

ELI LILLY AND COMPANY



DIABETES

2019 BUSINESS UPDATE

Lilly

Agenda

Introduction

Enrique Conterno, President, Lilly Diabetes & Lilly USA

Commercial Update

Ilya Yuffa, Vice President, U.S. Diabetes

Pipeline Update

Dr. Brad Woodward, Global Development Leader, Incretins

Closing Remarks

Enrique Conterno, President, Lilly Diabetes & Lilly USA

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; 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 Forms 10-K and 10-Q filed with the Securities and Exchange Commission.

The company undertakes no duty to update forward-looking statements

The background of the slide is a solid red color. Overlaid on this background is a faint, light-colored network diagram. This diagram consists of numerous circular nodes of varying sizes, connected by thin, light-colored lines. The nodes are distributed across the entire frame, creating a complex web-like structure. The word "INTRODUCTION" is centered in the middle of the slide in a bold, white, sans-serif font.

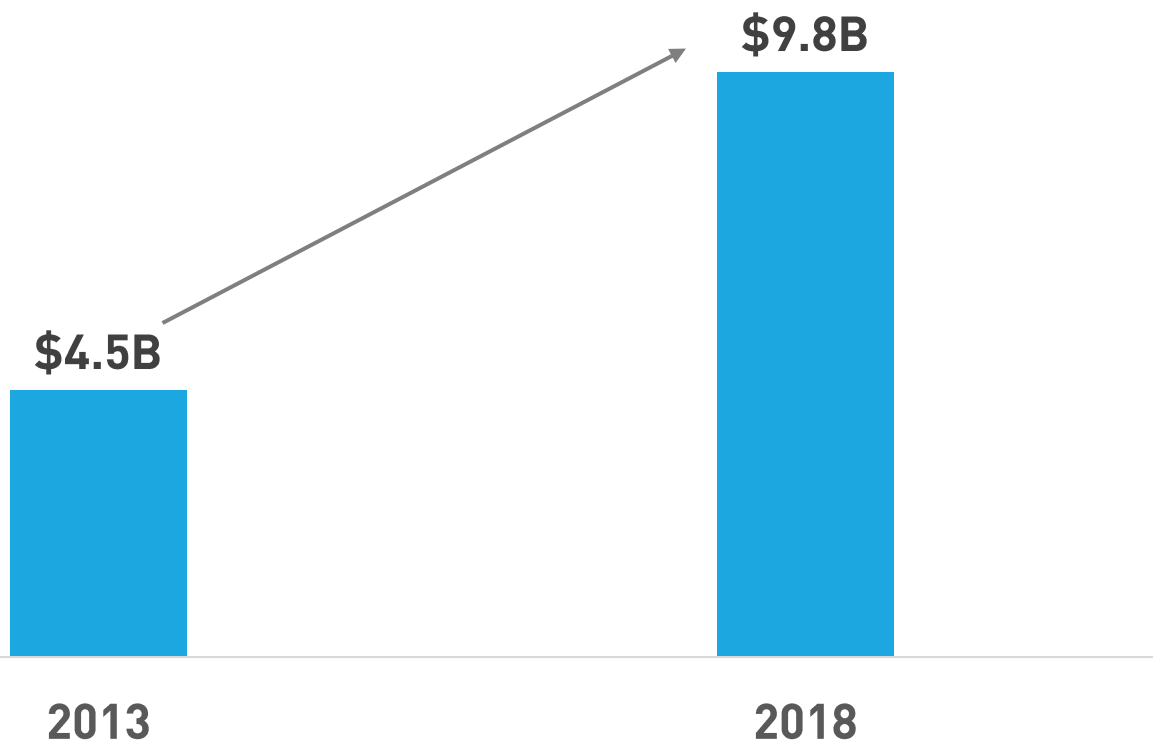
INTRODUCTION

ESTABLISHED LEADER IN DIABETES



SIGNIFICANT GROWTH

REVENUE FROM DIABETES NEARLY DOUBLED



WIDE RANGE OF THERAPIES

Orals	GLP-1	Insulins	Devices
Jardiance® Synjardy® Glyxambi® Tradjenta™ Jentadueto®	trulicity™ 	basaglar® Humalog® Humalog 200 units/mL KwikPen® Humulin® R U-500 Humulin®	

Note: Jardiance, Synjardy, Glyxambi, Tradjenta, Jentadueto and Basaglar are part of the Boehringer-Ingelheim and Lilly Diabetes Alliance.

The background of the image is a solid red color. Overlaid on this background is a network diagram consisting of numerous circular nodes of varying sizes, connected by thin, light-colored lines. The nodes are scattered across the frame, with some larger nodes acting as hubs and many smaller nodes branching off from them. The overall effect is a complex, interconnected web of points and lines.

COMMERCIAL UPDATE

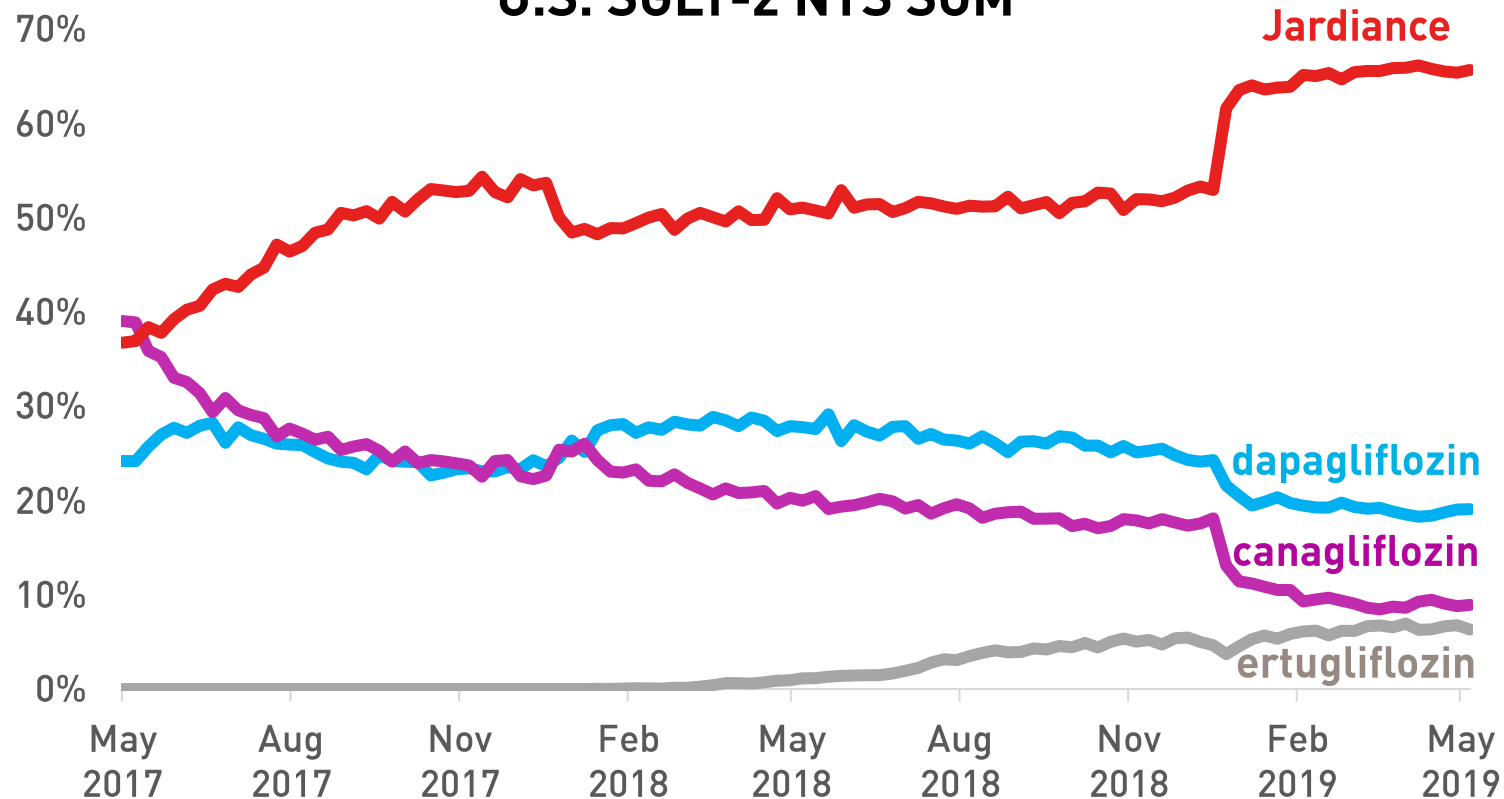
SGLT-2: JARDIANCE FAMILY

BEST-IN-CLASS WITH OPPORTUNITY TO BE FIRST BRANDED ORAL



PRODUCT PERFORMANCE

U.S. SGLT-2 NTS SOM



IQVIA NPA Weekly as of week ending 5.17.2019.

Note: Jardiance is part of the Boehringer-Ingelheim and Lilly Diabetes Alliance.

CLASS GROWTH

- SGLT-2 class growth is strong, New Therapy Starts (NTS) growing over 30% vs. prior year
- New prescriptions for SGLT-2s now exceed DPP-4s, as measured by New Therapy Starts
- Jardiance established as clear market leader within class:
 - 66% SOM New Therapy Starts
 - 52% SOM Total Prescriptions

SGLT-2: JARDIANCE FAMILY

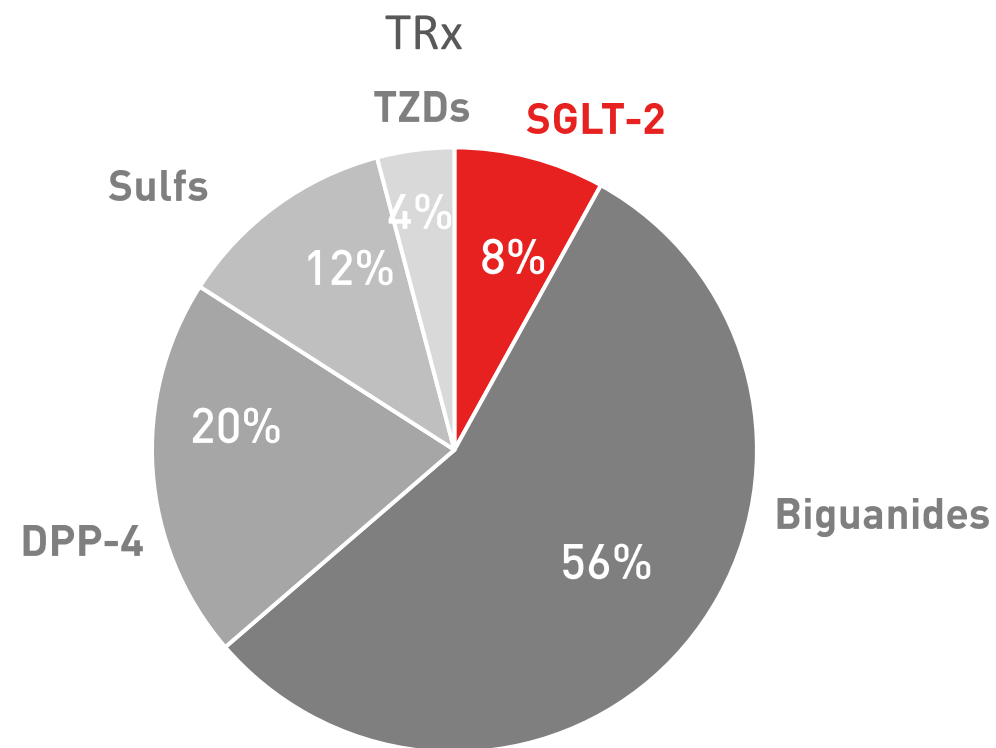
BEST-IN-CLASS WITH OPPORTUNITY TO BE FIRST BRANDED ORAL



GROWTH OPPORTUNITY

UPCOMING DATA READOUTS

U.S. Share of Oral Market



- Exercise ability in Chronic Heart Failure
 - Phase 3 data 2H 2019
- Chronic Heart Failure
 - Phase 3 data 2020 and 2021
- Chronic Kidney Disease
 - Phase 3 data 2022

IQVIA NPA Weekly as of week ending 5.17.2019.

Note: Jardiance is part of the Boehringer-Ingelheim and Lilly Diabetes Alliance.

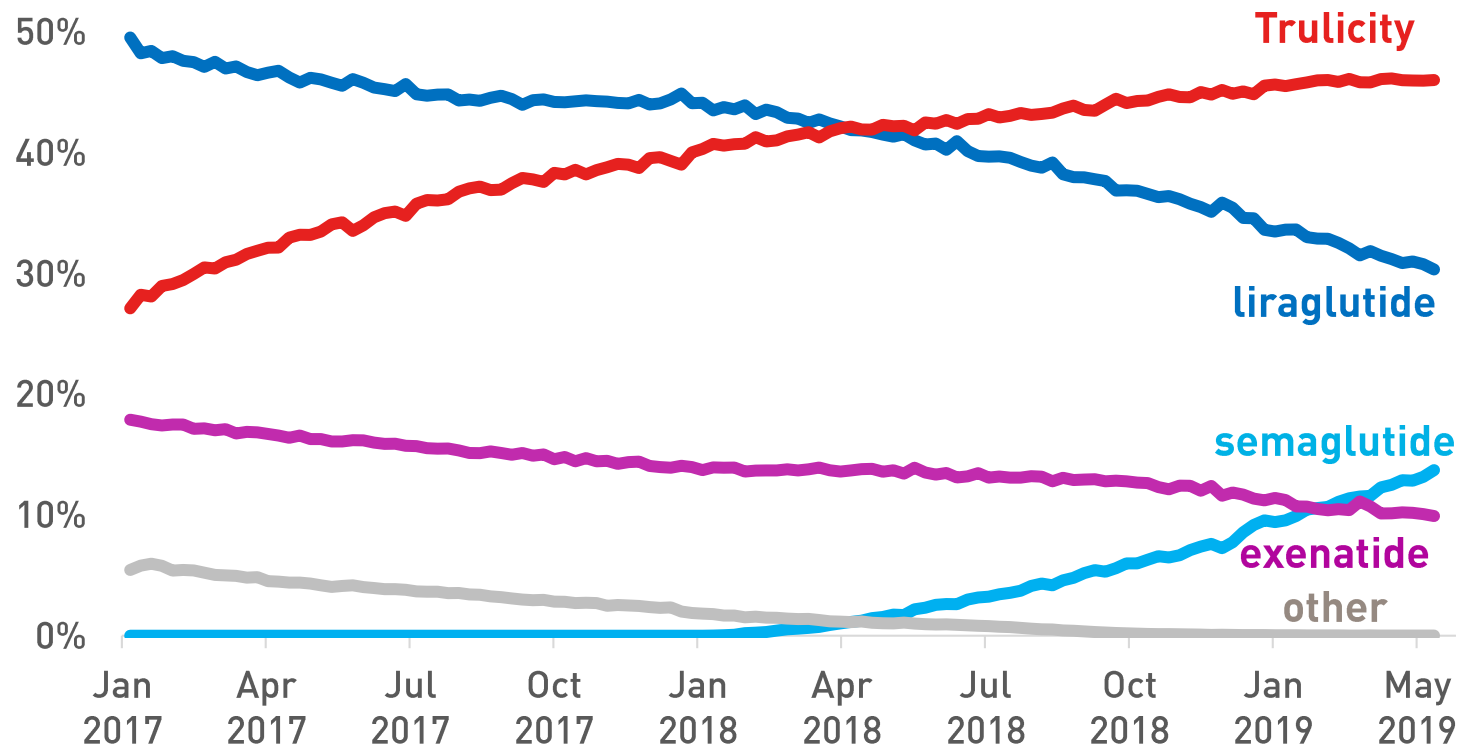
GLP-1: TRULICITY

TRANSFORMING THE FIRST INJECTABLE SPACE



PRODUCT PERFORMANCE

U.S. GLP-1 TRx SOM



U.S. GLP-1 market growing at 28%

IQVIA NPA Weekly as of week ending 5.17.19.

NEW DATA HIGHLIGHTS

- REWIND data submitted in U.S. and E.U.
 - Expect FDA and EMA action in 1H 2020
 - Label expected to align with dulaglutide cardiovascular outcome study population
- Phase 3 data evaluating 3.0 and 4.5mg doses of dulaglutide expected in 2019
 - Phase 2 demonstrated additional HbA1c reduction and weight loss

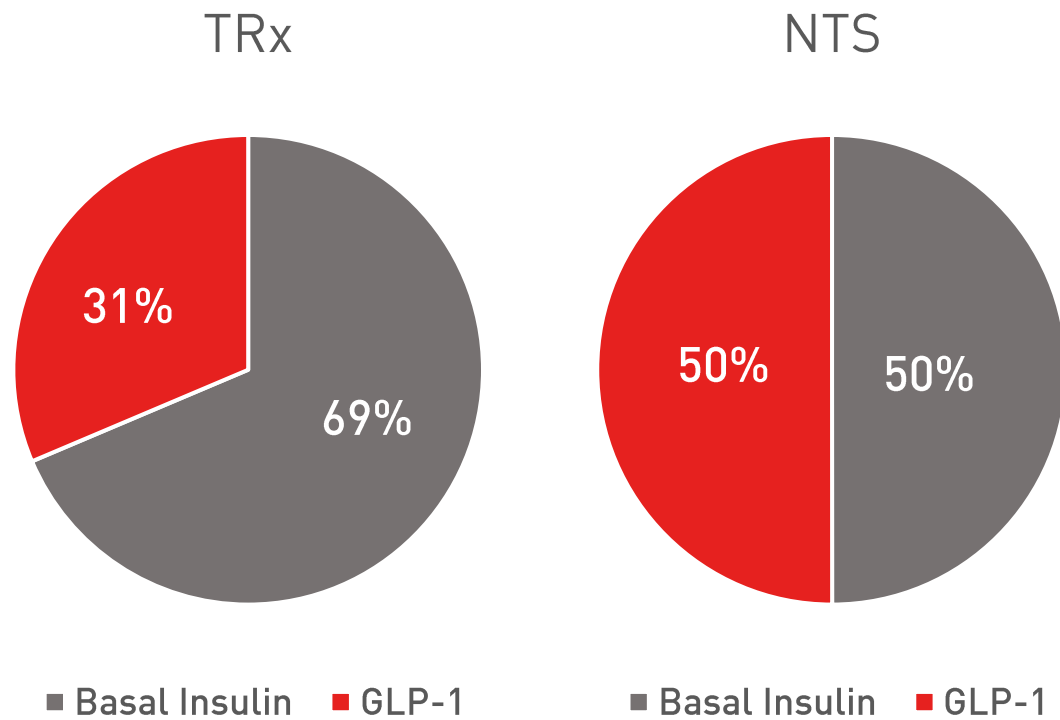
GLP-1: TRULICITY

TRANSFORMING THE FIRST INJECTABLE SPACE



GROWTH OPPORTUNITY

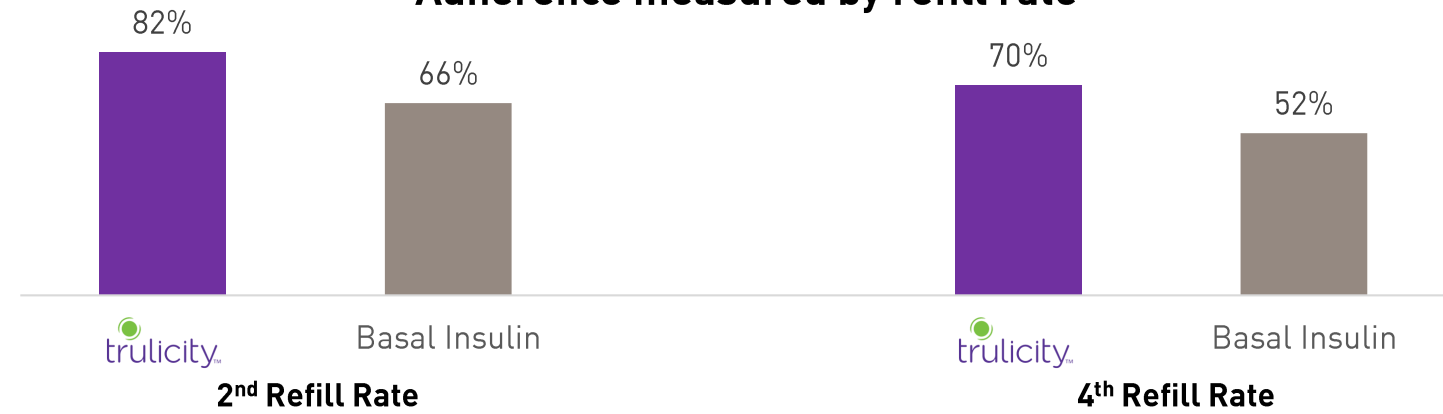
U.S. 1st Injection SOM



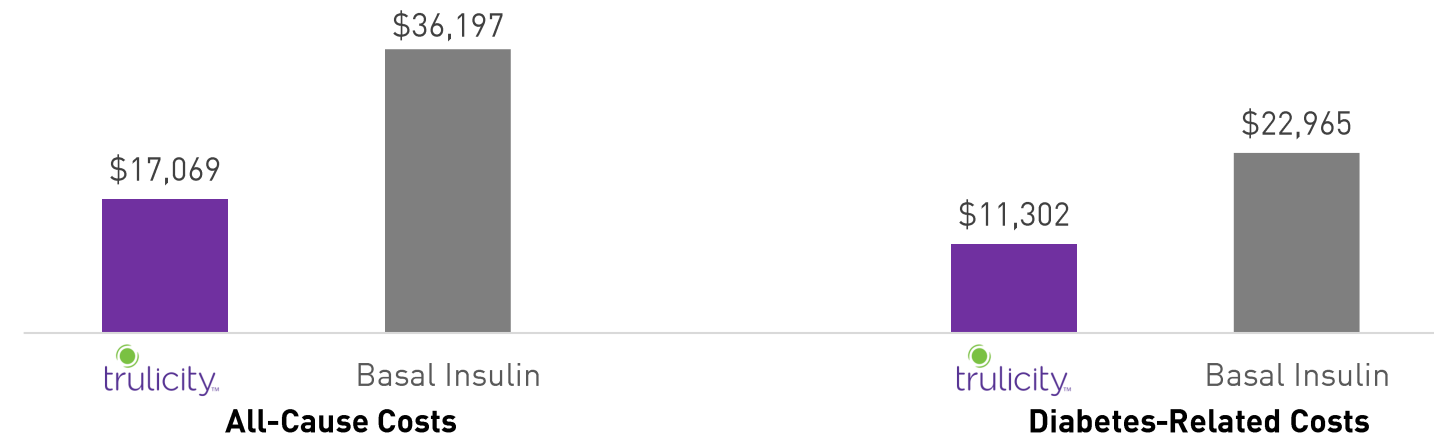
IQVIA NPA Weekly as of week ending 5.17.2019.

REAL WORLD DATA

Adherence measured by refill rate⁽¹⁾



Cost-Effectiveness measured by cost per 1% HbA1c reduction⁽²⁾



1) Source: IQVIA LRx data Aug 2017 – Jul 2018.

2) Source: Abstract PDB57: Presented at the ISPOR 24th Annual International Meeting; New Orleans, LA May 18-22, 2019.

CLINICAL GUIDELINE ADVANCEMENT

RECOMMENDATIONS FOR TYPE 2 DIABETES AND CARDIOVASCULAR RISK



CONSENSUS REPORTS

Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)
Diabetologia 2018

Standards of Medical Care in Diabetes—2019 (ADA)
Pharmacologic Approaches to Glycemic Treatment
Diabetes Care 2019

- For patients with clinical cardiovascular disease, an **SGLT2 inhibitor** or a **GLP-1 receptor agonist** with *proven cardiovascular benefit* is recommended
- For patients with chronic kidney disease or clinical heart failure and atherosclerotic cardiovascular disease, an **SGLT2 inhibitor** with proven benefit is recommended
- **GLP-1 receptor agonists** are generally recommended as the first injectable medication

The background features a network diagram with various sized nodes connected by thin lines, set against a solid red background. The nodes are arranged in a somewhat circular pattern, with some larger nodes and many smaller ones. The lines connecting them are thin and light red, creating a subtle grid-like structure.

PIPELINE UPDATE

TYPE 2 DIABETES AND CARDIOVASCULAR DISEASE



REWIND population represents a broad range of people with type 2 diabetes



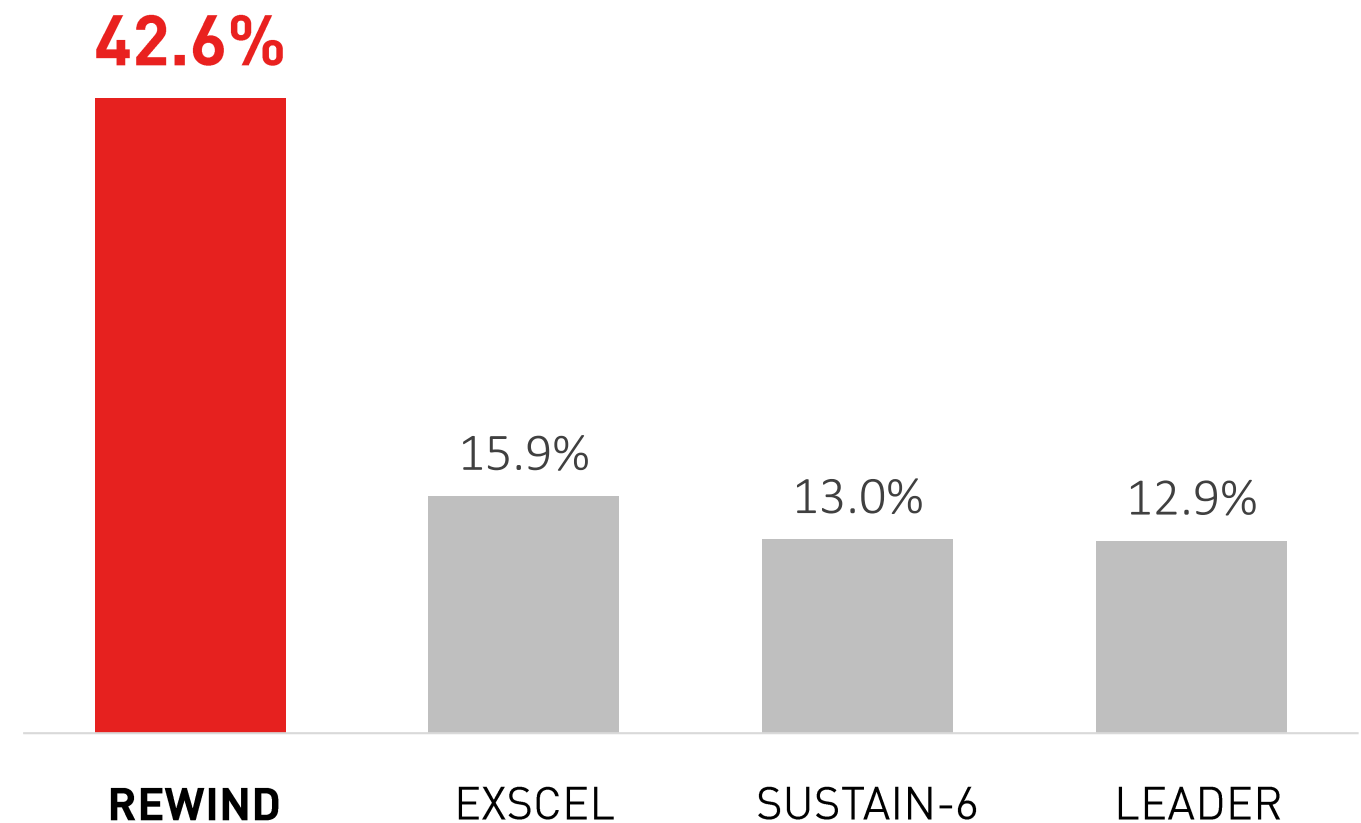
Cardiovascular disease is a leading cause of morbidity and mortality for individuals with diabetes



Study by Boye et al evaluated the extent to which the study populations in CVOT reflect the general **US population of adult patients with type 2 diabetes**

Boye et al, Diabetes Obes. Metab. 2019; 21:1299-1304.

Percentage of patients with type 2 diabetes that are estimated to fit all inclusion / exclusion criteria of each CVOT*



*The inclusion/exclusion criteria for each completed trial was applied against an RWE reference population, to estimate what percentage of people might have been enrolled in each study

TRULICITY CV OUTCOME TRIAL



REWIND KEY TRIAL ASPECTS

9901 participants with type 2 Diabetes



Key inclusion criteria

- Adults with type 2 diabetes and age ≥ 50 years with vascular disease; ≥ 55 years with subclinical vascular disease; or ≥ 60 years and multiple cardiovascular risk factors. HbA1c $\leq 9.5\%$

Study completed with high retention and assessment for the primary endpoint

- 97.1% Completers; 99.7% Vital Status Known; 83% of follow-up time on study drug

BASELINE CHARACTERISTICS

DATA PRESENTED AS MEAN VALUES	DULA 1.5MG	PLACEBO
Age (years)	66.2	66.2
Female (%)	46.6	46.1
Established CV disease* (%)	31.5	31.4
Prior CV event (MI or ischemic stroke) (%)	20.8	20.3
Prior heart failure (%)	8.5	8.7
Retinopathy (%)	9.1	8.9
Duration of diabetes (years)	10.5	10.6
HbA1c (%)	7.3	7.4
eGFR <60 ml/min/1.73m ² (%)	21.8	22.6

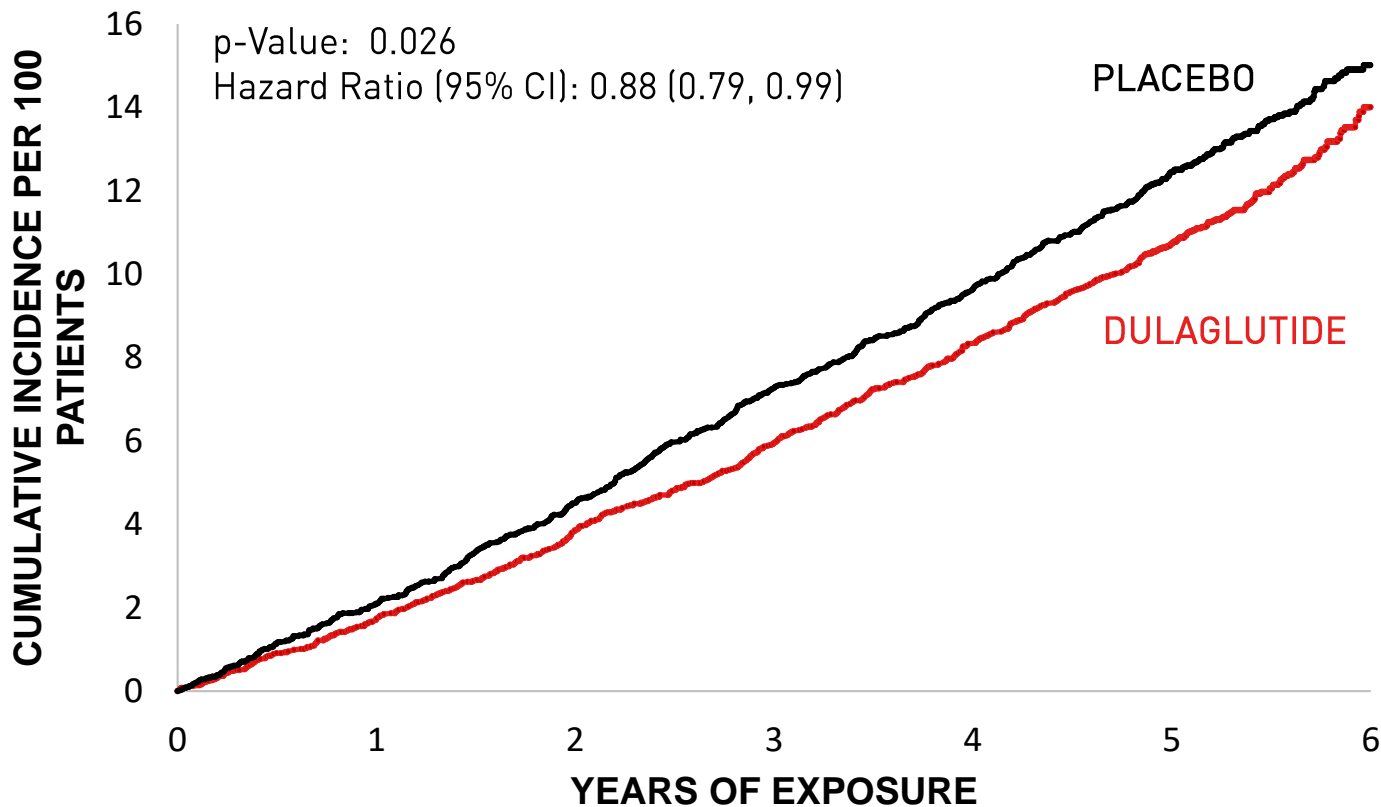
*REWIND defined established CV disease as including at least one of the following conditions: myocardial infarction (MI), ischemic stroke, unstable angina, revascularization, hospitalization for ischemia related events and/or documented myocardial ischemia.

TRULICITY CV OUTCOME TRIAL



PRIMARY MACE 3 RESULT

Dulaglutide significantly reduced the risk of Major Adverse Cardiovascular Events (MACE 3: CV death, non-fatal MI or non-fatal stroke) by 12% vs. placebo



Note: Hazard Ratio and its CI and p-value obtained from Cox Proportional Hazards Regression Model with treatment as a fixed effect.
Gerstein et al. Lancet 2019.

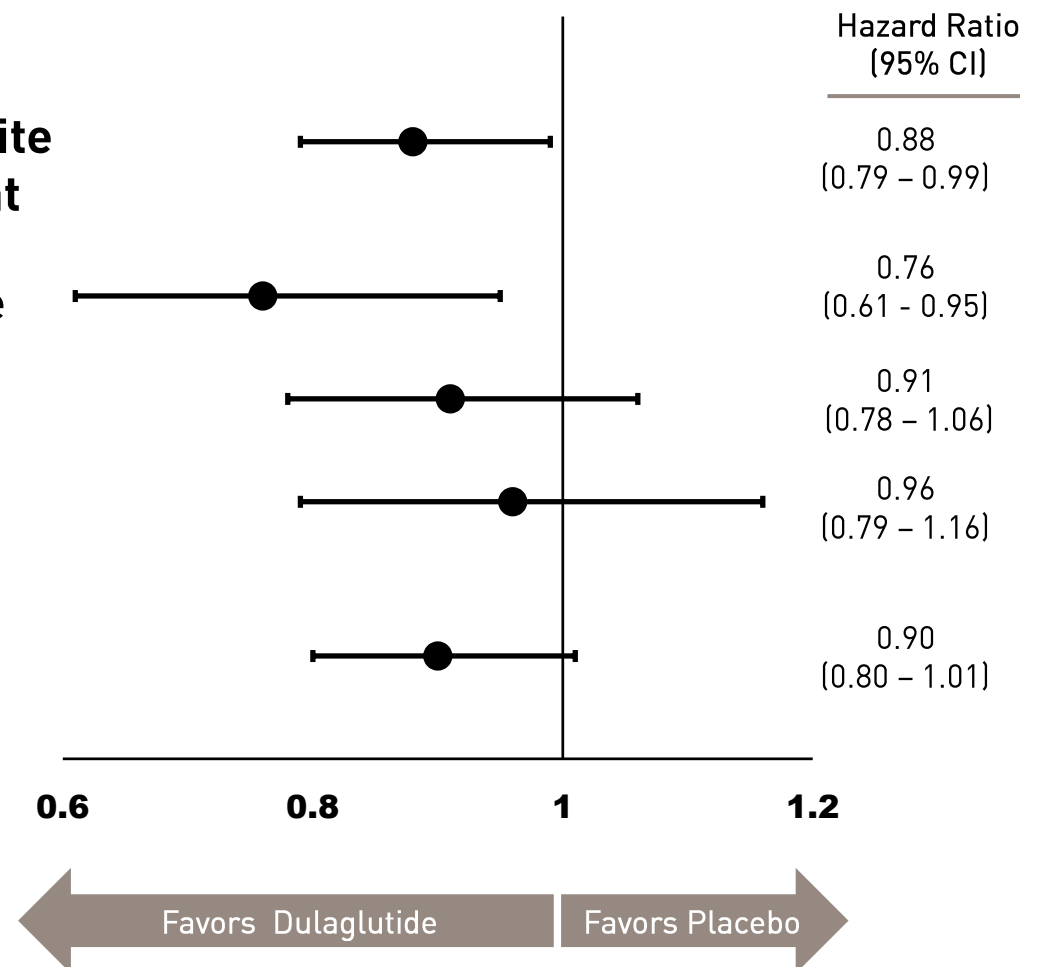
CV OUTCOMES

Consistent effect across three components of MACE, greatest difference observed in Nonfatal Stroke

MACE-3 Composite Primary Endpoint

Nonfatal Stroke
CV Death
Nonfatal MI

All Death



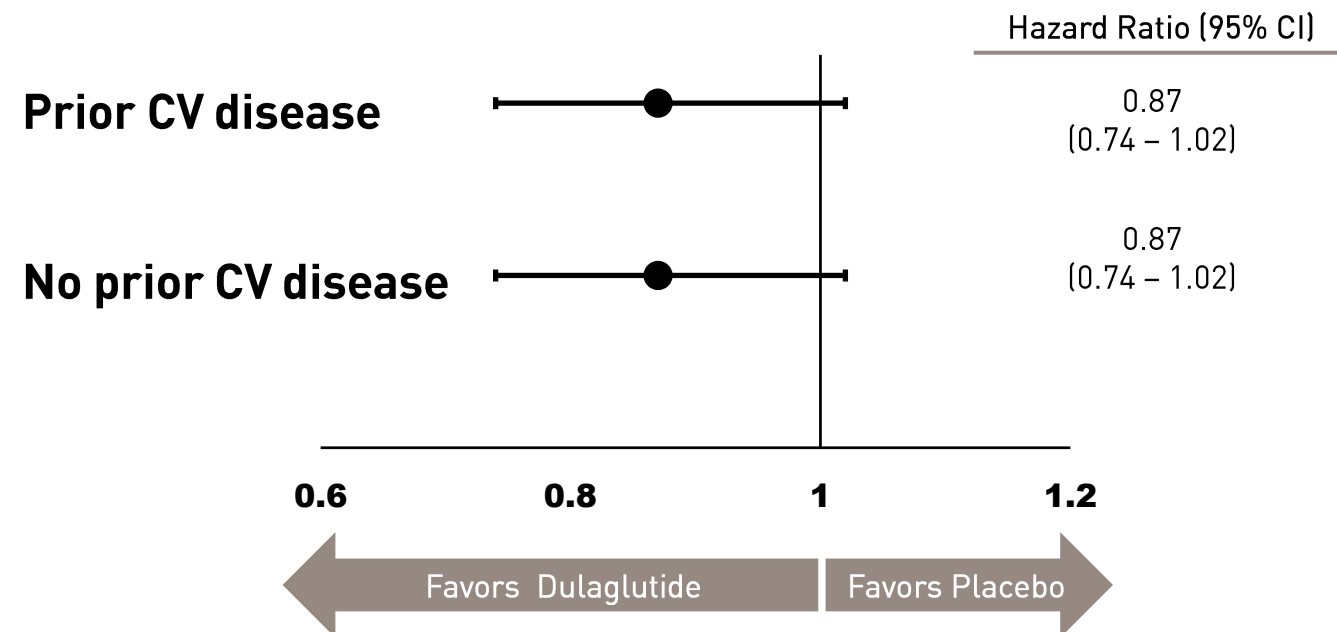
TRULICITY CV OUTCOME TRIAL



MACE 3 AND PRIOR CV DISEASE

- **Consistent MACE 3 effect observed in type 2 diabetes patients with and without prior CV disease*** (p-value for interaction 0.970)

PRESPECIFIED CV DISEASE SUBGROUP ANALYSIS



Gerstein et al. Lancet 2019.

KEY SUBGROUPS/RESULTS

- MACE effect consistent across key baseline characteristic subgroups including:
 - Age
 - Gender
 - Duration of diabetes
 - Baseline HbA1c
- Reduction in HbA1c
 - -0.46 dulaglutide vs. +0.16 placebo
- Reduction in weight
 - -2.95kg dulaglutide vs. -1.49 placebo, while on other background therapy

*REWIND defined established (prior) CV disease as including at least one of the following conditions: myocardial infarction (MI), ischemic stroke, unstable angina, revascularization, hospitalization for ischemia related events and/or documented myocardial ischemia.

TRULICITY CV OUTCOME TRIAL



Safety of dulaglutide in REWIND was consistent with the GLP-1 RA class

SELECT ADVERSE EVENTS

% unless otherwise specified	DULA 1.5MG	PLACEBO
Permanent discontinuation of study drug due to adverse event	9.1	6.3
Acute pancreatitis with imaging and enzymes confirmed	0.5 0.1	0.3 0.1
Any cancer	7.1	7.0
MTC or C-cell hyperplasia (n)	1	0
Thyroid cancer	0.1	0.1
Pancreatic cancer	0.4	0.2
Gastrointestinal event	47.4	34.1
Serious GI event	2.4	2.4
Severe hypoglycemia	1.3	1.5

Dulaglutide was well-tolerated and the safety profile was generally consistent with the GLP-1 RA class. More gastrointestinal adverse events were observed in participants receiving Trulicity

- Two composite microvascular endpoints evaluated:
- Nephropathy⁽¹⁾ – reduced composite renal outcomes versus placebo (HR = 0.85, 95% CI: 0.77-0.93)
 - Diabetic retinopathy⁽²⁾ – numerically higher in dulaglutide arm (HR = 1.24, 95% CI: 0.92-1.68, not statistically significant). Treatment-emergent adverse events of diabetic retinopathy were similar between groups, dulaglutide (4.1%) and placebo (3.9%)

⁽¹⁾ Urinary albumin-to-creatinine ratio >33.9mg/mmol, or ≥30% decline in eGFR, or chronic renal replacement therapy.

⁽²⁾ Photocoagulation, or anti-VEGF therapy, or vitrectomy.

REWIND KEY TAKEAWAYS



REWIND enrolled a precedent-setting population, representative of patients with type 2 diabetes

Lower baseline HbA1c versus other GLP CVOTs and nearly 70% of patients did not have established CV disease



REWIND enrolled a large population and included a long follow-up period

Nearly 10,000 patients and 5.4 year follow-up period



Trulicity demonstrated a clinically meaningful 12% reduction in major adverse cardiovascular events

Encouraging results in pivotal trial, with consistent effect across endpoints, and in patients with and without prior CVD

TIRZEPATIDE

DUAL GIP/GLP-1 RECEPTOR AGONIST



GOALS FOR TIRZEPATIDE PROGRAM



Launch first in new class of dual GIP and GLP-1 receptor agonists



Reset treatment expectations for glucose control and weight reduction

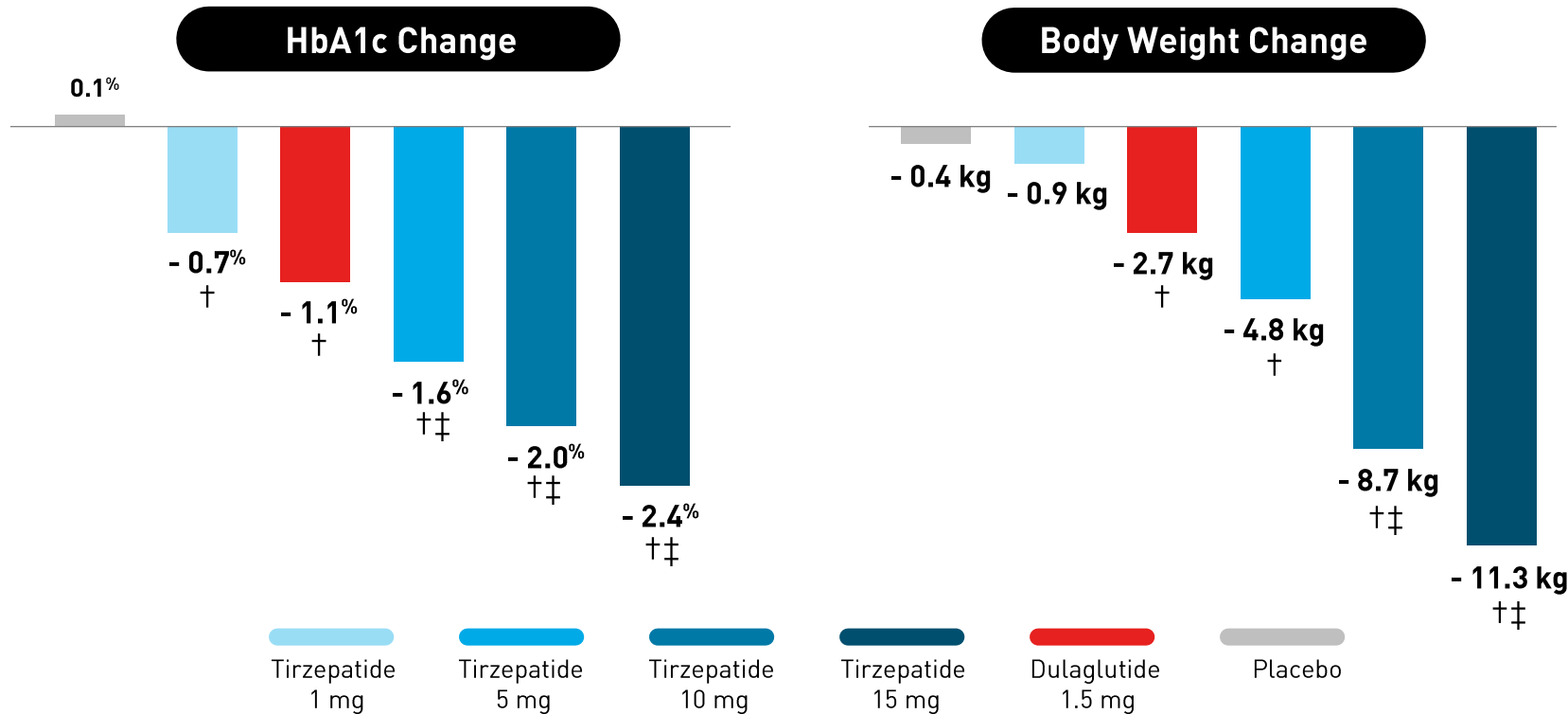


Deliver meaningful CV benefit



Replicate Trulicity's injection experience

PHASE 2B DATA AT 26 WEEKS



CLINICAL DEVELOPMENT MILESTONES



2018

T2DM **Phase 3** - started



2019

Obesity **Phase 3** - start
NASH **Phase 2** - start

Data for change in HbA1c and bodyweight presented are LS mean, MMRM on treatment analysis. † p<0.05 vs placebo and ‡ p<0.05 vs. dulaglutide 1.5 mg. Frias al. Lancet 2018;392(10160):2180-2193.

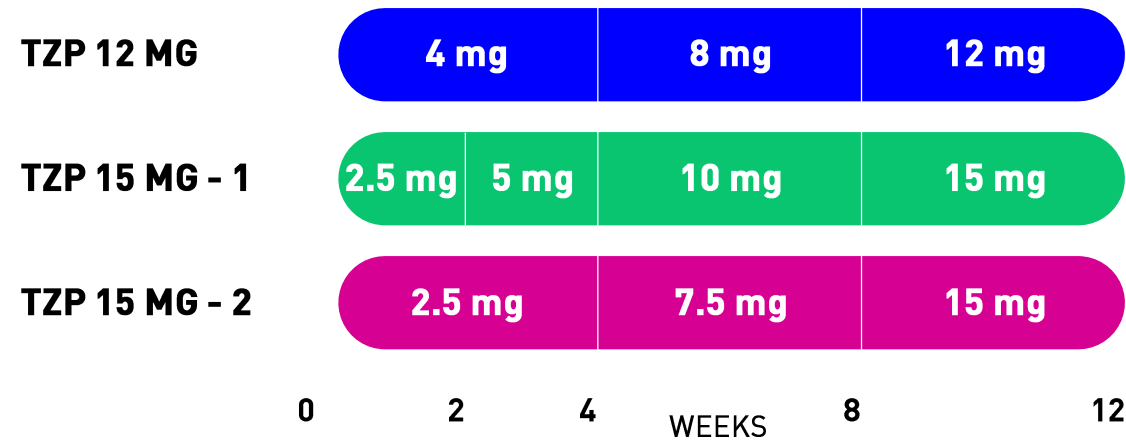
TIRZEPATIDE

TYPE 2 DIABETES DOSING STUDY AND RESULTS



PHASE 2 DOSING STUDY

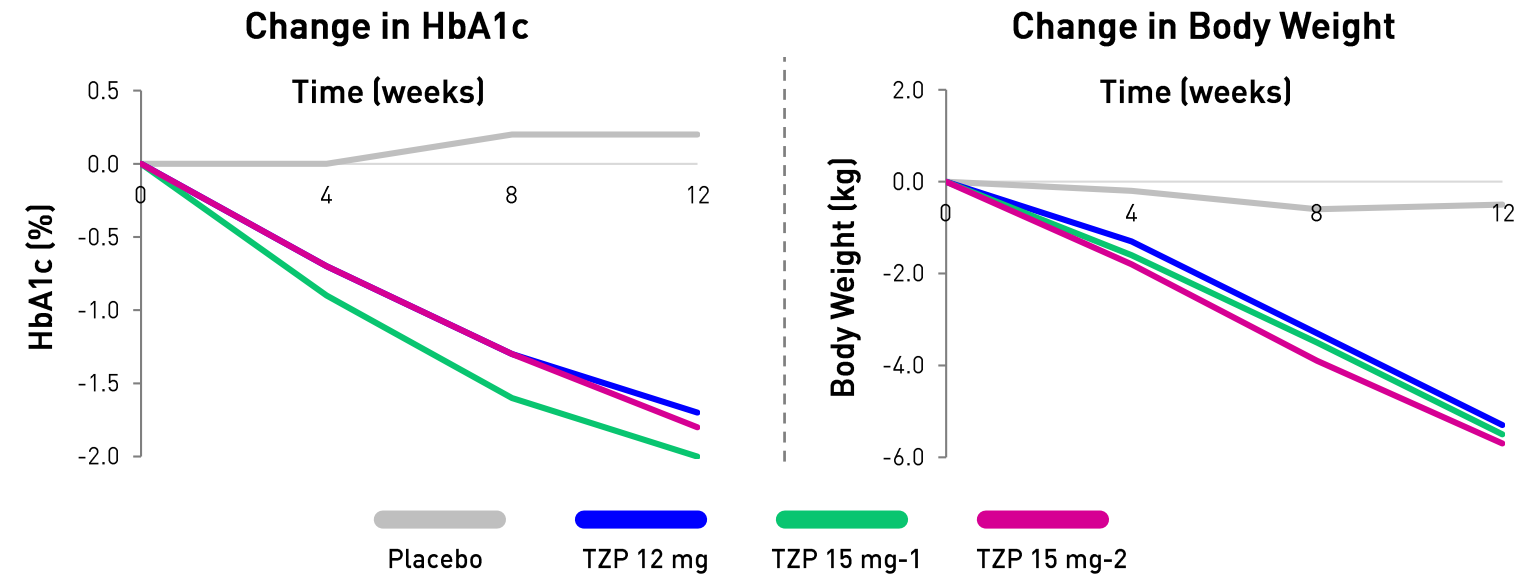
3 DOSING REGIMENS EVALUATED



Different tirzepatide starting doses and different dose escalation increments assessed

3-month, randomized, double-blind, placebo-controlled study with 111 total patients

EFFICACY AND SAFETY RESULTS⁽¹⁾



	Placebo	12 mg	15 mg-1	15 mg-2
HbA1c (%) Change from baseline	0.2	-1.7	-2.0	-1.8
Weight (Kg) Change from baseline	-0.5	-5.3	-5.5	-5.7
Adverse Events %	50.0	79.3	67.9	85.7
Overall Treatment Discontinuation %	23.1	6.9	21.4	7.1
Discontinuation due to Adverse Event %	3.8	3.4	3.6	0
Nausea (%)	7.7	24.1	39.3	35.7
Diarrhea (%)	7.7	31.0	35.7	32.1
Vomiting (%)	3.8	17.2	17.9	17.9

TIRZEPATIDE

TYPE 2 DIABETES PHASE 3 DOSING

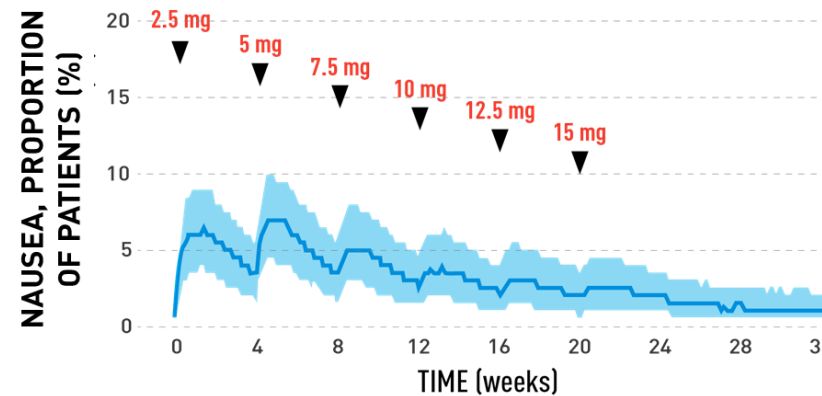


CONCLUSIONS FROM DOSING STUDY

- **Consistent efficacy:** HbA1c reduction and weight loss
- Dose escalation resulted in an **improved tolerability profile**
- Treatment **discontinuation rates were lower** vs. previously disclosed Phase 2b study
- **No discontinuation imbalance due to adverse events** vs. placebo

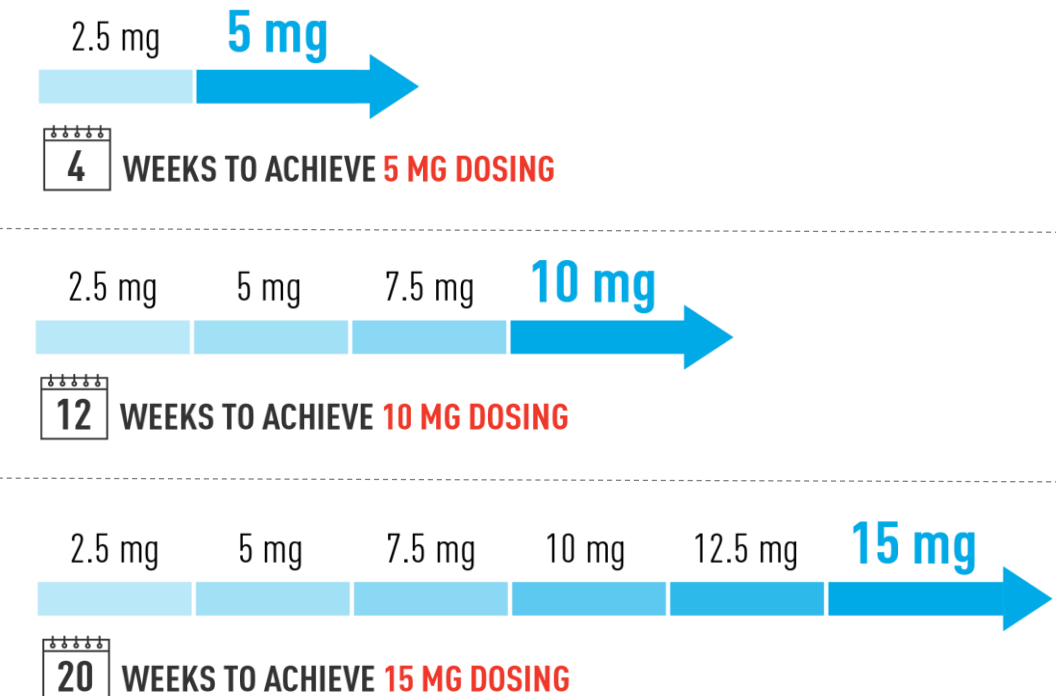


STUDY RESULTS AND EXPOSURE MODELING INFORMED PHASE 3 DOSING



PHASE 3 DOSE SCHEDULE

Step through doses (2.5mg increments) expected to improve tolerability profile while achieving breakthrough efficacy goals

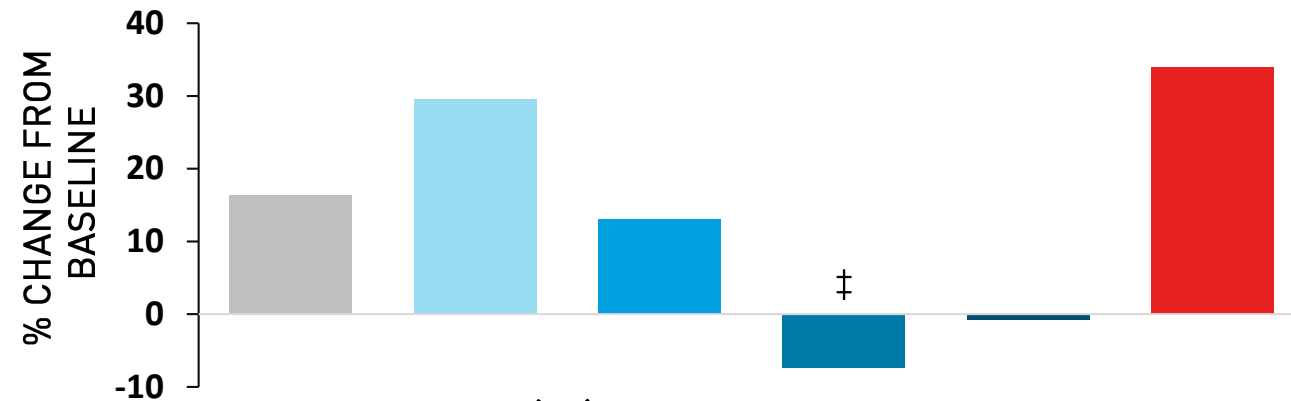


TIRZEPATIDE

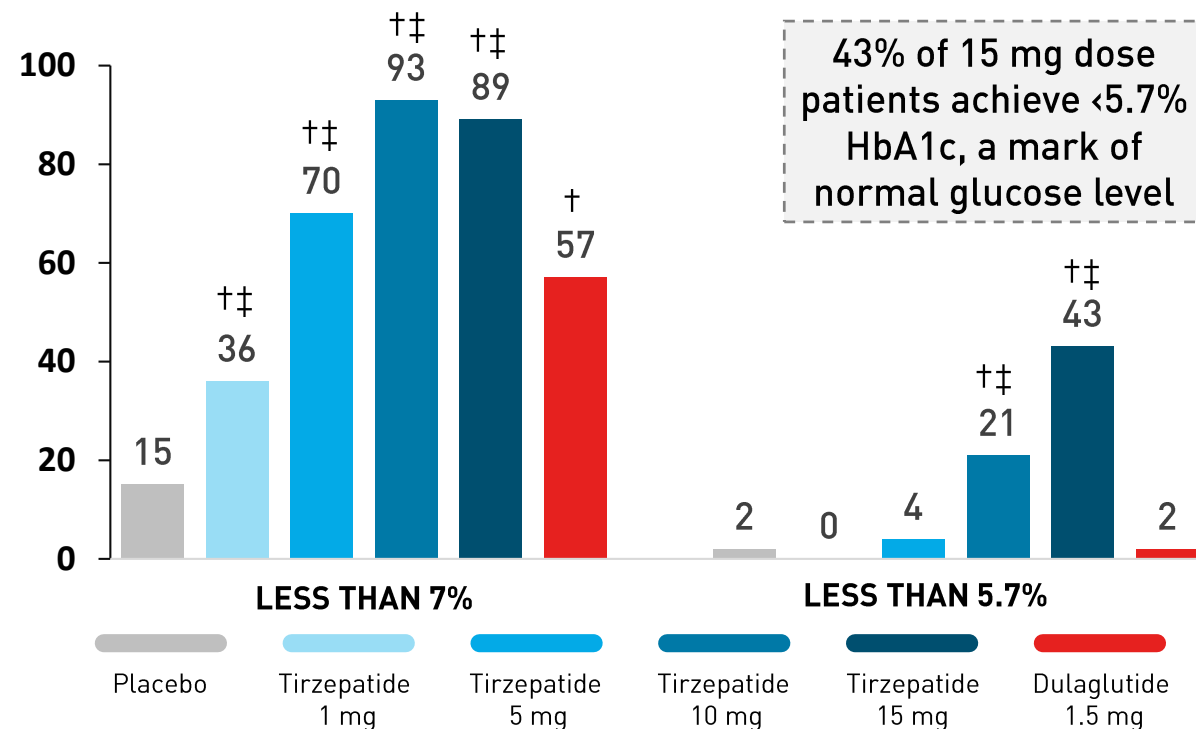
ADDITIONAL INSIGHTS FROM PHASE 2B



FASTING INSULIN⁽¹⁾



A1C (%) TO TARGET AT WEEK 26



43% of 15 mg dose patients achieve <5.7% HbA1c, a mark of normal glucose level

TIRZEPATIDE IMPROVED BETA-CELL FUNCTION AND INSULIN SENSITIVITY

- Insulin-sensitizing effects of tirzepatide are only partially attributable to weight loss
- Improved markers of pancreatic beta-cell function and insulin processing
- Improved glucose control with greater impact on insulin sensitivity and beta-cell function as compared with dulaglutide
- Further mechanistic studies in progress

⁽¹⁾Abstract 980-P. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.

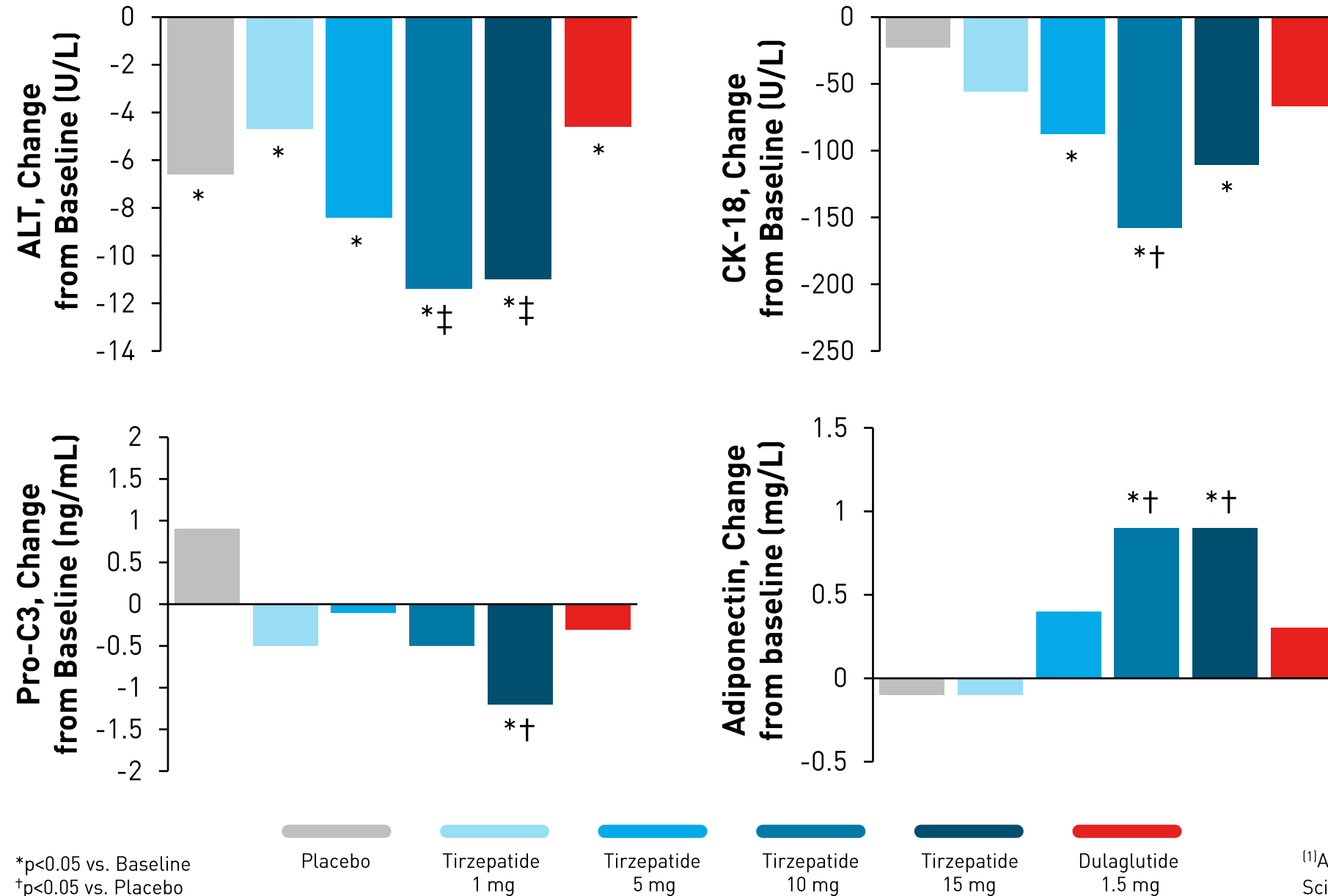
Data presented are from logistic regression, on treatment analysis.
[†] p<0.05 vs placebo and [‡] p<0.05 vs. dulaglutide 1.5 mg

TIRZEPATIDE

NASH RELATED BIOMARKERS SHOW POTENTIAL EFFICACY



PHASE 2B LIVER BIOMARKERS IN SERUM AT 26 WEEKS OF TREATMENT⁽¹⁾



*p<0.05 vs. Baseline
 †p<0.05 vs. Placebo
 ‡p<0.05 vs. Dulaglutide

NASH RELATED BIOMARKERS

Markers of apoptosis and fibrosis decreased and adiponectin increased with tirzepatide in Phase 2 type 2 diabetes

Along with the weight loss findings, supports further evaluation of tirzepatide in patients with NASH

⁽¹⁾Abstract 134-OR. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.

TIRZEPATIDE CLINICAL PROGRAM

OPERATIONAL UPDATE

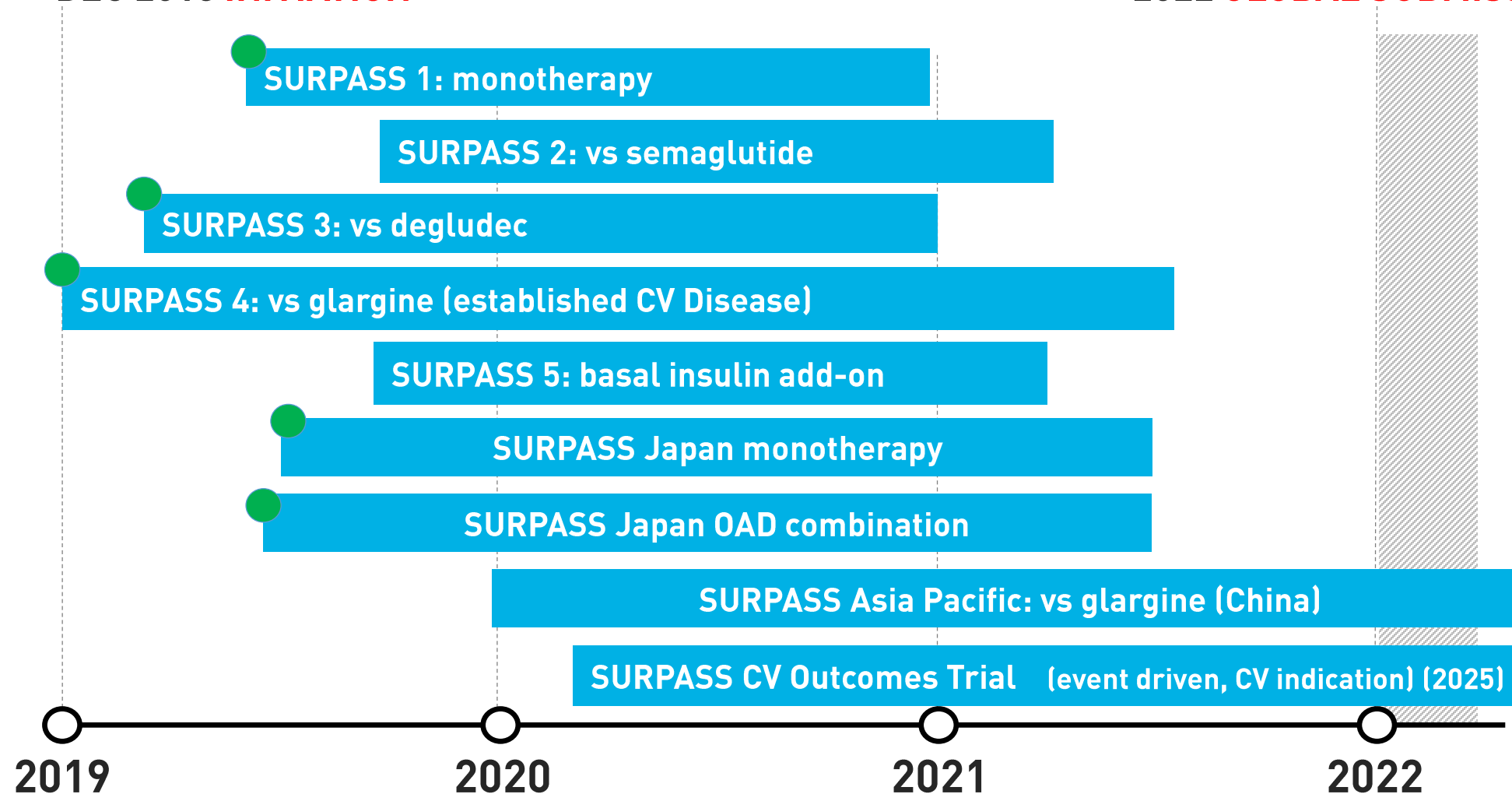


SURPASS TYPE 2 DIABETES PROGRAM

● Five type 2 diabetes Phase 3 studies initiated

DEC 2018 **INITIATION**

2022 **GLOBAL SUBMISSIONS**



OTHER INDICATIONS



Obesity **Phase 3** – start of SURMOUNT program

NASH **Phase 2** – start of SYNERGY-NASH program

Summary



Exciting time in Lilly Diabetes

Significant growth during five year period, nearly doubling revenue and expanding portfolio with new products



Strong commercial launch capabilities

Trulicity and Jardiance both established market leaders in fast growing diabetes classes



Trulicity REWIND data positive for patients

Precedent-setting trial produced superior CV results in a broad population of patients, and had a consistent effect in patients with and without prior CVD



Continuing to raise the bar with tirzepatide

Additional insights shared for the dosing regimen, mechanism of action and support for development in NASH and obesity



QUESTIONS AND ANSWERS

**LILLY UNITES
CARING WITH DISCOVERY
TO CREATE MEDICINES THAT
MAKE LIFE BETTER
FOR PEOPLE
AROUND THE WORLD**

Lilly