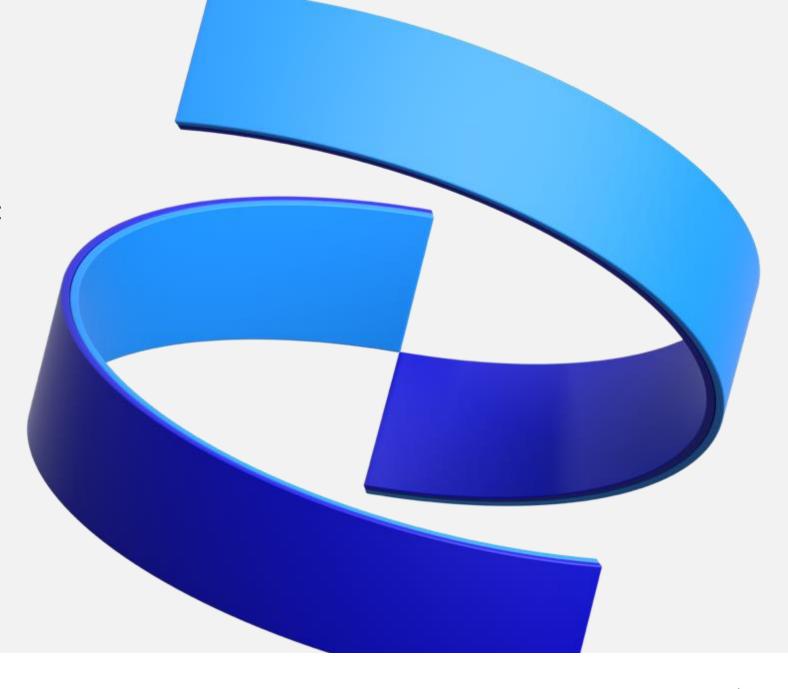
Analyst and Investor Call to Review Oral GLP-1 Data: Scientific Data

The European Association for the Study of Diabetes (EASD) Annual Meeting, Stockholm

September 21, 2022





## Forward-Looking Statements and Other Notices

This presentation and our discussions during this conference call will include forward-looking statements that are subject to substantial risks and uncertainties, many of which are beyond our control, that could cause actual results to differ materially from those expressed or implied by such statements. We may include forward-looking statements about, among other topics, Pfizer's oral GLP-1 candidates, danuglipron and PF-07081532, including anticipated regulatory submissions, data read-outs, study starts, approvals, clinical trial results and other developing data, potential market opportunity, revenue contribution, growth, performance, timing of exclusivity and potential benefits; anticipated operating and financial performance; capital allocation objectives; future opportunities and strategies; and growth potential. Among other things, any statements regarding growth; the development or commercial potential of the product pipeline, inline products, product candidates and additional indications, including expected clinical trial protocols, the timing of the initiation and progress of clinical trials and data read-outs from trials; the timing for the submission of applications for and receipt of regulatory approvals; expected profile and product labeling; and expected breakthrough, best or first-in-class or blockbuster status of products are forward-looking and are estimates that are subject to change and clinical trial and regulatory success. These statements are subject to risks, uncertainties and other factors that may cause actual results to differ materially from past results, future plans and projected future results.

Additional information regarding these and other factors affecting such statements can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in our subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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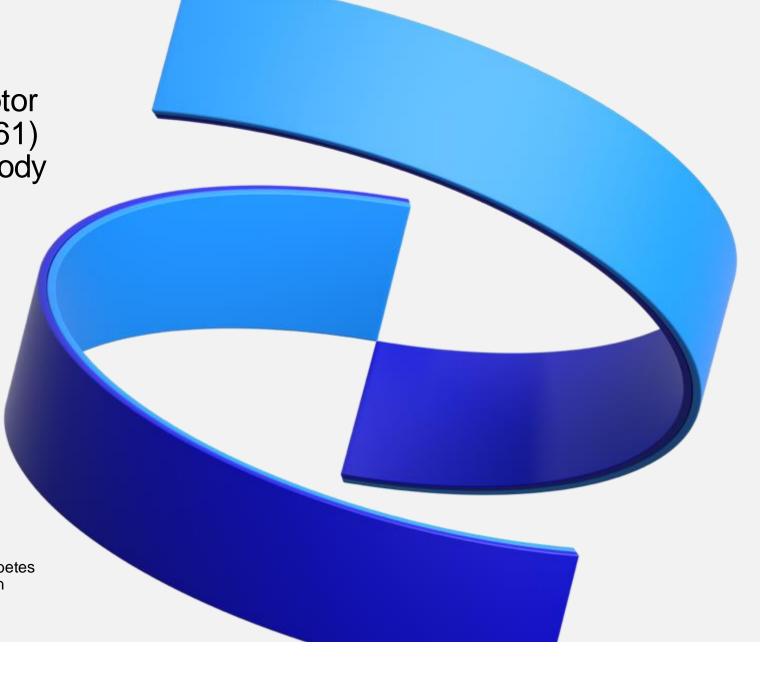
Oral small molecule GLP-1 receptor agonist danuglipron (PF-06882961) results in glucose lowering and body weight loss over 16 weeks in a Phase 2b study in adults with Type 2 diabetes mellitus

<u>Aditi R Saxena<sup>1</sup></u>, Juan Frias<sup>2</sup>, Lisa S Brown<sup>3</sup>, Donal N Gorman<sup>4</sup>, Nikolaos Tsamandouras<sup>1</sup>, Morris J Birnbaum<sup>1\*</sup>

<sup>1</sup>Pfizer Worldwide Research, Development, and Medical, Cambridge, MA, USA; <sup>2</sup>Velocity Clinical Research, Los Angeles, CA, USA; <sup>3</sup>Pfizer Worldwide Research and Development, Collegeville, PA, USA; <sup>4</sup>Pfizer Worldwide Research and Development, Cambridge, UK

\*At the time of the study

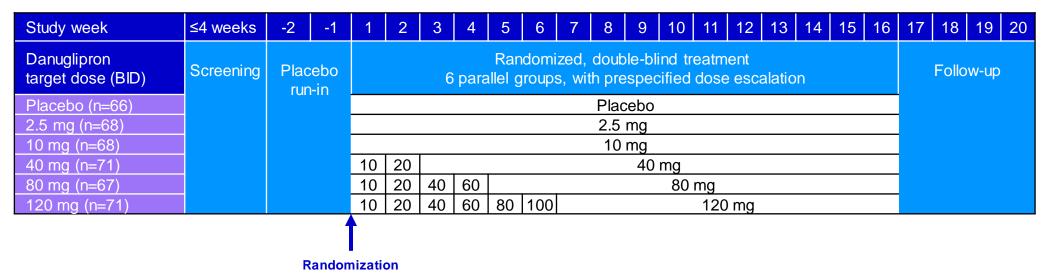
#589, Presented at the European Association for the Study of Diabetes (EASD) Annual Meeting, September 20, 2022, Stockholm, Sweden





## Introduction, Objectives and Study Design

- Objectives and study design: Phase 2b, randomized, placebo-controlled, parallel group, dose-ranging study to examine the effect of danuglipron on efficacy, safety, tolerability and pharmacokinetics over 16 weeks in adults with T2D (NCT03985293)
- Primary efficacy endpoint: change from baseline in HbA1c at Week 16
- Key secondary endpoints: changes from baseline in FPG and body weight at Week 16
- Study was conducted during the early stages of the pandemic, July 2020 to July 2021
- 411 participants were randomized and dosed, and 316 (77%) completed double-blind treatment



BID, twice daily; FPG, fasting plasma glucose; GLP-1R, glucagon-like peptide-1 receptor; HbA1c, glycated hemoglobin; T2D, Type 2 diabetes



## Eligibility Criteria and Baseline Characteristics



#### **Key Eligibility Criteria**

- T2D treated with diet and exercise, with or without metformin
- HbA1c ≥7% and ≤10.5%
- Stable body weight
- Body mass index<sup>b</sup> 24.5–45.4 kg/m<sup>2</sup>



## Demographics and Baseline Characteristics of the Overall Population<sup>a</sup>

• **Age:** 58.6 ± 9.33 years

• Female: 49.1%

• Race: White 83.5%, other 16.5%

• Ethnicity: Hispanic or Latino 31.1%, other 68.9%

• Duration of T2D:  $8.8 \pm 6.68$  years

• Metformin use: 91.5%

• **HbA1c:**  $8.07 \pm 0.92\%$ 

• **FPG**:  $169.3 \pm 41.65 \text{ mg/dL}$ 

• **Body weight:**  $91.3 \pm 17.89 \text{ kg}$ 

• **Body mass index:** 32.8 ± 5.25 kg/m<sup>2</sup>

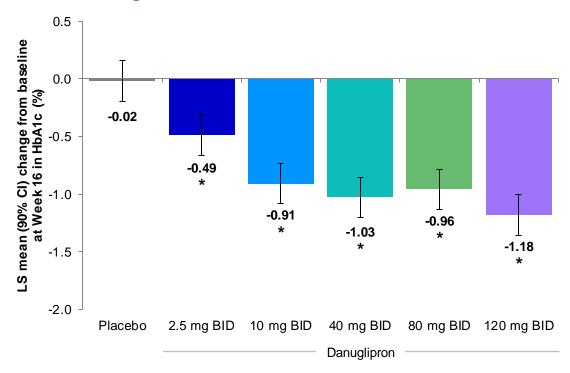
a. Proportion of participants for categorical data and mean ± standard deviation for continuous data. b. Minimum for North America/Europe w as 24.5 kg/m²; minimum for Asia w as 22.5 kg/m². FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; T2D, type 2 diabetes



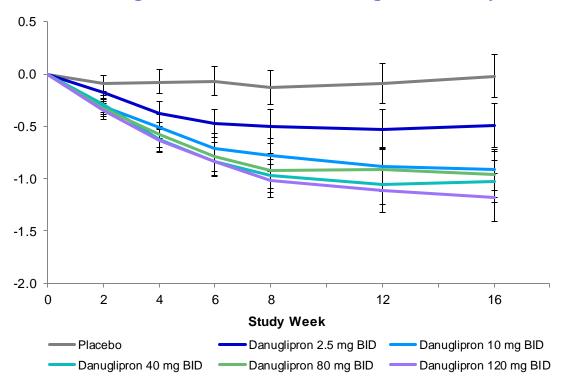
## Significant, Dose-responsive Declines in HbA1c

All danuglipron groups demonstrated statistically significant dose-responsive declines from baseline in HbA1c at Week 16 compared with placebo (all P<0.0001, except 2.5 mg BID which was P<0.01)

#### **HbA1c: Change from Baseline at Week 16**



#### **HbA1c: Change from Baseline Through the Study**



<sup>\*</sup>Prespecified two-sided P<0.1 (statistically significant) versus placebo. Mixed model repeated measures analysis including treatment, time, strata (metformin vs diet/exercise), and treatment-time interaction as fixed effects; baseline as covariate; and baseline-time interaction with time fitted as a repeated effect and participant as a random effect.

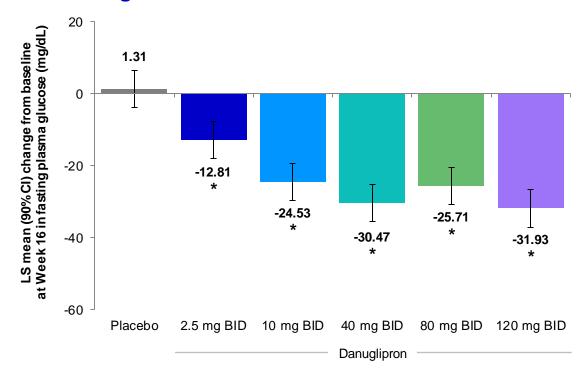
BID, twice daily; CI, confidence interval; HbA1c, glycated haemoglobin; LS, least squares



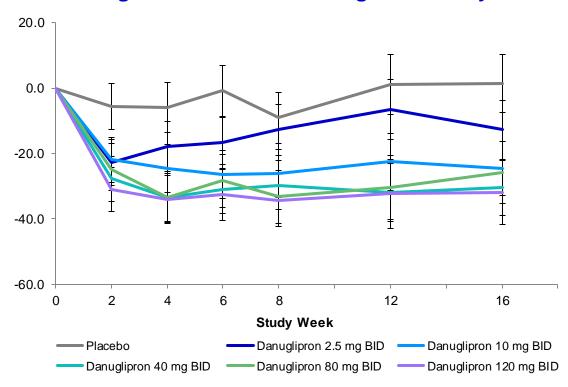
## Significant Reduction in Fasting Plasma Glucose Over 16 weeks

At Week 16, FPG was statistically significantly reduced with all Danuglipron doses compared with placebo (P<0.001 for all doses ≥10 mg BID; P<0.1 for 2.5 mg BID)

#### FPG: Change from baseline at Week 16



#### **FPG: Change from Baseline Through The Study**



\*Prespecified two-sided P<0.1 (statistically significant) versus placebo. Mixed model repeated measures analysis including treatment, time, strata (metformin vs diet/exercise), and treatment-time interaction as fixed effects; baseline as covariate; and baseline-time interaction with time fitted as a repeated effect and participant as a random effect.

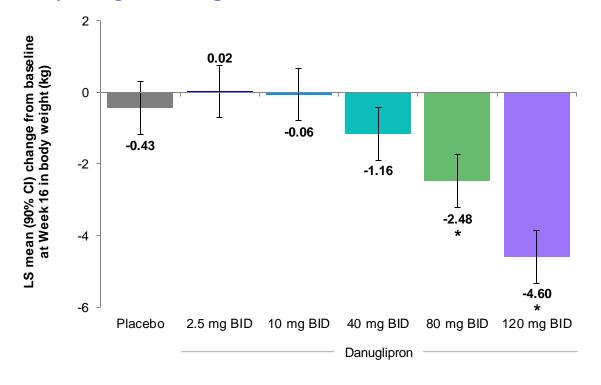
BID, twice daily; CI, confidence interval; FPG, fasting plasma glucose; LS, least squares



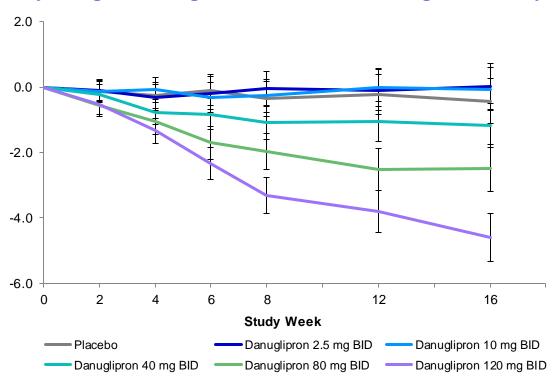
## Significant Decline in Body Weight Over 16 Weeks

Body weight was statistically significantly reduced at Week 16 in the Danuglipron 80 mg BID and 120 mg BID groups (both P<0.001), compared with placebo

#### **Body Weight: Change from Baseline at Week 16**



#### **Body Weight: Change from Baseline Through the Study**



<sup>\*</sup>Prespecified two-sided P<0.1 (statistically significant) versus placebo. Mixed model repeated measures analysis including treatment, time, strata (metformin vs diet/exercise), and treatment-time interaction as fixed effects; baseline as covariate; and baseline-time interaction with time fitted as a repeated effect and participant as a random effect.

BID. twice daily: CI, confidence interval; LS, least squares



## Safety & Tolerability Profile Consistent with Mechanism

- The majority of AEs were mild, with nausea, diarrhoea and vomiting most common
- No episodes of severe hypoglycemia
- No clinically significant, adverse trends in laboratory measures, electrocardiogram or vital sign abnormalities

		Danuglipron								
Participants, n (%)	Placebo (n=66)	2.5 mg BID (n=68)	10 mg BID (n=68)	40 mg BID (n=71)	80 mg BID (n=67)	120 mg BID (n=71)	Total (N=411)			
Participants who discontinued study medication due to AE	5 (7.6)	2 (2.9)	3 (4.4)	8 (11.3)	15 (22.4)	24 (33.8)	57 (13.9)			
Participants with ≥1 AE	32 (48.5)	32 (47.1)	31 (45.6)	42 (59.2)	43 (64.2)	44 (62.0)	224 (54.5)			
Participants with ≥1 AE										
Nausea	2 (3.0)	5 (7.4)	5 (7.4)	11 (15.5)	22 (32.8)	23 (32.4)	68 (16.5)			
Diarrhoea	2 (3.0)	3 (4.4)	4 (5.9)	8 (11.3)	12 (17.9)	7 (9.9)	36 (8.8)			
Vomiting	0	0	1 (1.5)	5 (7.0)	11 (16.4)	18 (25.4)	35 (8.5)			
Dyspepsia	0	4 (5.9)	3 (4.4)	2 (2.8)	9 (13.4)	2 (2.8)	20 (4.9)			
Gastro-oesophageal reflux disease	0	1 (1.5)	2 (2.9)	2 (2.8)	4 (6.0)	5 (7.0)	14 (3.4)			
Abdominal distension	1 (1.5)	0	1 (1.5)	4 (5.6)	3 (4.5)	2 (2.8)	11 (2.7)			

Treatment-emergent AEs, all causality. Participants counted once per treatment per event. Includes all data collected since the first dose of double-blind study medication. Participants who discontinued study medication might still have continued in the study. Gastrointestinal AEs (preferred terms) with ≥5% in any treatment arm are shown.

AE, adverse event; BID, twice daily



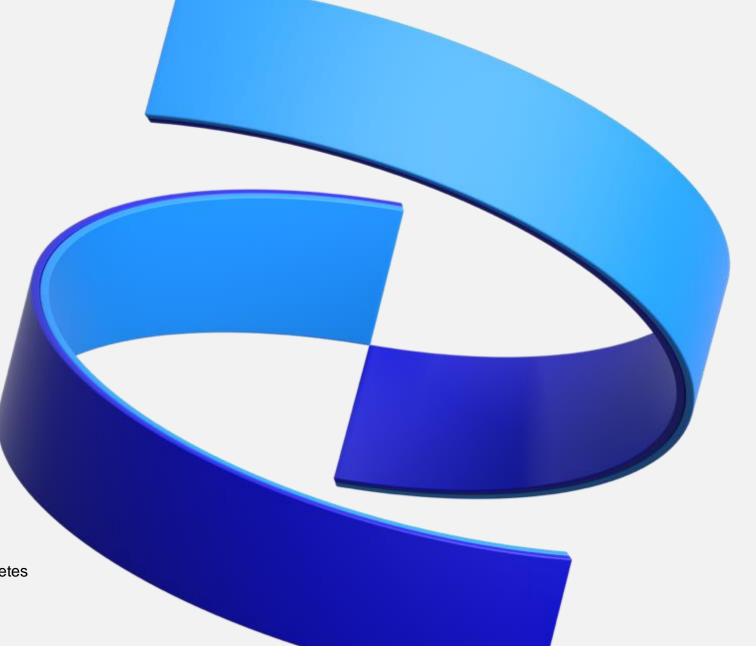
Efficacy, safety and tolerability of danuglipron (PF-06882961) over 12 weeks in Phase 2a study in adults with Type 2 diabetes mellitus

Donal N Gorman<sup>1</sup>, Aditi R Saxena<sup>2</sup>, Juan Frias<sup>3</sup>, Rene N Lopez<sup>4</sup>, Nikolaos Tsamandouras<sup>2</sup>, Morris J Birnbaum<sup>2\*</sup>

<sup>1</sup>Pfizer Worldwide Research and Development, Cambridge, UK; <sup>2</sup>Pfizer Worldwide Research, Development, and Medical, Cambridge, MA, USA; <sup>3</sup>Velocity Clinical Research, Los Angeles, CA, USA; <sup>4</sup>Pfizer Inc, Groton, CT, USA.

\*At the time of the study

#588, Presented at the European Association for the Study of Diabetes (EASD) Annual Meeting, September 20, 2022, Stockholm, Sweden





Breakthroughs that change patients' lives

## Danuglipron 12-Week Phase 2a Study Overview

- Danuglipron: an oral small molecule GLP-1R agonist being investigated for T2D and/or obesity
- Objectives and study design: phase 2a, randomised, double-blind, placebo-controlled, parallel-group study to
  assess the tolerability, safety and pharmacodynamic effects over 12 weeks of different danuglipron dose
  escalation schemes in adults with T2D treated with metformin (NCT04617275)
- Endpoints: tolerability (primary) and changes from baseline in HbA1c, FPG and body weight at Week 12
- Study was conducted in the US during the pandemic, January 2021 to November 2021

Danuglipron target dose (BID)   Dose escalation schedule <sup>a</sup>   Participants	Study week			≤4 weeks	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13-16
80 mg (n=20) LS T2D  80 mg (n=22) HS T2D  10 20 40 60 80  120 mg (n=22) LF T2D  120 mg (n=22) HF T2D  120 mg (n=22) HF T2D  10 20 40 60 80 100 120  120 mg (n=21) HF T2D  10 20 40 60 80 100 120  120 mg (n=6) - Obesity  10 20 40 60 80 100 120 140 160 180 200			Participants	Screening										Follow-up					
80 mg (n=22)	Placebo (n=16)	-	T2D				Placebo												
120 mg (n=22)     LF     T2D       120 mg (n=22)     HF     T2D       200 mg (n=21)     HF     T2D       Placebo (n=6)     -     Obesity         5     10     20     40     60     80     100     120       10     20     40     60     80     100     120       10     20     40     60     80     100     120     140     160     180     200	80 mg (n=20)	LS	T2D		5 10 20 40 60 80						80								
120 mg (n=22)     HF     T2D       200 mg (n=21)     HF     T2D       Placebo (n=6)     -     Obesity         10     20     40     60     80     100     120     140     160     180     200       Placebo     -     Obesity	80 mg (n=22)	HS	T2D				10 20 40 60 80												
200 mg (n=21)     HF     T2D       Placebo (n=6)     -     Obesity         10     20     40     60     80     100     120     140     160     180     200       Placebo	120 mg (n=22)	LF	T2D				5	10	20	40	60	80	100			120			
Placebo (n=6) - Obesity Placebo	120 mg (n=22)	HF	T2D				10 20 40 60 80 100 120												
	200 mg (n=21)	HF	T2D				10	20	40	60	80	100	120	140	160	180	2	00	
200 mg (n=22) HF Obesity 10 20 40 60 80 100 120 140 160 180 200	Placebo (n=6)	-	Obesity				Placebo												
200 mg (1 22) 10   00   100   100   100   100   200	200 mg (n=22)	HF	Obesity				10	20	40	60	80	100	120	140	160	180	2	00	

Randomisation

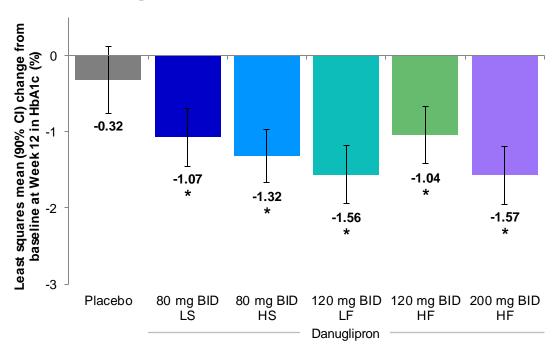
<sup>&</sup>lt;sup>a</sup> Danuglipron dose was escalated to target dose (80 mg BID, 120 mg BID, or 200 mg BID) using low (L, 5 mg BID) or high (H, 10 mg BID) starting dose and fast (F, 1 week) or slower (S, 2 weeks) escalation steps. BID, twice daily; FPG, fasting plasma glucose; GLP-1R, glucagon-like peptide-1 receptor; HbA1c, glycated haemoglobin; T2D, type 2 diabetes; US, United States



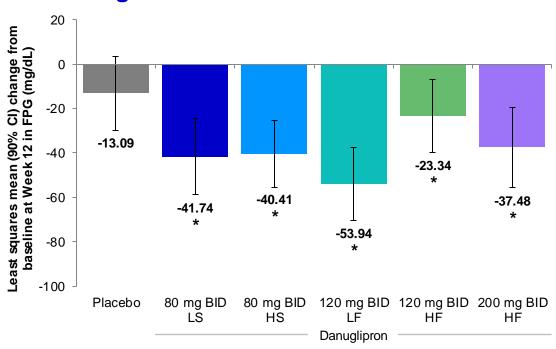
## Declines in HbA1c and FPG with Danuglipron at Week 12 in T2D

Statistically significant reductions from baseline in HbA1c in all Danuglipron groups, and FPG across most groups, at Week 12 were demonstrated compared with placebo

#### HbA1c: Change from baseline at week 12 in T2D



#### FPG: Change from baseline at week 12 in T2D



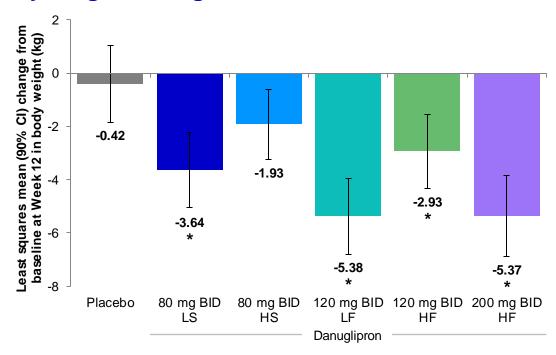
<sup>\*</sup> Prespecified one-sided P<0.05 (statistically significant) versus placebo. Mixed model repeated measures analysis including trætment, time, strata (defined as male vs female) and the treatment-by-time interaction as fixed effects; baseline as a covariate; and the baseline-by-time interaction with time fitted as a repeated effect and participant as a random effect.

BID, twice daily; CI, confidence interval; F, fast; FPG, fasting plasma glucose; H, high; HbA1c, glycated haemoglobin; L, low; S, slow er; T2D, type 2 diabetes



## Declines in Body Weight with Danuglipron at Week 12

#### Body weight: Change from baseline at week 12 in T2D



#### • T2D

 Statistically significant reductions in body weight in all Danuglipron groups at Week 12 were demonstrated compared with placebo (except for Danuglipron 80 mg BID HS)

#### Obesity without T2D

- Least squares mean difference did not reach statistical significance (one-sided P=0.0826)
- Observed (mean ± SD) reductions from baseline at Week 12:
  - **Danuglipron 200 mg BID**: **–7.17** ± 7.24 kg (n=6 who completed double-blind treatment)
  - Placebo: -0.30 ± 2.19 kg (n=5)

<sup>\*</sup> Prespecified one-sided P<0.05 (statistically significant) versus placebo. Mixed model repeated measures analysis including trætment, time, strata (defined as male vs female) and the treatment-by-time interaction as fixed effects; baseline as a covariate; and the baseline-by-time interaction with time fitted as a repeated effect and participant as a random effect.

BID, twice daily; CI, confidence interval; F, fast; H, high; L, low; S, slow er; SD, standard deviation; T2D, type 2 diabetes



## Tolerability and Safety of Danuglipron in 12 Week Phase 2 Study

 Majority of AEs were mild, with nausea, vomiting and diarrhoea most commonly reported; incidence of nausea and vomiting was generally greater at higher doses

		Obesity v	Obesity without T2D					
Participants, n (%)	Placebo (n=16)	Danuglipron 80 mg BID LS (n=20)	Danuglipron 80 mg BID HS (n=22)	Danuglipron 120 mg BID LF (n=22)	Danuglipron 120 mg BID HF (n=22)	Danuglipron 200 mg BID HF (n=21)	Placebo (n=6)	Danuglipron 200 mg BID HF (n=22)
Participants who discontinued study medication due to AE	1 (6.3)	6 (30.0)	4 (18.2)	6 (27.3)	7 (31.8)	8 (38.1)	0	12 (54.5)
Participants with ≥1 AE	8 (50.0)	12 (60.0)	14 (63.6)	16 (72.7)	15 (68.2)	14 (66.7)	4 (66.7)	18 (81.8)
Participants with ≥1 AE (preferred term)								
Nausea	2 (12.5)	4 (20.0)	5 (22.7)	6 (27.3)	8 (36.4)	10 (47.6)	0	13 (59.1)
Vomiting	2 (12.5)	5 (25.0)	4 (18.2)	6 (27.3)	9 (40.9)	6 (28.6)	0	10 (45.5)
Diarrhoea	2 (12.5)	2 (10.0)	1 (4.5)	5 (22.7)	5 (22.7)	1 (4.8)	0	1 (4.5)
Dyspepsia	0	1 (5.0)	1 (4.5)	2 (9.1)	5 (22.7)	1 (4.8)	0	1 (4.5)
Abdominal pain upper	1 (6.3)	1 (5.0)	3 (13.6)	2 (9.1)	1 (4.5)	0	0	3 (13.6)
Constipation	0	1 (5.0)	1 (4.5)	1 (4.5)	1 (4.5)	2 (9.5)	0	2 (9.1)
Gastro-oesophageal reflux disease	1 (6.3)	2 (10.0)	1 (4.5)	1 (4.5)	0	1 (4.8)	0	1 (4.5)
Abdominal pain	0	2 (10.0)	2 (9.1)	0	0	1 (4.8)	0	0
Eructation	0	1 (5.0)	2 (9.1)	0	1 (4.5)	0	0	0
Abdominal distension	0	1 (5.0)	0	0	0	2 (9.5)	0	1 (4.5)

Treatment-emergent AEs, all causality. Participants were counted only once per treatment per event. Includes all data collected since the first dose of double-blind study medication. Participants who discontinued study medication might still have continued in the study. Gastrointestinal AEs with ≥5% in any treatment arm are shown.

AE, adverse event; BID, twice daily; F, fast; H, high; L, low; S, slower; T2D, type 2 diabetes



### Summary of Danuglipron Phase 2 Data

- These Phase 2 clinical data with an oral small molecule GLP-1R agonist demonstrate that danuglipron was generally safe, with a tolerability profile consistent with the mechanism of action<sup>1,2</sup>
- Danuglipron reduced HbA1c, FPG and body weight in T2DM at multiple dose levels at Weeks 12-16, compared with placebo, and was administered without fasting restrictions
  - Declines in HbA1c up to -1.57% and body weight up to -5.38 kg were observed in T2D over this duration
- Adverse events (AEs) were generally mild in nature, and the most common AEs were gastrointestinal and consisted of nausea, diarrhea and vomiting
- The efficacy and safety data are in line with Phase 1 data for danuglipron<sup>3</sup> and Phase 2 data for peptidic GLP-1R agonists over similar durations of time<sup>4-6</sup>

<sup>1.</sup> Bain EK, et al. *Diabetes Obes Metab*. 2021;23(Suppl 3):30-9. 2. Drucker DJ. *Cell Metab* 2018;27:740-56. 3. Saxena AR, et al. *Nat Med*. 2021;27:1079-87. 4. Skrivanek Z, et al. *Diabetes Obes Metab*. 2014;16:748-56. 5. Davies M, et al. *JAMA*. 2017;318:1460-70. 6. Nauck MA, et al. *Diabetes Care*. 2016;39:231-41. AE, adverse event; FPG, fasting plasma glucose; GLP-1R, glucagon-like peptide-1 receptor; HbA1c, glycated haemoglobin; T2D, type 2 diabetes

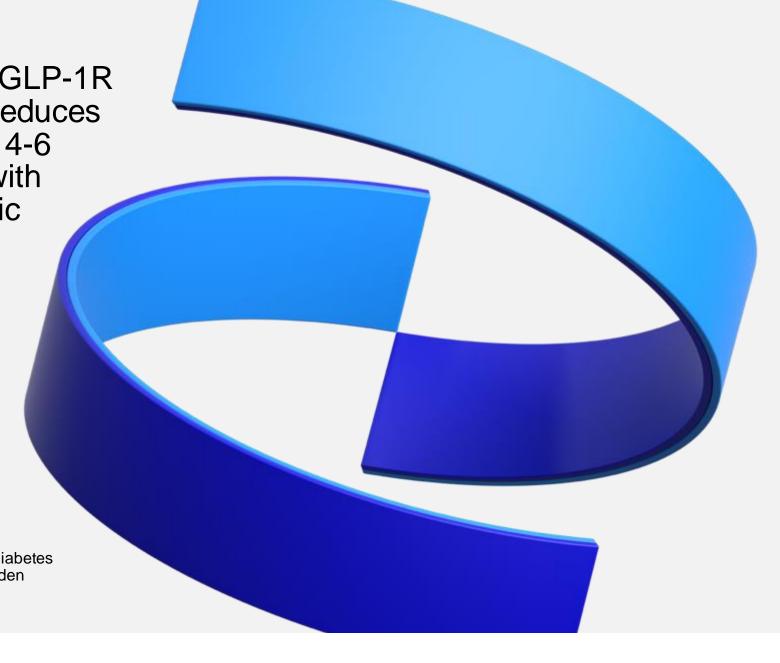


Once-daily oral small molecule GLP-1R agonist PF-07081532 robustly reduces glucose and body weight within 4-6 weeks in a Phase 1b in adults with Type 2 diabetes and non-diabetic adults with obesity

Clare Buckeridge<sup>1</sup>, Nikolaos Tsamandouras<sup>1</sup>, Santos Carvajal-Gonzalez<sup>1</sup>, Lisa S Brown<sup>2</sup>, Kristin L Chidsey<sup>1</sup>, Aditi R Saxena<sup>1</sup>

<sup>1</sup>Pfizer Worldwide Research, Development, and Medical, Cambridge, MA, USA; <sup>1</sup>Pfizer Worldwide Research, Development, and Medical, Collegeville, PA, USA

#114, Presented at the European Association for the Study of Diabetes (EASD) Annual Meeting, September 21, 2022, Stockholm, Sweden

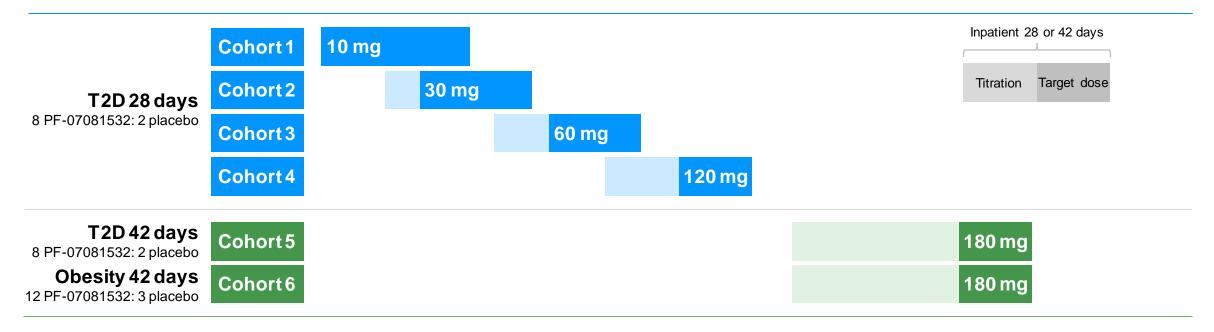




Breakthroughs that change patients' lives

## Study Design Overview

- Inpatient study (NCT05158244) conducted at 2 clinical research units in the United States
- 6 cohorts were enrolled: 5 cohorts of participants with T2D and 1 cohort with obesity
- PF-07081532 or placebo administered once daily, with breakfast
- Rapid titration used to achieve higher doses
- Dosing took place during the early stages of the COVID-19 pandemic: mid-2020 to mid-2021



COVID-19, coronavirus disease 2019; T2D, type 2 diabetes



## Population and Key Endpoints



#### **Adult Participants**

#### With type 2 diabetes:

- T2D
   (stable metformin ≥ 500 mg)
- HbA1c 7%–10.5%
- BMI 24.5–45.5 kg/m<sup>2</sup>

#### With obesity:

- HbA1c < 6.5%
- BMI 30.5–45.5 kg/m<sup>2</sup>



### **Key Safety and Tolerability Endpoints**

- Adverse events (AEs), discontinuations due to AEs
- Laboratory tests, vital signs, 12-lead ECGs



#### **Other Assessments**

- Change from baseline in mean daily glucose and fasting plasma glucose
- Change from baseline in HbA1c and body weight over 4–6 weeks
- Pharmacokinetic parameters

AE, adverse event; BMI, body mass index; ECG, electrocardiogram; HbA1c, glycated haemoglobin; T2D, type 2 diabetes



## Key Baseline Demographic and Disease Characteristics

#### A total of 66 participants were randomised

T2D: 51 participants; 40 for dosing duration of 28 days and 11 for dosing duration of 42 days

**Obesity**: 15 participants for dosing duration of 42 days

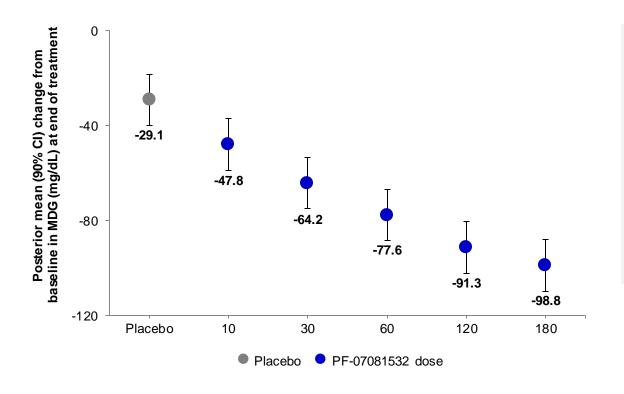
	T2D	Obesity
Age, years	58.6 (8.3)	53.3 (9.1)
Male, %	52.9	53.3
T2D duration, years	10.7 (5.4)	N/A
MDG, mg/dL	207.8 (36.9)	N/A
FPG, mg/dL	194.1 (38.7)	N/A
HbA1c, %	8.6 (1.0)	5.6 (0.5)
Body weight, kg	89.7 (19.3)	98.2 (12.2)
BMI, kg/m <sup>2</sup>	32.1 (5.8)	32.9 (6.9)

Arithmetic mean (standard deviation) for all except % for male.

Body w eight measured at Screening Visit; FPG and HbA1c were defined as the measurement on Day -1, 0 hours. MDG was defined as the AUC24 of glucose/24 hours on Day -1. BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; N/A, not applicable; MDG, mean daily glucose; T2D, type 2 diabetes



## Robust Declines in Mean Daily Glucose with Once-daily PF-07081532 in Participants with T2D



Observed mean reductions from baseline in MDG were dose-dependent

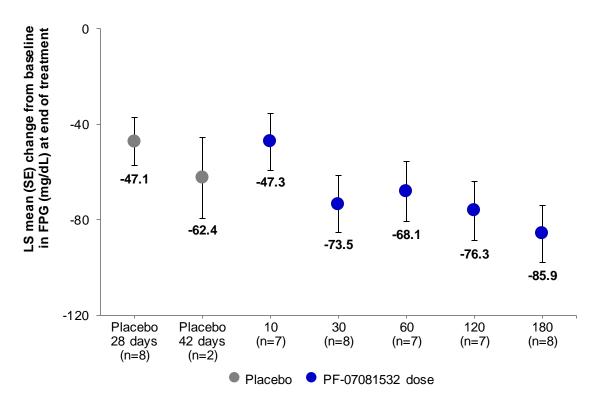
Each of the PF-07081532 doses were statistically significantly different to placebo

A Bayesian 4-parameter dose-response Emax model was applied to the change from baseline on Day 28 or Day 42. The model included stable dose as a continuous variable and baseline as a covariate. Stable dose refers to the PF-07081532 dose (or placebo) that participants received during Days 24 to 28 (28-day) or Days 38 to 42 (42-day). Placebo data were pooled across 5 T2D cohorts with 28 or 42 days of dosing.

Cl. confidence interval: MDG, mean daily glucose; T2D, type 2 diabetes



## Fasting Plasma Glucose Approaching Non-diabetic Thresholds with Once-daily PF-07081532 in Participants with T2D



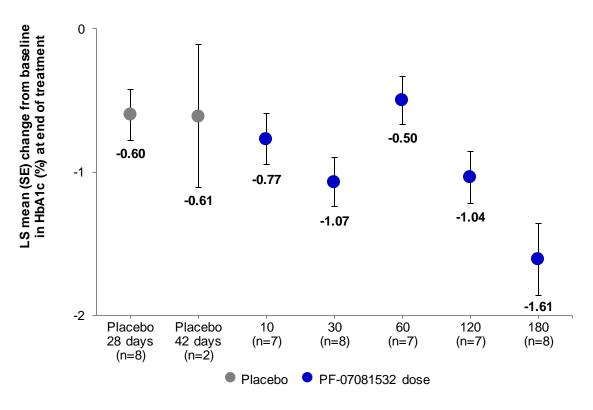
Observed average reductions from baseline in FPG were up to -79 mg/dL over 28 days and up to -102 mg/dL over 42 days

By Day 28, all PF-07081532 treatment groups >10 mg had observed average fasting plasma glucose levels of ≤126 mg/dL

Baseline is defined as the measurement collected at Day -1, 0 hours. FPG, fasting plasma glucose; LS, least squares; SE. standard error; T2D, type 2 diabetes



## HbA1c Reduction with Once-daily PF-07081532 for 4 to 6 Weeks in Participants with T2D

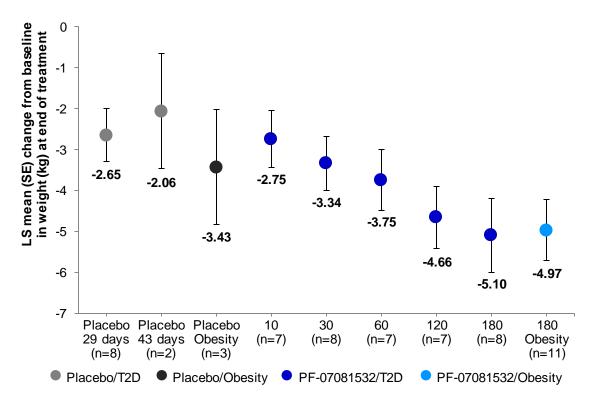


While longer duration of intervention is required to assess the effect of treatment on HbA1c, reductions were observed following dosing with PF-07081532, with modelled mean decreases of up to -1.61% in 6 weeks

Baseline is defined as the measurement collected at Day -1, 0 hours. LS, least squares; HbA1c, glycated haemoglobin; SE, standard error; T2D, type 2 diabetes



## Dose-responsive Weight Reduction with Once-daily PF-07081532 for 4 to 6 Weeks



While longer duration of intervention is required to assess the effect of treatment on body weight, reductions were observed following dosing with PF-07081532 for 4 to 6 weeks: mean decreases from baseline of up to approx. -5.5% in participants with T2D and approx. -5.2% in participants with obesity

Baseline is defined as the pre-dose measurement on Day 1. LS, least squares: SE, standard error: T2D, type 2 diabetes



## Observed Adverse Effect Profile of PF-07081532 in Phase 1b Study is Consistent with the Mechanism of Action

**Adverse Events**: Most events (87% for T2D; 94% for obesity) were reported as mild in intensity, with gastrointestinal disorders most common across groups, in line with the mechanism of action. None of the events listed below were severe or serious

Safety Laboratory, ECG, Vitals: No clinically significant adverse trends

			T2D 28 day	/S	T2D 4	-2 days	Obesity 42 days		
	Placebo	10 mg	30 mg	60 mg	120 mg	Placebo	180 mg	Placebo	180 mg
Randomised (n)	9	7	8	8	8	2	9	3	12
Discontinued study drug due to AE (n)	0	0	0	1	1	0	0	0	1
Participants with AE (n)	7	3	7	8	8	2	9	3	11
Number (%) of participar	nts with all-ca	usality treati	ment-emerger	nt AEs of intere	est, by Preferre	d Term			
Nausea	2 (22.2)	0	2 (25.0)	4 (50.0)	5 (62.5)	1 (50.0)	8 (88.9)	1 (33.3)	7 (58.3)
Diarrhoea	2 (22.2)	1 (14.3)	4 (50.0)	2 (25.0)	4 (50.0)	0	2 (22.2)	1 (33.3)	5 (41.7)
Constipation	2 (22.2)	0	1 (12.5)	2 (25.0)	4 (50.0)	1 (50.0)	3 (33.3)	2 (66.7)	6 (50.0)
Headache	2 (22.2)	0	2 (25.0)	4 (50.0)	3 (37.5)	0	3 (33.3)	1 (33.3)	2 (16.7)
Vomiting	1 (11.1)	0	1 (12.5)	3 (37.5)	3 (37.5)	0	2 (22.2)	1 (33.3)	3 (25.0)
Decreased Appetite	0	1 (14.3)	0	3 (37.5)	2 (25.0)	0	3 (33.3)	1 (33.3)	4 (33.3)

Participants were counted once per treatment per event. One participant with SAE reported in follow -up phase, 30-mg group; no other participant with severe or serious AE; no deaths. Low overall frequency of generally mild hypoglycaemia (no cases of severe hypoglycaemia). AE, adverse event; ECG, electrocardiogram; T2D, type 2 diabetes; SAE, serious adverse event



### PF-07081532 Pharmacokinetic Profile Following Last Dose

- PF-07081532 exposure (AUC24 and Cmax) generally increased in an approximately dose-proportional manner across the dose range studied
- Observed half-life is supportive of once-daily administration
- No substantial differences in exposure observed between participants with T2D and those with obesity

		Participants with Obesity				
	10 mg (n=7)	30 mg (n=8)	60 mg (n=8)	120 mg (n=8)	180 mg (n=9)	180 mg (n=12)
AUC <sub>24</sub> , ng.hr/mL	26380 (23)	78930 (20)	177000 (58)	265400 (62)	496500 (44)	521300 (38)
C <sub>max</sub> , ng/mL	2263 (19)	5631 (26)	12860 (51)	18520 (47)	30600 (33)	35000 (37)
T <sub>max</sub> , hr	2.0 (2.0-4.0)	4.0 (1.0–12.0)	4.0 (1.0–10.0)	4.0 (4.0–12.0)	8.0 (6.0–12.0)	4.0 (1.0–12.0)
t <sub>½</sub> , hr	26.5 (4.6)	26.4 (6.3)	23.7 (3.8)	24.5 (5.4)	23.1 (5.9)	20.7 (4.4)

Geometric mean (geometric % coefficient of variation) for all except median (range) for  $T_{max}$  and arithmetic mean (SD) for  $t_{k}$ ; PK parameters refer to total PF-07081532 plasma concentrations; AUC<sub>24</sub>, area under the plasma concentration time profile from time 0 to time 24 hours;  $C_{max}$ , maximum plasma concentration; n, total number of participants in the treatment group;  $t_{k}$ , terminal half life;  $T_{max}$ , time to  $C_{max}$ ; T2D, type 2 diabetes;



# Phase 1b Data with PF-07081532 Over 4-6 Weeks in T2D and Obesity Support Potential Best-in-Class in Efficacy and Tolerability

- Dose-dependent reductions from baseline in MDG, FPG and HbA1c in participants with T2D
- Declines in body weight, with higher doses of PF-07081532 demonstrating greater reductions
- Tolerability profile consistent with the mechanism of action
- Pharmacokinetic profile suitable for once-daily dosing
- Plasma concentrations of PF-07081532 increased approximately dose-proportionally, with similar plasma exposure observed in participants with T2D and participants with obesity

