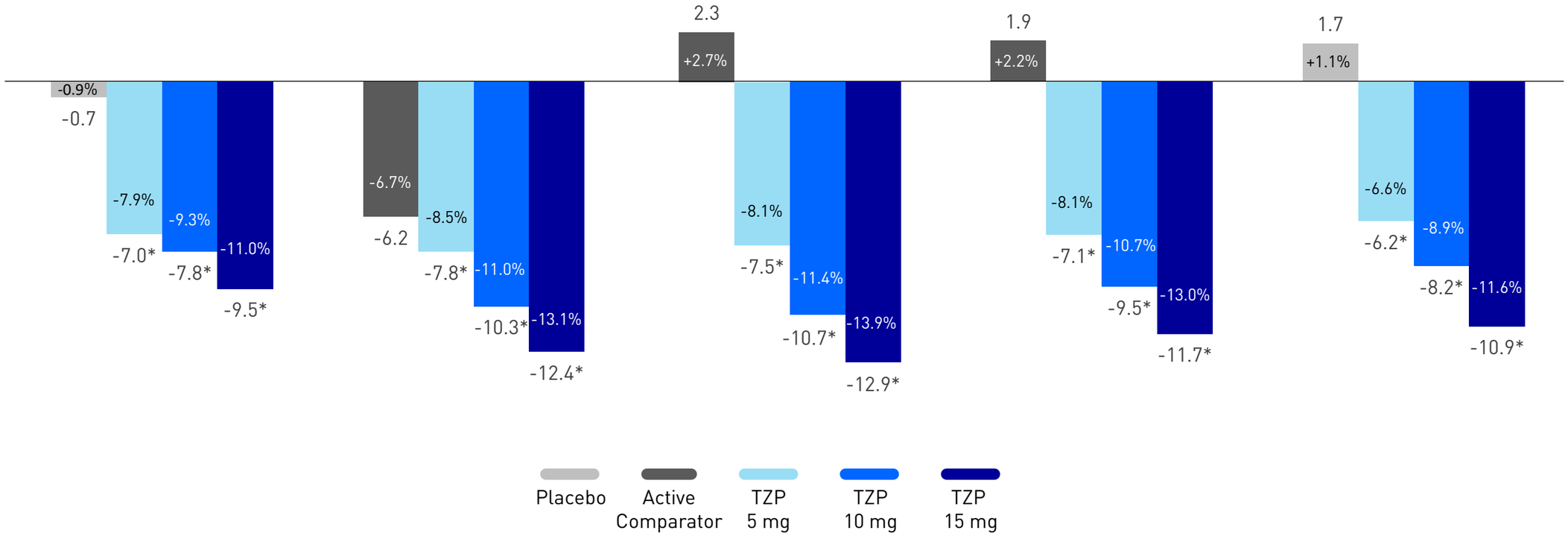
*denotes statistical significance to comparator; + denotes not controlled for type 1 error
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

CONSISTENT WEIGHT LOSS ACROSS SURPASS TRIALS

TIRZEPATIDE WAS STATISTICALLY SIGNIFICANT IN WEIGHT REDUCTION VERSUS ALL COMPARATORS STUDIED

	SURPASS-1 vs. placebo (40 weeks)	SURPASS-2 vs. semaglutide 1mg (40 weeks)	SURPASS-3 vs. insulin degludec (52 weeks)	SURPASS-4 vs. insulin glargine (52 weeks)	SURPASS-5 add on to insulin glargine (40 weeks)
Baseline Weight (kg)	85.9	93.7	94.3	90.3	95.2

Body weight reduction (kg)

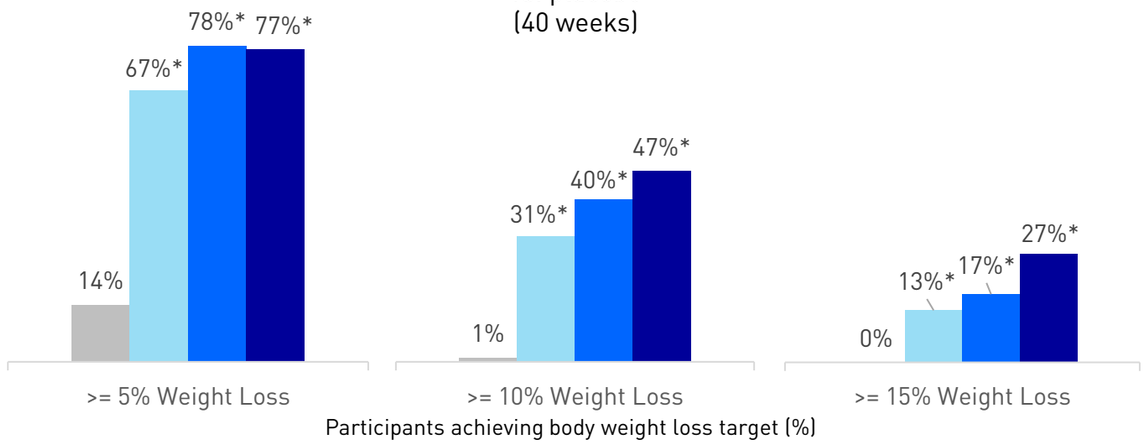


*denotes statistical significance to comparator
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

PROPORTION OF PARTICIPANTS ACHIEVING WEIGHT LOSS GOALS

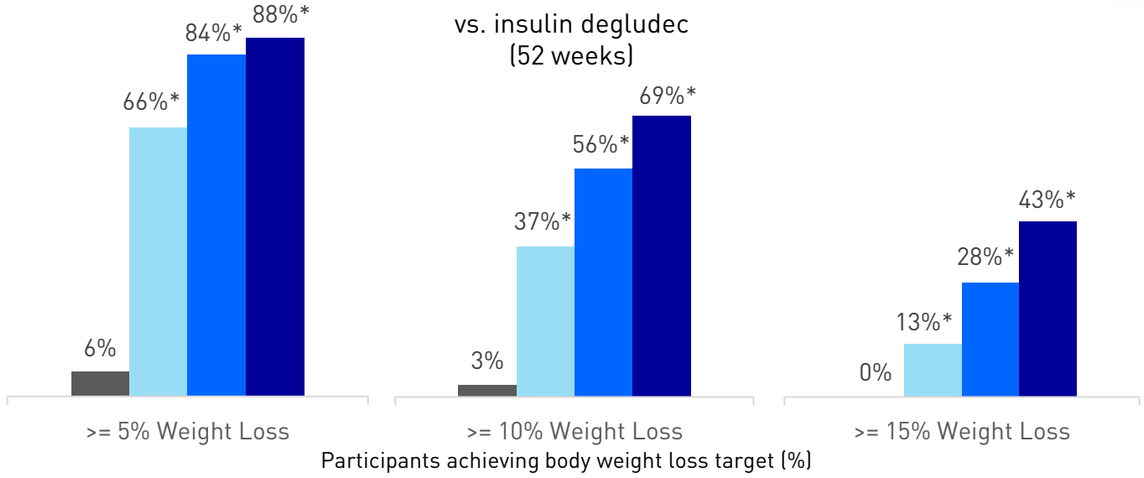
TIRZEPATIDE HELPED UP TO 43% OF PATIENTS ACHIEVE A WEIGHT LOSS TARGET OF GREATER OR EQUAL TO 15%

SURPASS-1
vs. placebo
(40 weeks)



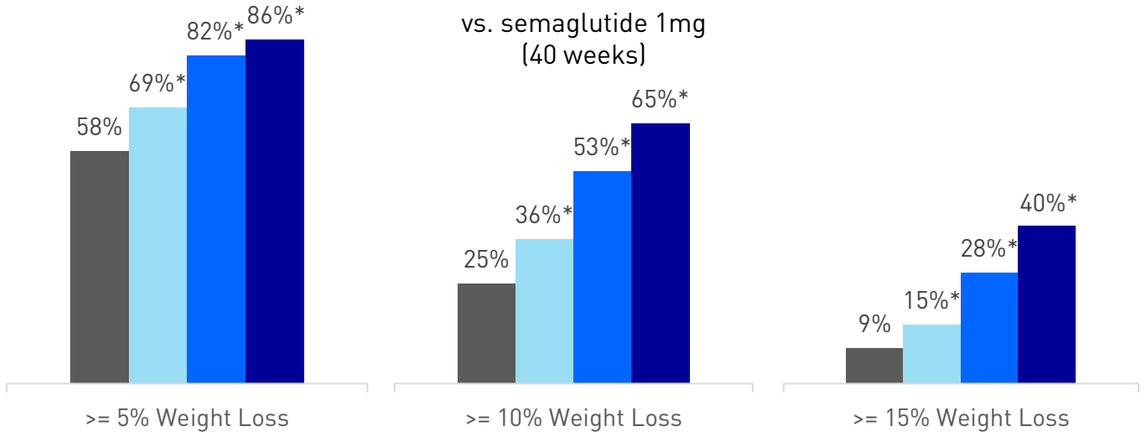
Participants achieving body weight loss target (%)

SURPASS-3
vs. insulin degludec
(52 weeks)



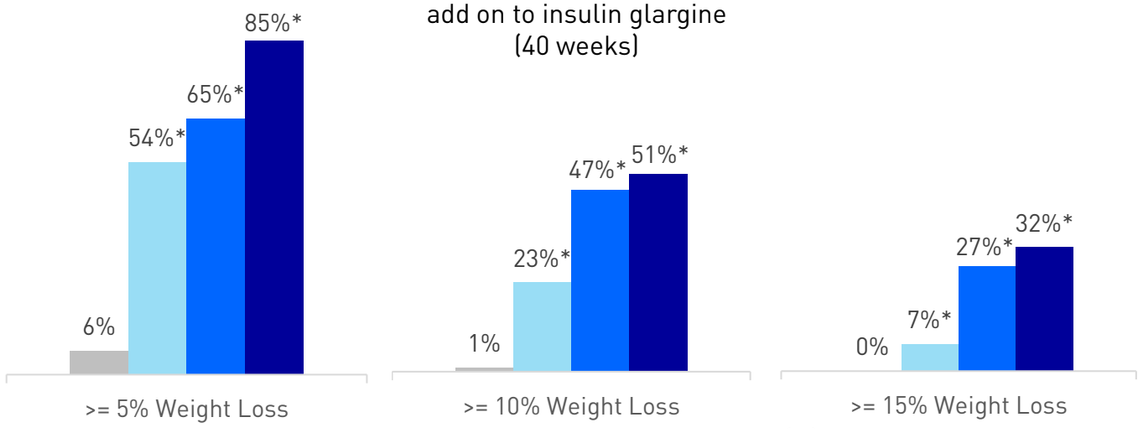
Participants achieving body weight loss target (%)

SURPASS-2
vs. semaglutide 1mg
(40 weeks)



Participants achieving body weight loss target (%)

SURPASS-5
add on to insulin glargine
(40 weeks)



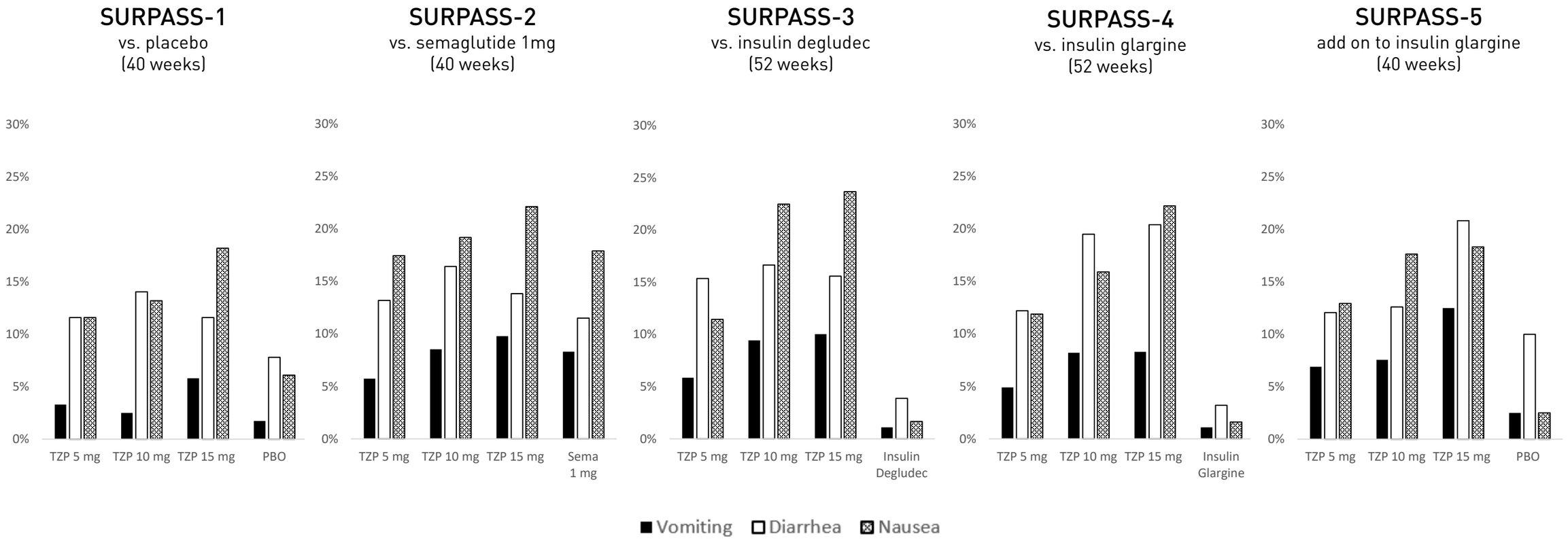
Participants achieving body weight loss target (%)

Placebo | Active Comparator | TZP 5 mg | TZP 10 mg | TZP 15 mg

*denotes statistical significance to comparator; All TZP arms were not controlled for type 1 error
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

SURPASS GI TOLERABILITY

TOLERABILITY PROFILE CONSISTENT WITH THE WELL ESTABLISHED GLP-1 RECEPTOR AGONIST CLASS



Most cases of nausea, vomiting and diarrhea were mild-to-moderate and most frequently occurred during the dose-escalation period across all doses of tirzepatide and SURPASS studies

GI = gastrointestinal; TZP = tirzepatide; sema = semaglutide; PBO = placebo

SURPASS SAFETY PROFILE

SAFETY AND CV DATA FROM REGISTRATION TRIALS OFFER CONFIDENCE IN TIRZEPATIDE

SAFETY TAKEAWAYS

- Overall safety profile consistent with GLP-1 receptor agonist class in the patient populations studied
- Most frequent adverse events were mild-to-moderate, gastrointestinal-related and occurred during the dose escalation period
- Discontinuation of study drug due to adverse events ranged from 3% to 11%
- Hypoglycemia was low in the SURPASS program when tirzepatide was not combined with a sulfonylurea or insulin

CARDIOVASCULAR TAKEAWAYS

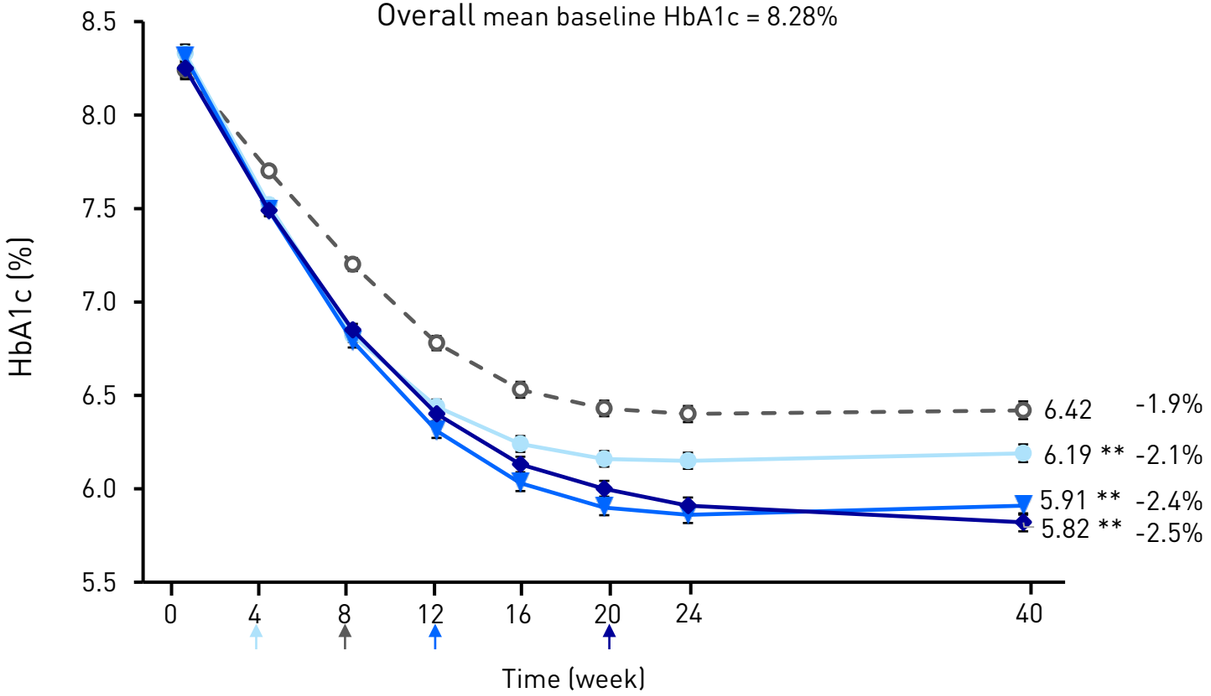
- The SURPASS program has met regulatory submission requirements for evaluating cardiovascular risk
- Hazard ratio of 0.81 attained for pooled SURPASS data of MACE-4 events; (97.85% CI, 0.52 to 1.26)
- SURPASS-4 contributed the majority of the MACE-4 events with a hazard ratio of 0.74; (95% CI, 0.51 to 1.08)
- SURPASS-CVOT, which will assess cardiovascular benefit, was initiated in June 2020 and is expected to read out in 2024
- Phase 3 SUMMIT study evaluating tirzepatide in HFpEF initiated in Q2 2021

MACE-4 = a composite endpoint of death from cardiovascular or undetermined causes, myocardial infarction, stroke and hospitalization for unstable angina; CI = Confidence interval

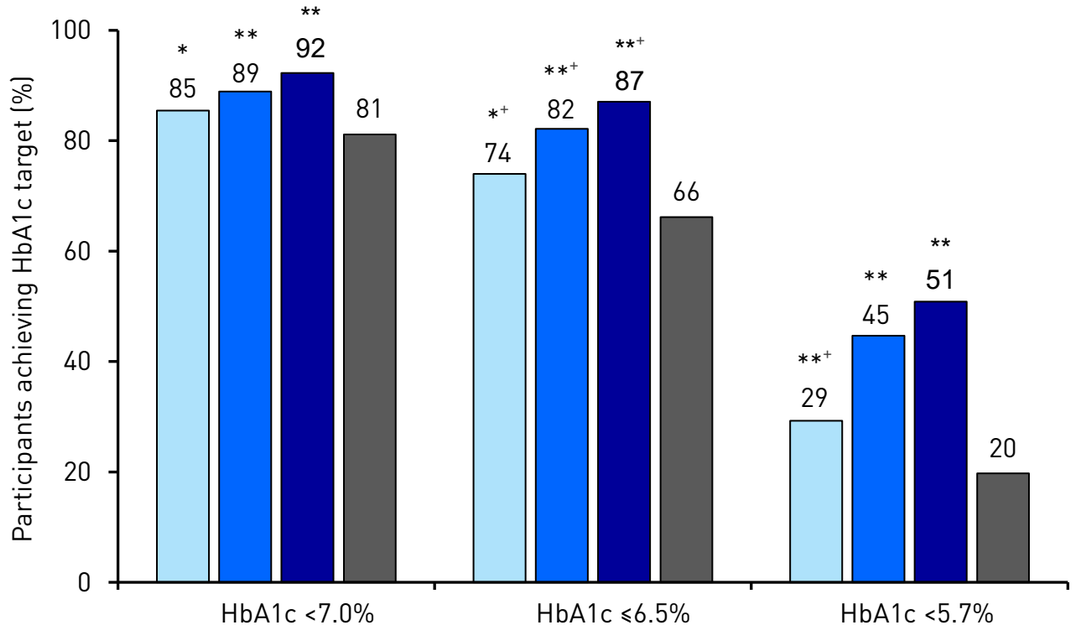
SURPASS-2: HBA1C IMPROVEMENT

TIRZEPATIDE SHOWED SUPERIOR A1C REDUCTION AS COMPARED TO SEMAGLUTIDE ACROSS DOSES

HBA1C OVER TIME



HBA1C TARGET THRESHOLDS

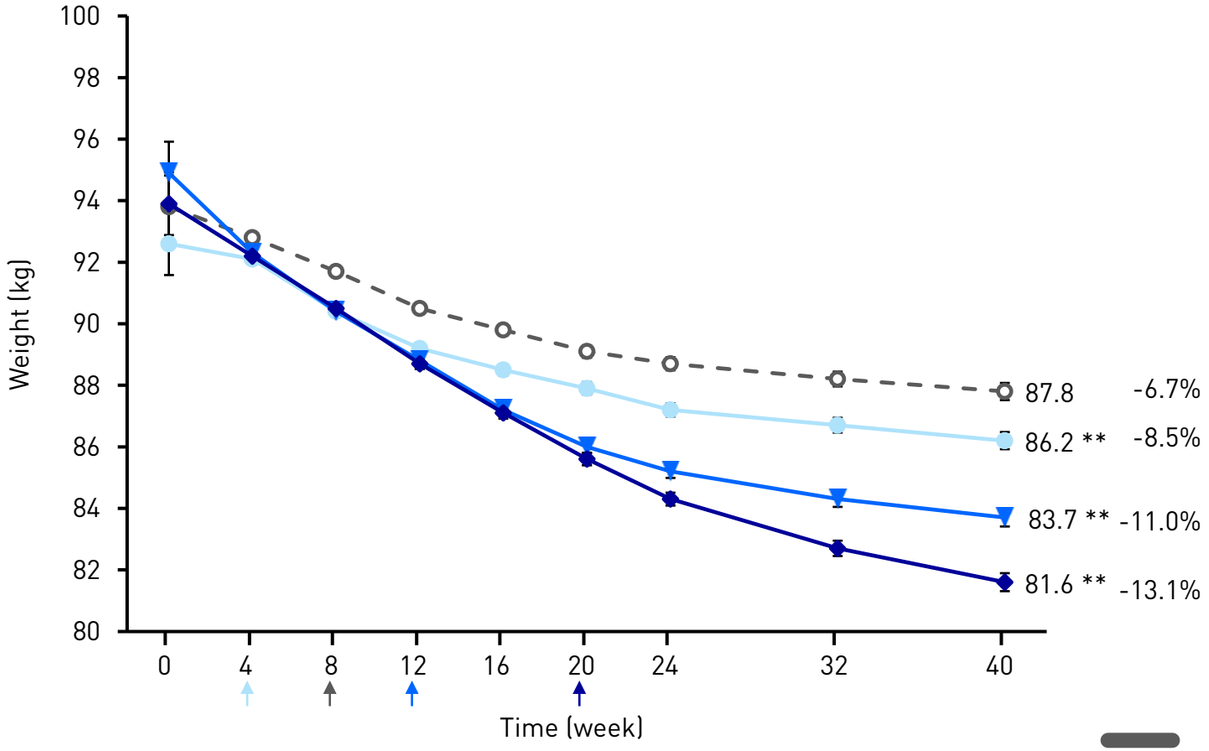


TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia
HBA1C over time: Data are LSM (SE); mITT (efficacy estimand) ANOVA analysis (week 0) and MMRM analysis (week 40); ITT is any patient who is randomized, and mITT is any patient who is randomized and has had one dose of the treatment; Arrows indicate when the maintenance dose of tirzepatide 5 mg, 10 mg and 15 mg and semaglutide 1 mg are achieved. **p<0.001 vs. semaglutide 1 mg
HBA1C target thresholds: Data are estimated mean; mITT (full analysis set). Logistic regression. *p<0.05, **p<0.001 vs. semaglutide 1 mg ; + denotes not controlled by type 1 error

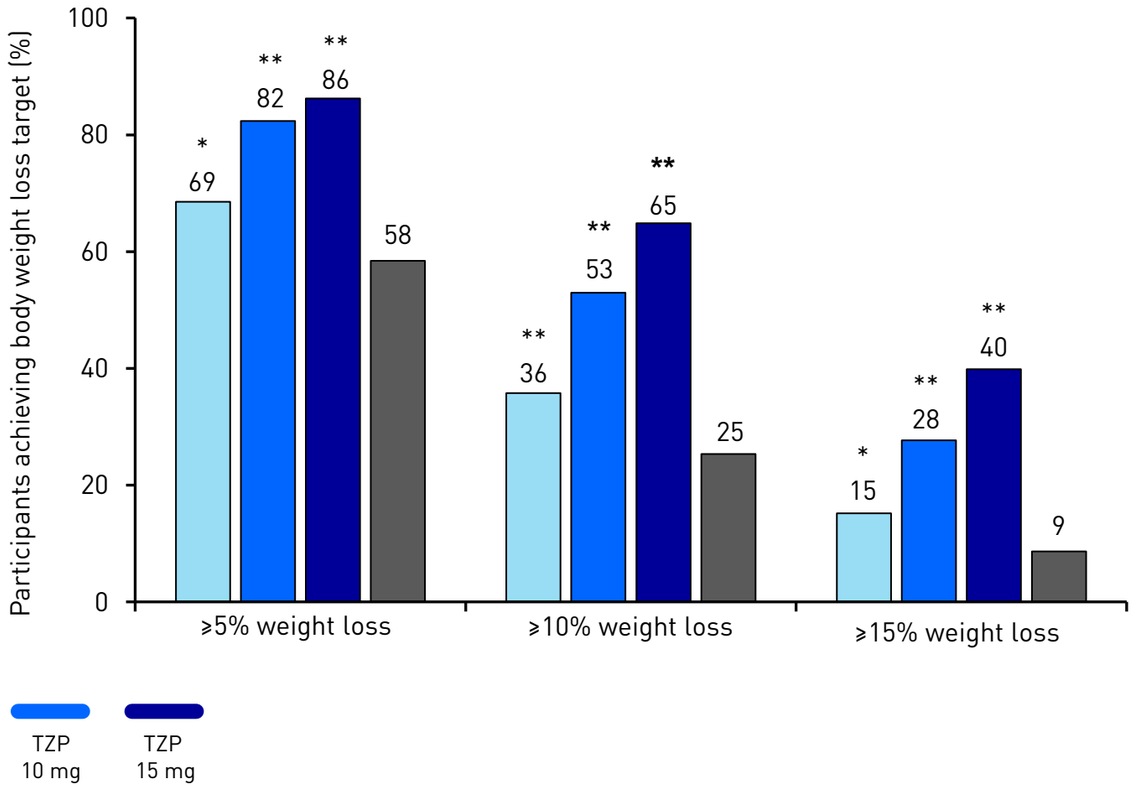
SURPASS-2: WEIGHT LOSS

TIRZEPATIDE SHOWED SUPERIOR WEIGHT LOSS AS COMPARED TO SEMAGLUTIDE ACROSS DOSES

BODY WEIGHT OVER TIME



WEIGHT LOSS THRESHOLDS



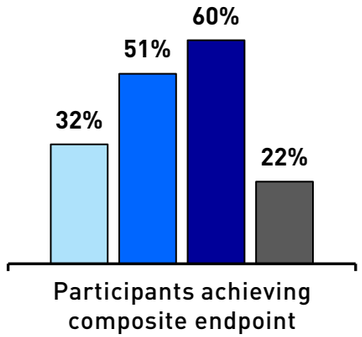
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia
Body weight over time: Data are LSM (SE); mITT (efficacy estimand) ANOVA analysis (week 0) and MMRM analysis (week 40). ITT is any patient who is randomized, and mITT is any patient who is randomized and has had one dose of the treatment; Arrows indicate when the maintenance dose of tirzepatide 5 mg, 10 mg and 15 mg and semaglutide 1 mg are achieved. **p<0.001 vs. semaglutide 1 mg
Weight loss thresholds: Data are estimated mean; mITT (full analysis set). Logistic regression. *p<0.05, **p<0.001 vs. semaglutide 1 mg; All TZP arms were not controlled for type 1 error

SURPASS-2: ADDITIONAL DATA

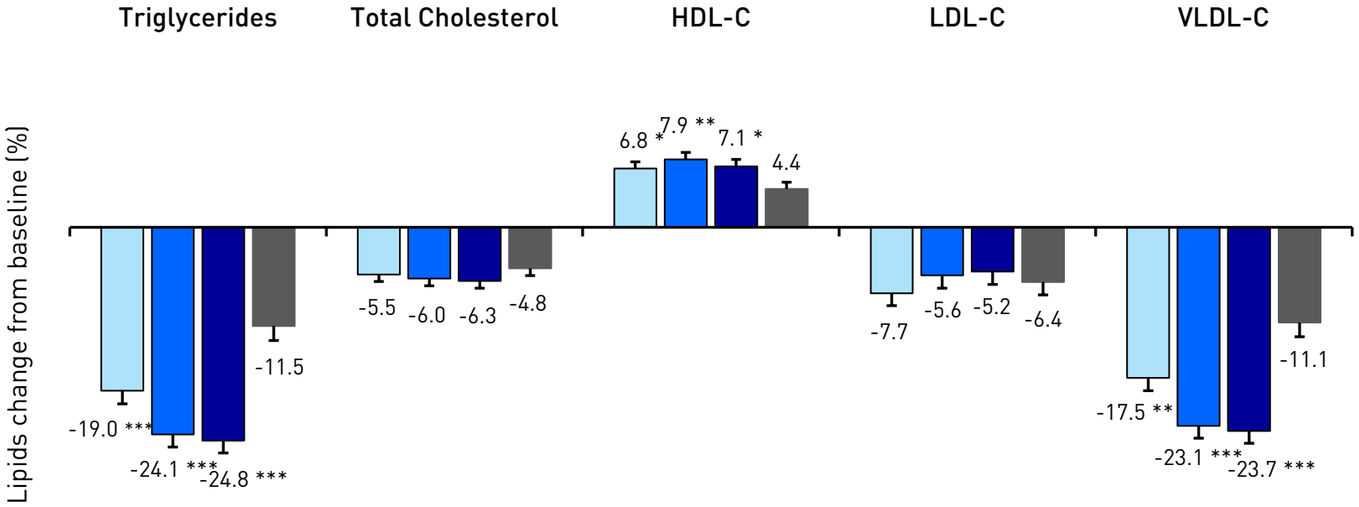
TIRZEPATIDE SHOWED BENEFIT FOR COMPOSITE ENDPOINT AND LIPID PROFILE COMPARED TO SEMAGLUTIDE

COMPOSITE ENDPOINT

- **Prespecified exploratory composite endpoint comprised of participants who:**
  - Achieved an A1C <= 6.5%
  - Achieved weight loss >= 10%
  - Did not experience hypoglycemia < 54 mg/dL or severe hypoglycemia
- **Up to 60% of participants on tirzepatide achieved composite endpoint compared to 22% on semaglutide**



LIPID PROFILE



- Patients on tirzepatide had improved lipid profile, blood pressure, biomarkers of insulin sensitivity and liver enzymes
- Near normal glycemia, weight loss, blood pressure decrease and lipid control increase confidence in potential overall metabolic health improvement

Semaglutide 1 mg | TZP 5 mg | TZP 10 mg | TZP 15 mg

MMRM analysis, mITT population (efficacy analysis set). ITT is any patient who is randomized, and mITT is any patient who is randomized and has had one dose of the treatment; Data presented are the estimated means ± standard errors; TZP vs. semaglutide at 40 weeks: *p<0.05, **p<0.01, ***p<0.001; All TZP arms were not controlled for type 1 error; HbA1c below 5.7% is considered normal levels based on ADA guidelines; HDL-C = High-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; VLDL-C = very low-density lipoprotein cholesterol

TIRZEPATIDE GIP/GLP-1 MECHANISM OF ACTION

COMPREHENSIVE SET OF MOA STUDIES IN PATIENTS WITH AND WITHOUT DIABETES

Insulin Secretion and Insulin Action Study

- People with type 2 diabetes
- Tirzepatide vs placebo vs semaglutide
- Evaluated effects on α and β-cell function, insulin sensitivity and energy balance
- Study completed, will be included in type 2 diabetes submission (NCT03951753)

Hypoglycemia Recovery Study

- People with type 2 diabetes
- Tirzepatide vs placebo
- Will evaluate ability to recover from hypoglycemia and effects on glucagon concentration during induced hypoglycemia
- Study recruiting (NCT04050553)

Energy Expenditure and Food Intake Study

- People with obesity and other comorbidities
- Tirzepatide vs placebo
- Will evaluate effects on sleep metabolic rate and 24 hour energy expenditure, food intake and appetite
- Study recruiting (NCT04081337)

Brain Activation Study

- People with obesity or who are overweight
- Tirzepatide vs placebo vs liraglutide
- Will evaluate effects on appetite and reward pathways in the brain in relation to regulation of food intake
- Study recruiting (NCT04311411)

MOA = mechanism of action

NEXT STEPS FOR TYPE 2 DIABETES

SURPASS PROGRAM

- Submission requirements have been met
- SURPASS-4, Insulin Secretion and Insulin Action MoA Study, SURPASS-3 CGM and SURPASS-3 MRI studies to be presented at EASD
- Global submissions expected by the end of 2021
- SURPASS-CVOT trial expected to read out in 2024

COMMERCIAL OPPORTUNITIES

- Evolution in incretin innovation for the treatment of patients with type 2 diabetes
- Early and unsurpassed A1C and weight reductions for people with type 2 diabetes across doses
- Possible expansion of the incretin market
- Potential to be a best-in-class incretin based on efficacy even at the 5 mg dose

MoA = mechanism of action; CGM = continuous glucose monitoring; MRI = magnetic resonance imaging

TIRZEPATIDE DEVELOPMENT PROGRAM

FIVE INDICATIONS BEING STUDIED DRIVEN BY POTENTIAL FROM GIP/GLP-1 MECHANISM

Type 2 Diabetes
SURPASS Phase 3 data may disrupt the current treatment paradigm

Cardiovascular Disease
SURPASS-CVOT primary completion estimated for 2024

Obesity
Phase 3 SURMOUNT studies initiated

TIRZEPATIDE
Dual GIP/GLP-1 Agonist

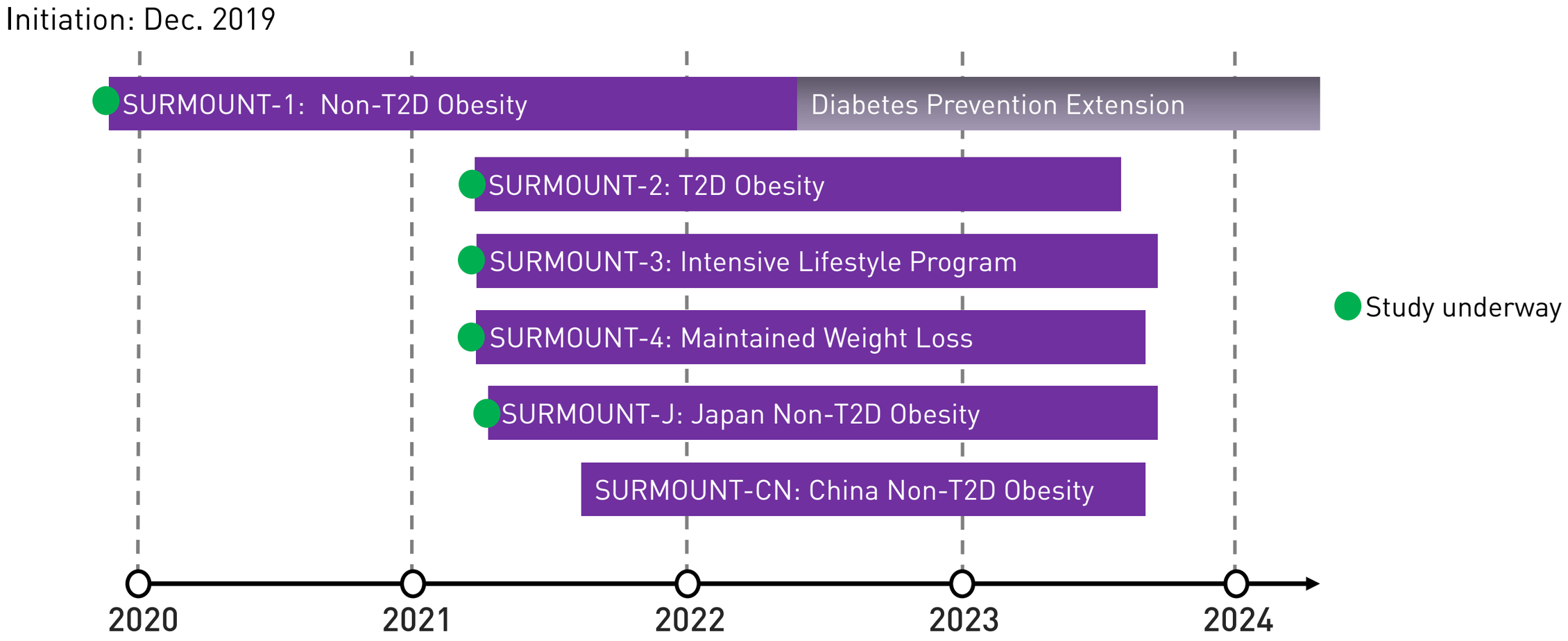
NASH
Phase 2 SYNERGY-NASH study initiated in Q4 2019

HFpEF
Phase 3 SUMMIT study initiated in Q2 2021

CVOT = Cardiovascular outcomes trial; NASH = Non-alcoholic steatohepatitis (nonalcoholic fatty liver disease)

SURMOUNT PHASE 3 PROGRAM

DESIGNED TO DELIVER ROBUST DATASET IN OBESITY WITH DIVERSE SET OF TRIALS



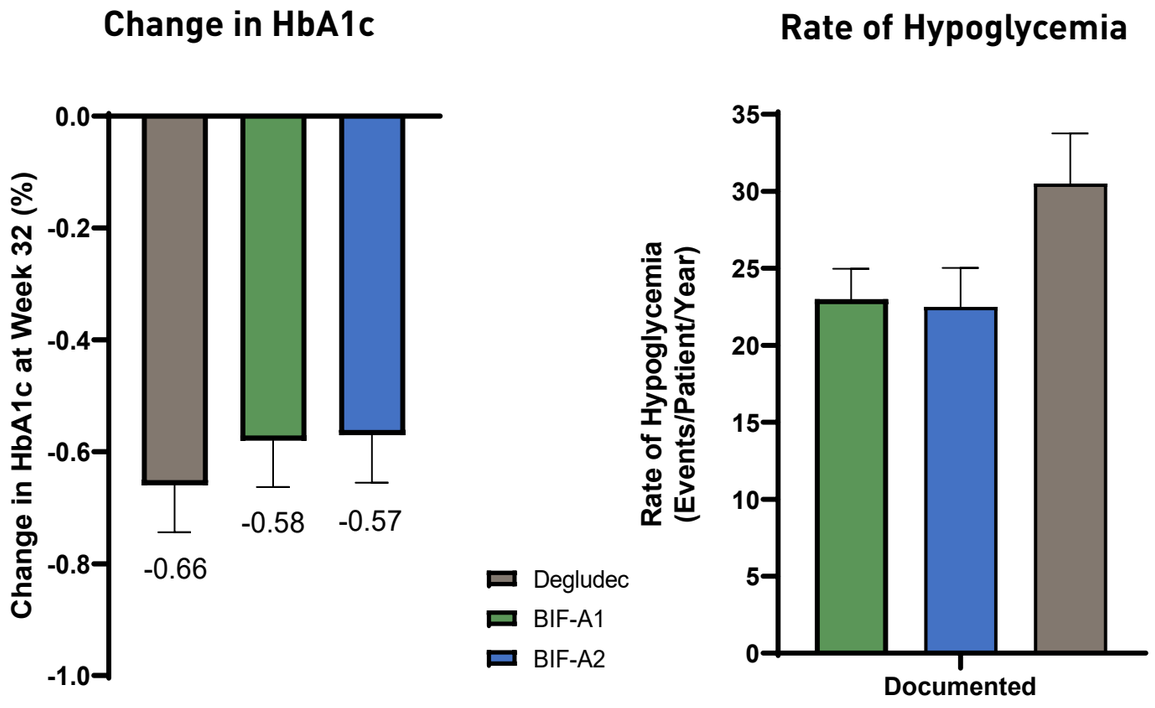
T2D = type 2 diabetes; Estimated study completion based on clinicaltrials.gov as of July 1, 2021

EARLY PHASE PIPELINE

BASAL INSULIN FC (BIF)

WEEKLY INSULIN COULD BE THE NEXT FRONTIER IN INSULIN THERAPY

PHASE 2 DATA



KEY TAKEAWAYS

- Simple once-weekly titration regimen could result in **earlier adoption of insulin therapy and better compliance**
- Flat peak-to-trough profile could provide **more consistent and predictable glycemic control compared to daily basal insulins**
- Phase 2 study in a basal switch population has shown similar efficacy with lower hypoglycemia rates compared to insulin degludec
- CGM data has shown that BIF has lower within-day glucose variability compared to insulin degludec
- Two additional Phase 2 studies underway (T1D, insulin naïve T2D). Phase 3 is planned for 2022

BIF-A1 target fasting glucose algorithm was 140 mg/dL; BIF-A2 target fasting glucose algorithm was 120 mg/dL; Degludec target fasting glucose algorithm was ≤100 mg/dL
CGM= continuous glucose monitoring; T1D = type 1 diabetes; T2D = type 2 diabetes

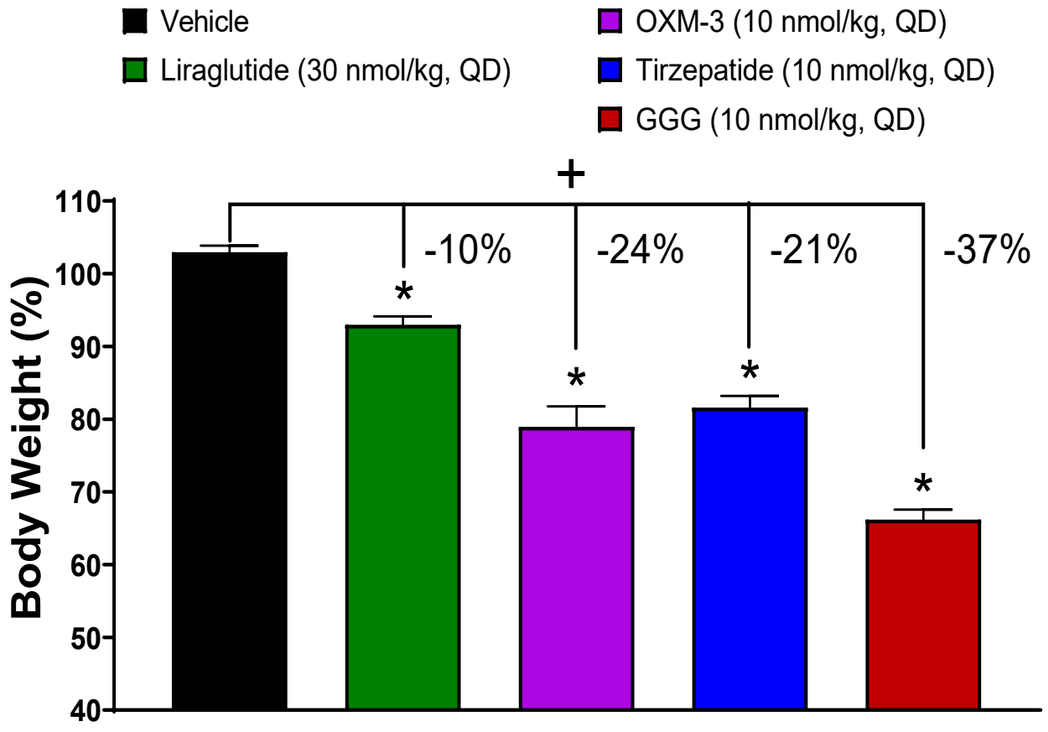
GIP, GLP-1 AND GLUCAGON TRIPLE RECEPTOR AGONIST (GGG)

APPROACH OFFERS POTENTIAL FOR BARIATRIC SURGERY-LIKE WEIGHT LOSS WITH ADDITIONAL LIVER BENEFITS

GGG OVERVIEW

- GGG (LY3437943) is a single peptide derived from a GIP peptide backbone with triple-agonist activity for GIP, GLP-1, and glucagon receptors
- This molecule is built with the goal of maintaining tirzepatide pharmacology and adding balanced glucagon receptor activation as additional pharmacology
- In preclinical models, GGG shows improved weight loss compared to oxyntomodulin, tirzepatide and selective GLP-1 RA. Decreased food intake and increased energy expenditure both contribute to weight loss
- GGG may have a differentiated efficacy in NASH due to additional direct effects of glucagon on the liver. In preclinical models, liver fat and liver enzymes are decreased by GGG

GGG PRECLINICAL DATA



Diet-induced obese mice are treated daily for 18 days

LY3437943 = GGG; OXM-3 = Oxyntomodulin; GLP-1 RA = glucagon-like peptide-1 receptor agonist; NASH = non-alcoholic fatty liver disease
*p<0.05 vs Vehicle and +p<0.05 vs LY3437943

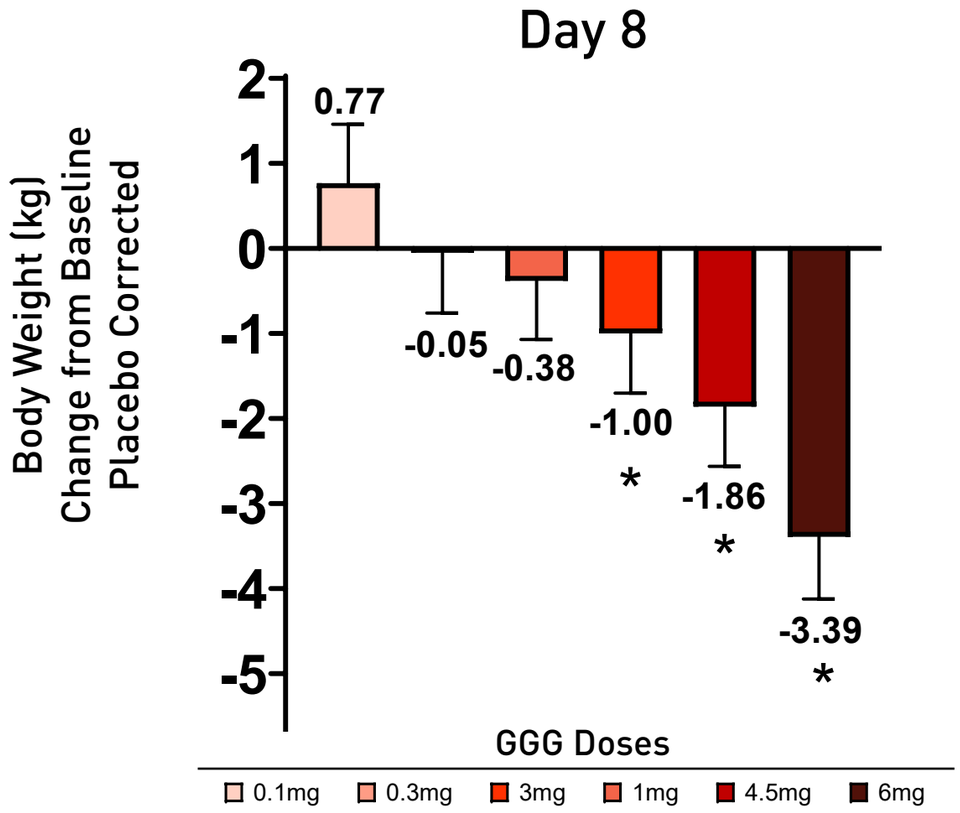
GIP, GLP-1 AND GLUCAGON TRIPLE RECEPTOR AGONIST (GGG)

PHASE 1 DATA CONFIRMS PRECLINICAL PROFILE

GGG CLINICAL TAKEAWAYS

- Single dose study in healthy volunteers:
  - Weight loss of up to 3.5 kg after a single dose, sustained beyond initial drug exposure with weight loss up to 2.5 kg at day 43
  - Mean half-life of ~6 days supports once-weekly dosing
- 12-week MAD/PoC study in patients with T2D:
  - Substantially more weight loss than what was seen with tirzepatide in similar patient population
  - Robust glucose control, potential to be similar to tirzepatide
- Safety and tolerability profile in SAD and MAD studies consistent with GLP-1 RA
- Phase 2 studies in T2D and obesity (including assessment of liver fat) have been initiated

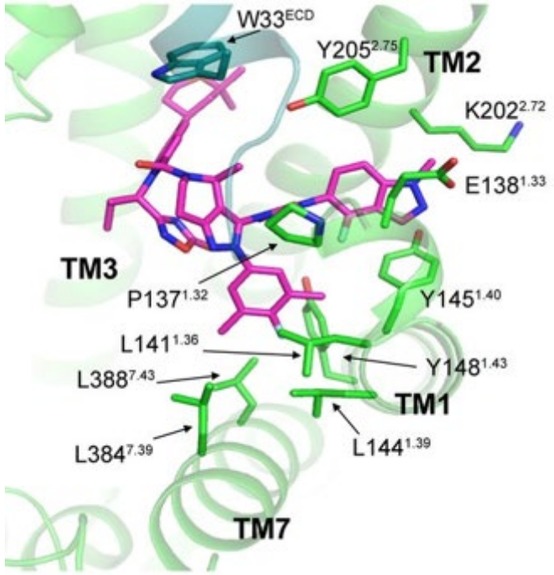
GGG PHASE 1 DATA (SAD)



MAD = multiple ascending dose; SAD = single ascending dose; PoC = proof of concept; T2D = type 2 diabetes; GLP-1 RA = glucagon-like peptide-1 receptor agonists; Data is expressed as difference in least squares means (GGG-Placebo) with 90% confidence interval for the difference (lower, upper) *statistically significant compared to placebo

ORAL INCRETINS

GLP-1R NPA (LY3502970) IS LILLY'S MOST ADVANCED ORAL INCRETIN



Kawai et al. PNAS 2020;117:47:29959

LY3502970 bound to the GLP-1R

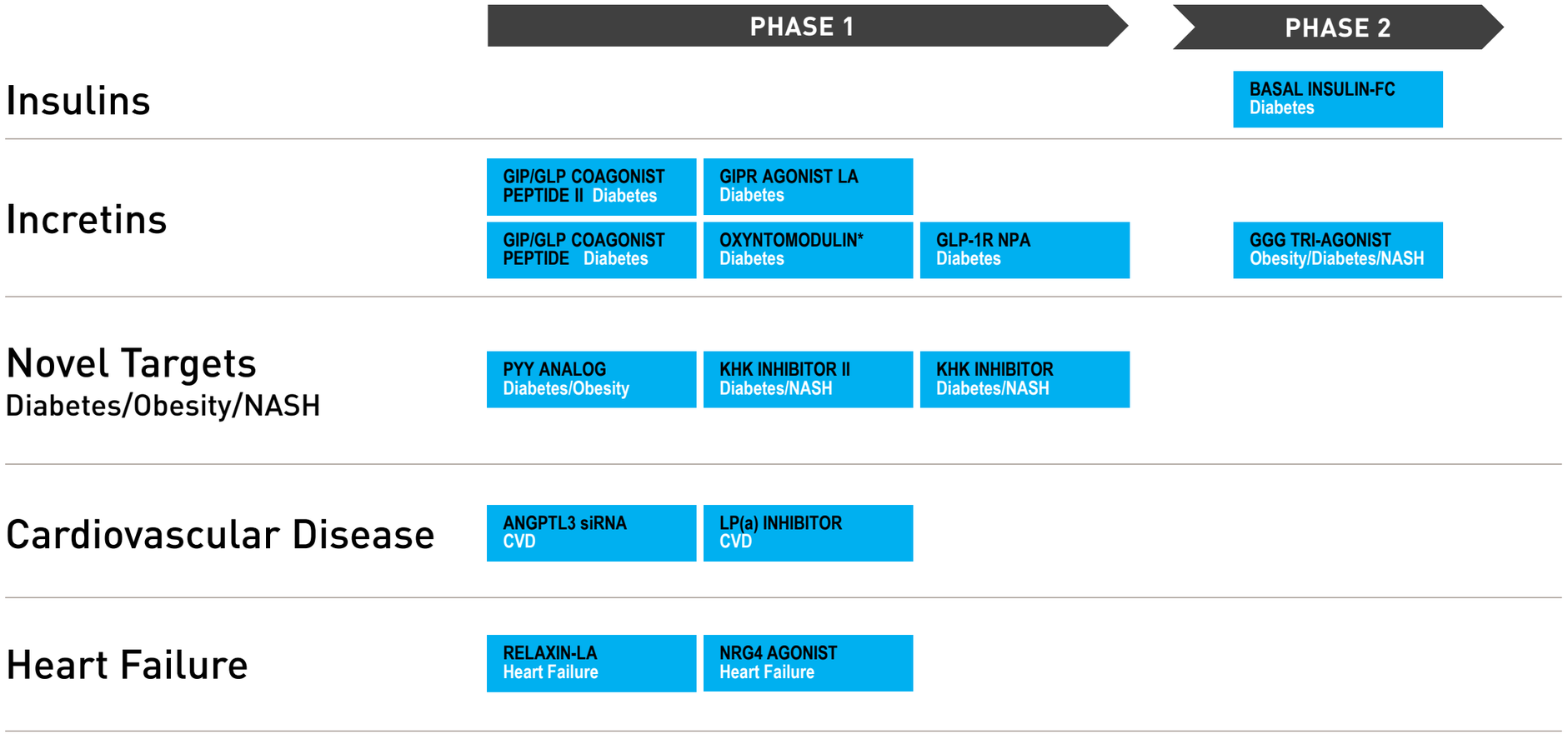
- GLP-1R NPA (LY3502970) is a selective, partial and biased agonist at the GLP-1 receptor. Molecule is differentiated compared to other GLP-1R NPAs
- Preclinical data show efficacy similar to injectable incretins
- Phase 1 clinical data support **once-daily dosing** with **no food or water restrictions.**
- A 12-week proof of concept study in T2D is ongoing (NCT04426474)
- Potential for Phase 2 initiation in late 2021/early 2022

Additional efforts aim for tirzepatide-like efficacy using orally-delivered peptides (LY3537031, LY3493269)

Note: GLP-1R NPA (LY3502970) is licensed from Chugai; GLP-1R NPA = GLP-1 receptor non-peptidic agonist; PK = pharmacokinetics

LILLY DIABETES EARLY PHASE NME PORTFOLIO

OPPORTUNITIES ACROSS CLASSES AND INDICATIONS



*China rights for oxyntomodulin are partnered with Innovent; NME = new molecular entity; NASH = Non-alcoholic steatohepatitis; CVD = cardiovascular disease

Summary

Tremendous growth in diabetes over the past decade with momentum from Trulicity and Jardiance with future growth opportunities in both diabetes and related metabolic disorders

Potential for tirzepatide to be a foundational medicine with outstanding clinical results in type 2 diabetes and exciting opportunities in obesity, NASH and heart failure

Continue to innovate in our early phase diabetes pipeline as we invest in next generation incretins and our weekly basal insulin

QUESTIONS AND ANSWERS