biomea FUSION™

2026 J.P. Morgan Healthcare Conference

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Biomea Fusion

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Biomea Fusion – Development Candidates

Icovamenib

- **Diabetes**
- **Oral**
- **Small molecule**

COVALENT-111 (Phase 2)

- Insulin-deficient Type 2 Diabetes (T2D)
- GLP-1 inadequately controlled

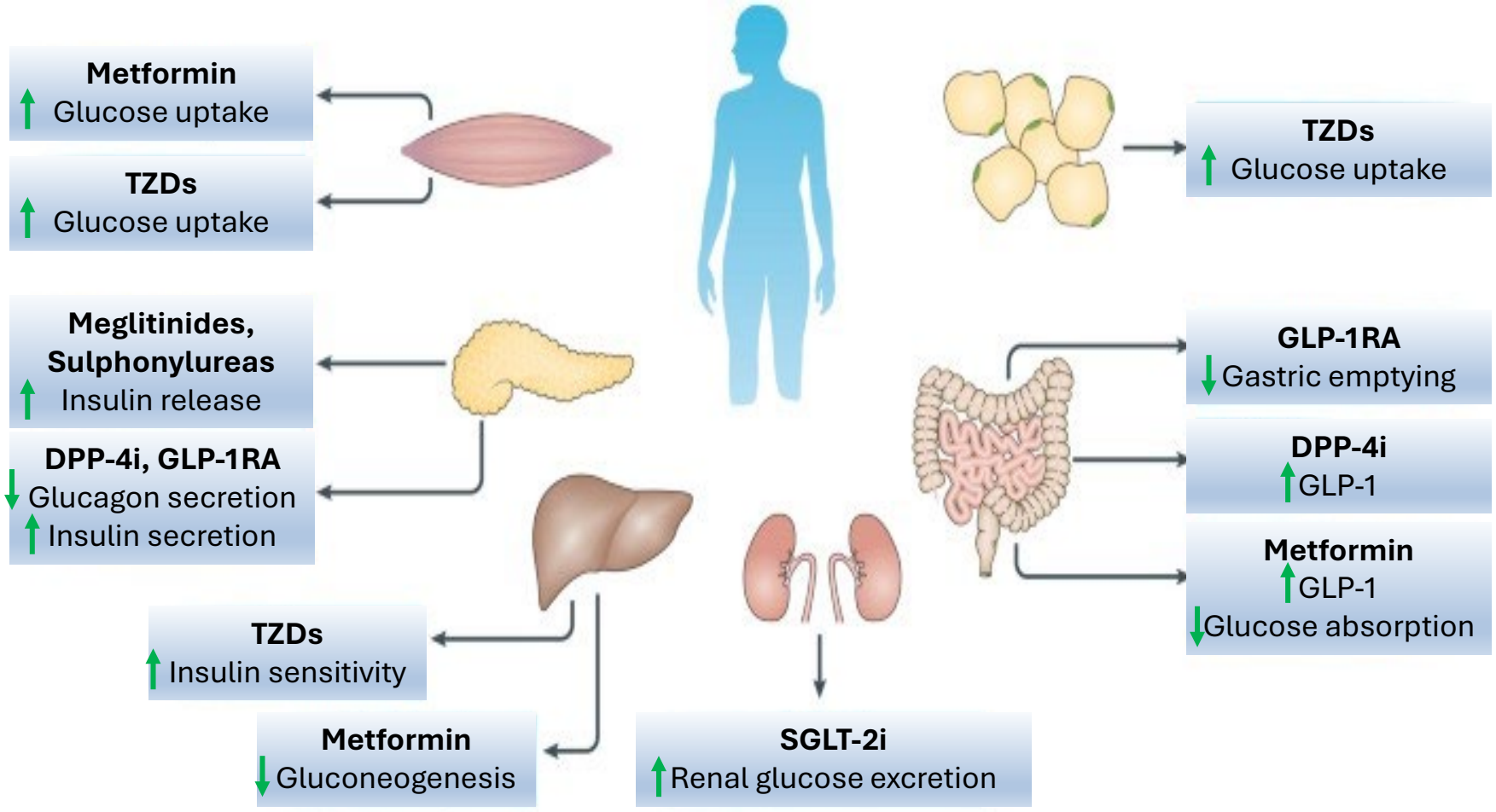
BMF-650 (GLP-1 RA)

- **Weight loss**
- **Oral**
- **Small molecule**

GLP-131 (Phase 1)

Obese (BMI ≥30kg/m^2)

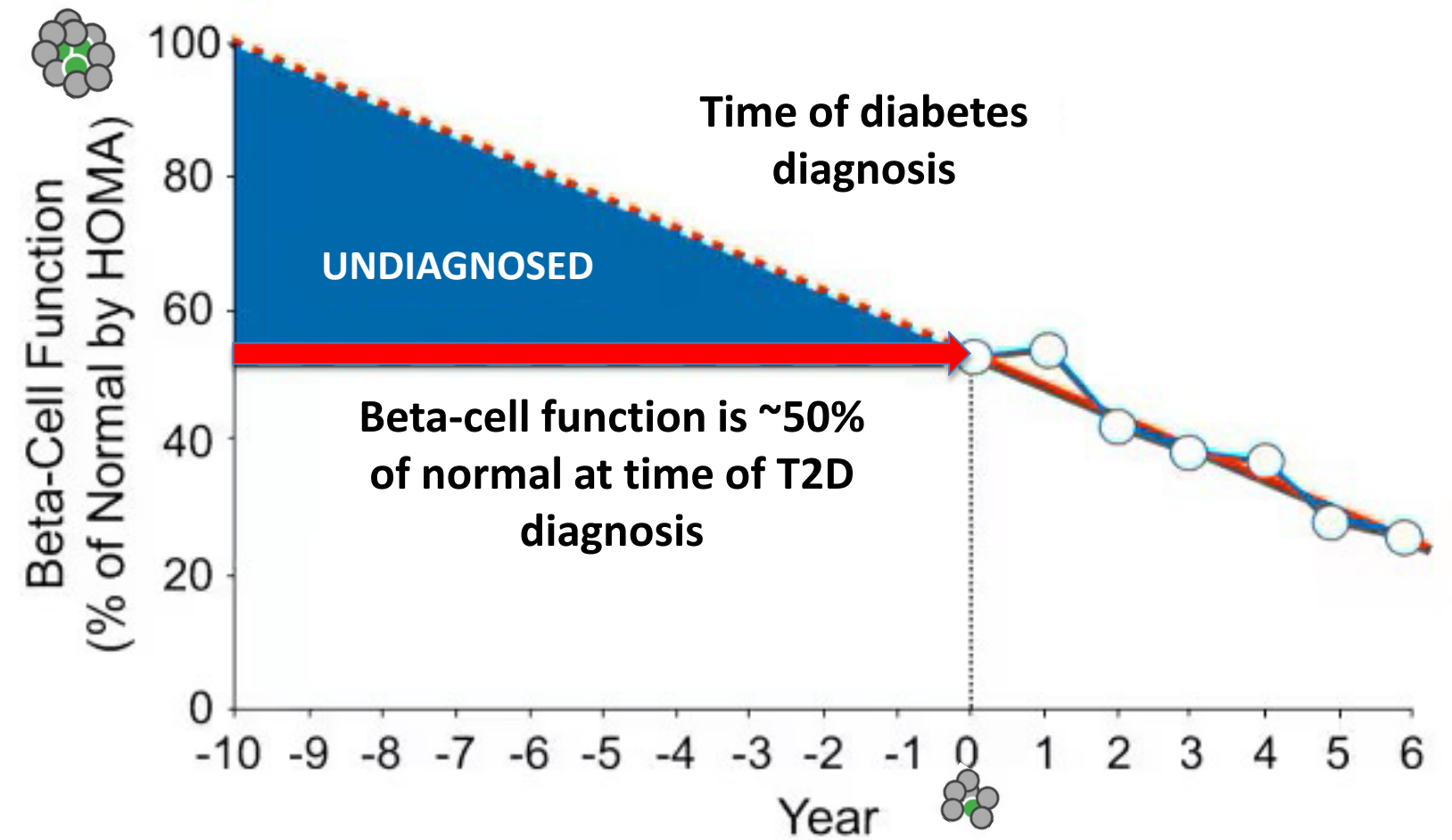
Existing T2D Treatments Address Symptoms, Not Disease Progression



- Existing T2D therapies primarily address downstream metabolic symptoms
- **Icovamenib** is a selective and partial menin inhibitor, targeting a previously unaddressed pathway

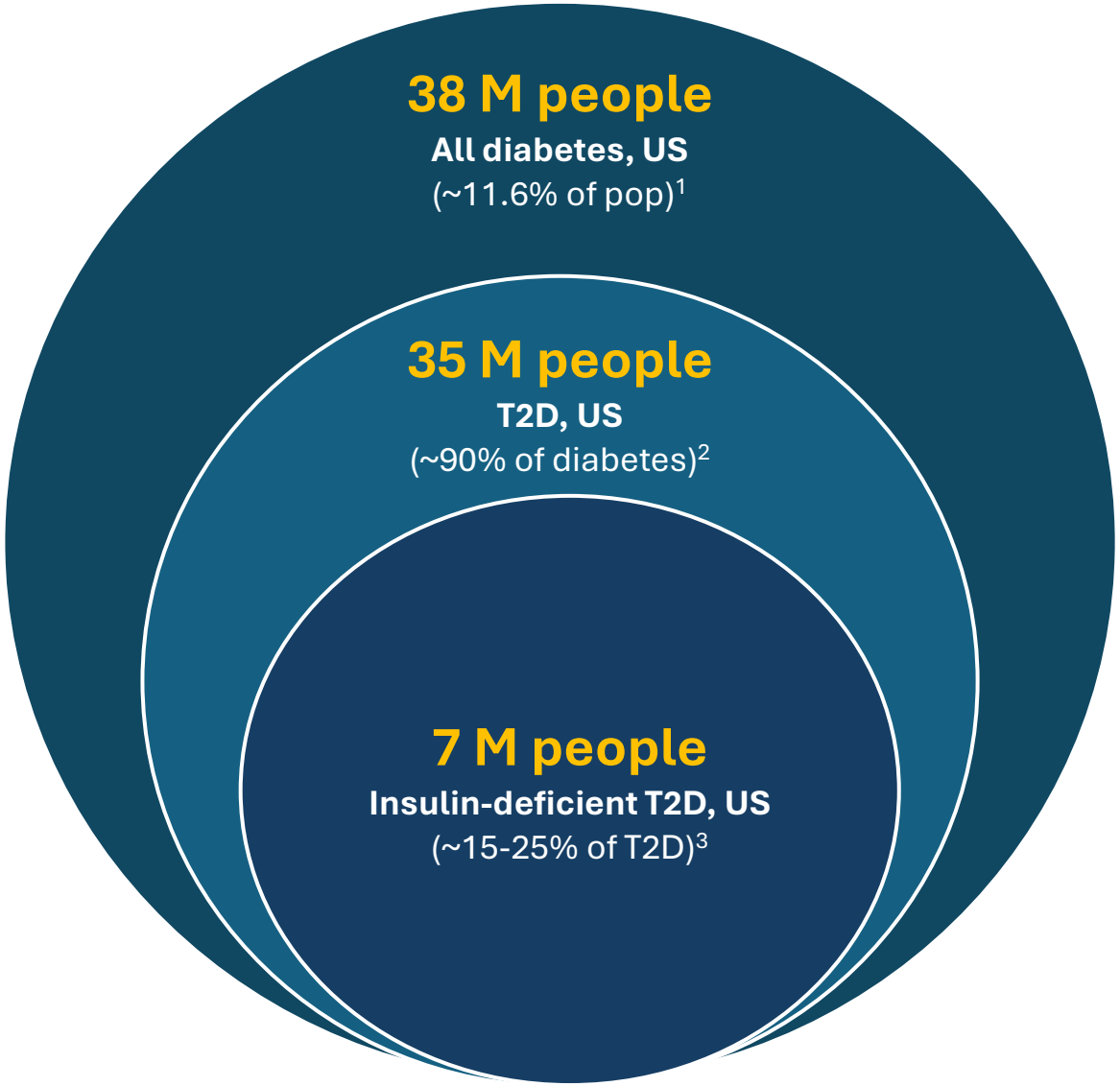
Zhou, Nat Rev Endocrinol, 2016

The Root Cause of Diabetes: T2D is driven by progressive beta-cell failure



Adapted from Lebovitz, Diabetes Rev, 1999

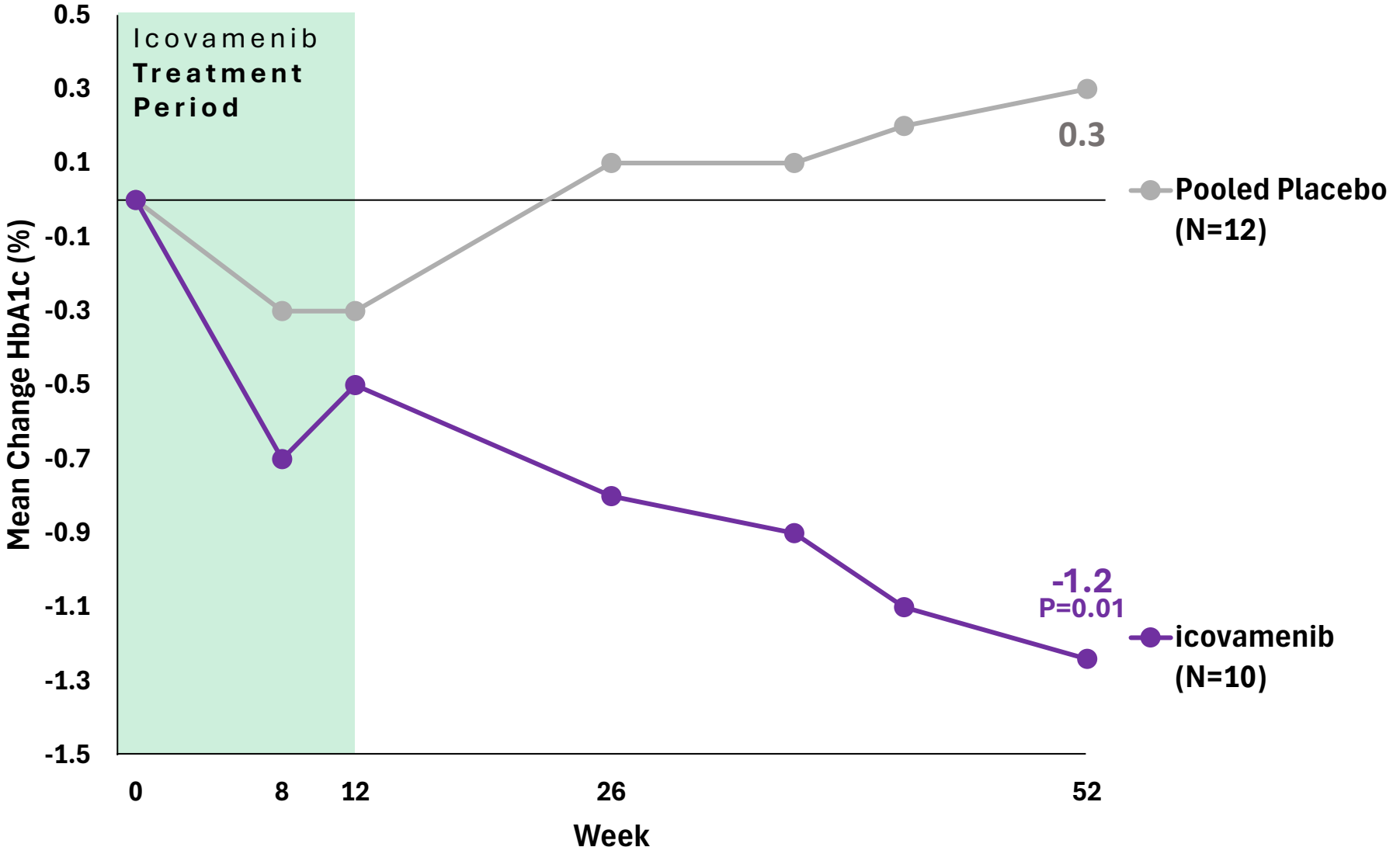
T2D Remains a Growing Health Burden in the US



[1]CDC, Natl. Diabetes Stat. Rep., 2022; [2]ADA, Standards of Care in Diabetes, Diabetes Care, 2024; [3]Ahlqvist, Lancet Diabetes Endocrinol., 2018

Severe Insulin-Deficient Diabetes Patients | 12 Weeks of icovamenib Dosing

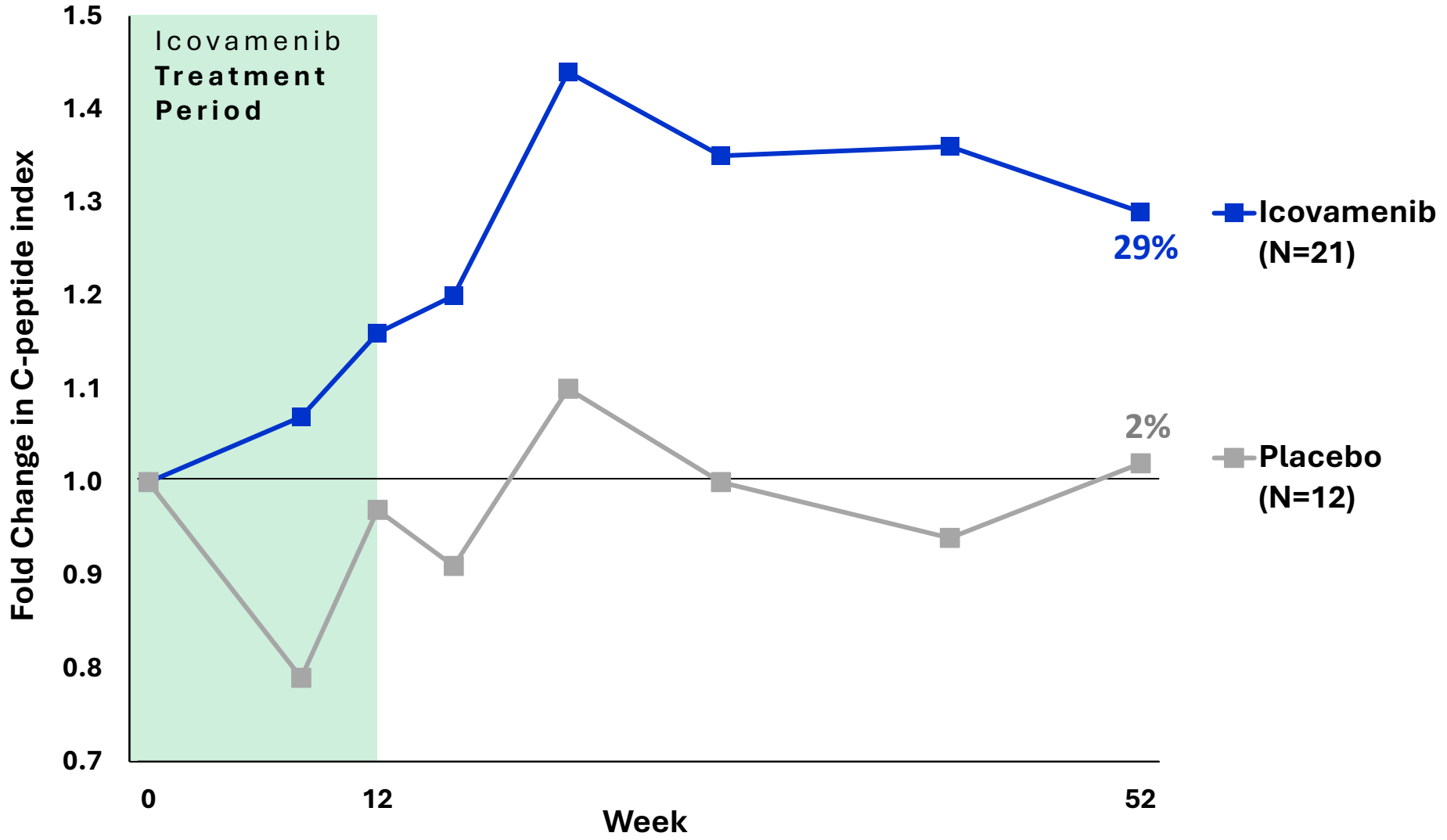
(9 Months After Last Dose)



Arm A was excluded from this analysis because it included only 8 weeks of dosing which the company is not planning to pursue

Icovamenib Increased Insulin Secretion as Measured by C-peptide Index

All severe insulin-deficient patients (All Arms)



Data censored at onset of rescue medication, defined as any modification in antihyperglycemic therapy

Why did HbA1c decrease beyond 12 weeks?

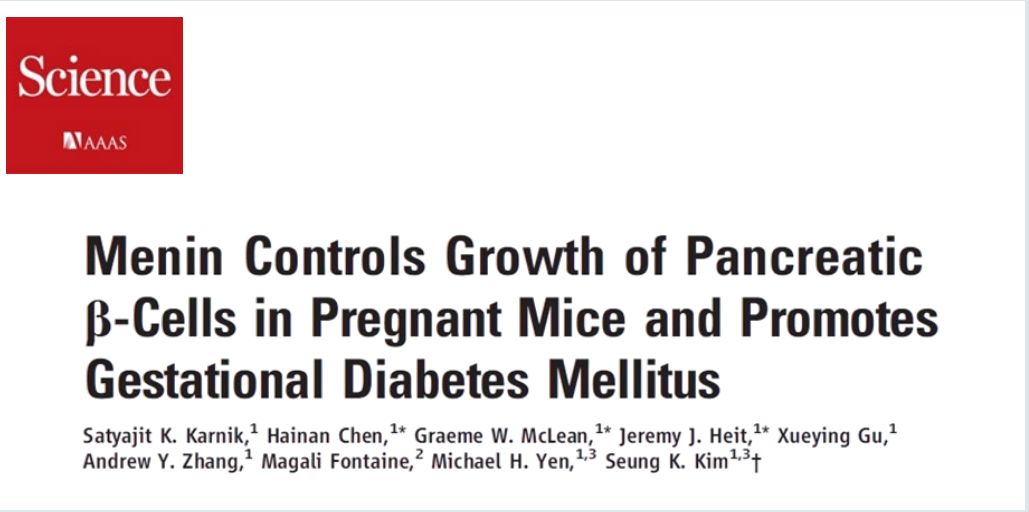
- **Menin suppressed beta-cell proliferation and function**
  - Demonstrated to act as a biological brake on insulin-producing cells in T2D
- **Menin inhibition was shown to lift this brake**
  - Enabled control on beta-cell regeneration and restoration of insulin secretory capacity
- **A short 12-week dosing period induced durable epigenetic reprogramming**
  - Allowed beta-cell functional regeneration to continue post-treatment and driving sustained HbA1c improvements

Physiologic Suppression of Menin Can Expand Beta-Cell Mass

- Physiologic states such as pregnancy and lactation suppress menin, enabling beta-cell expansion and increased insulin output

- Preclinical and human data consistently link reduced menin signaling to improved beta-cell mass and function

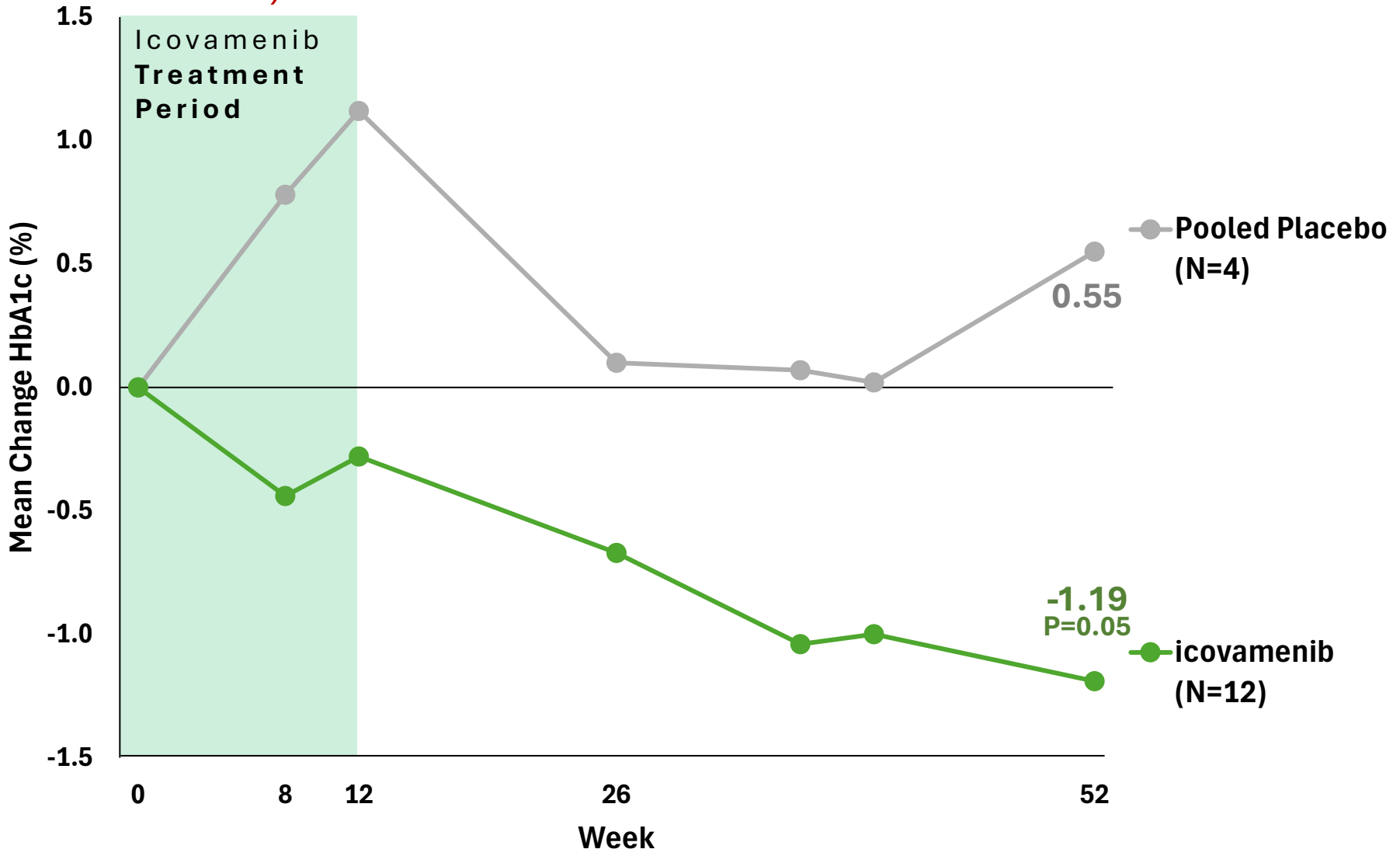
- **Icovamenib** has been shown to directly inhibit menin, aiming to pharmacologically replicate a naturally occurring, validated biologic process



Karnik, Science, 2007

Post-hoc Analysis of Patients on a GLP-1 Based Therapy Not Achieving Target HbA1c <7% at Enrollment

(9 Months After Last Dose)



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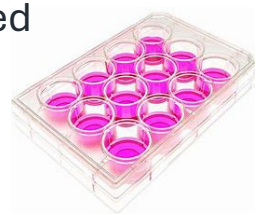
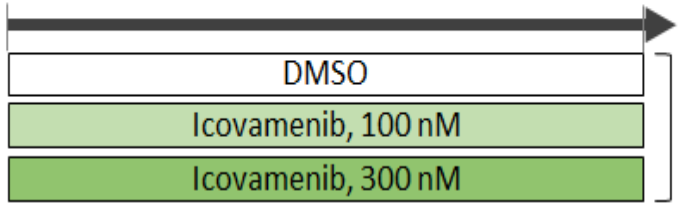
Icovamenib Enhanced GLP-1 Receptor and Insulin Transcript Levels

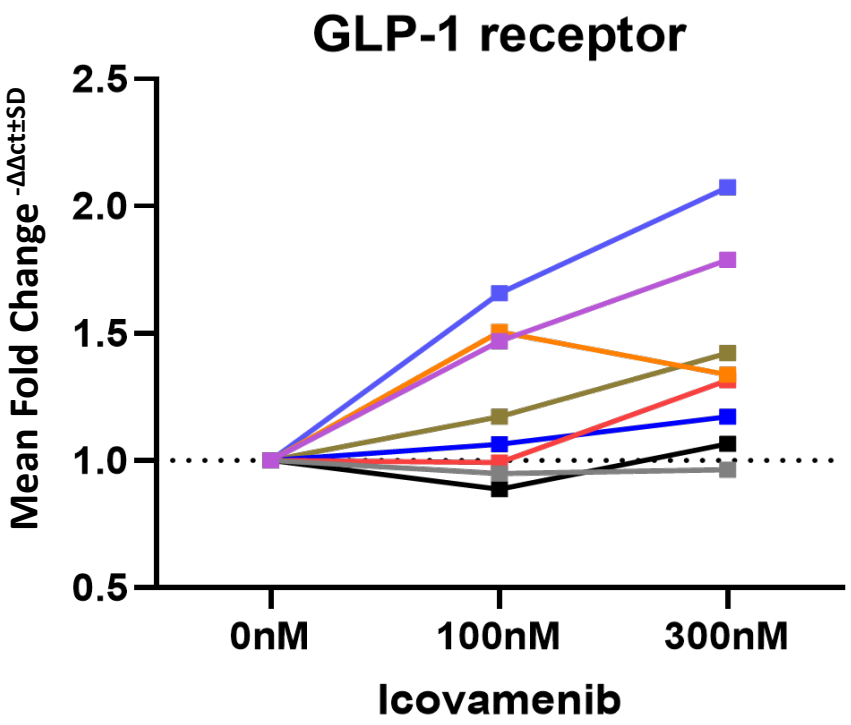
Culture 7 days under hyperglycemic conditions
(**8 mM glucose**)

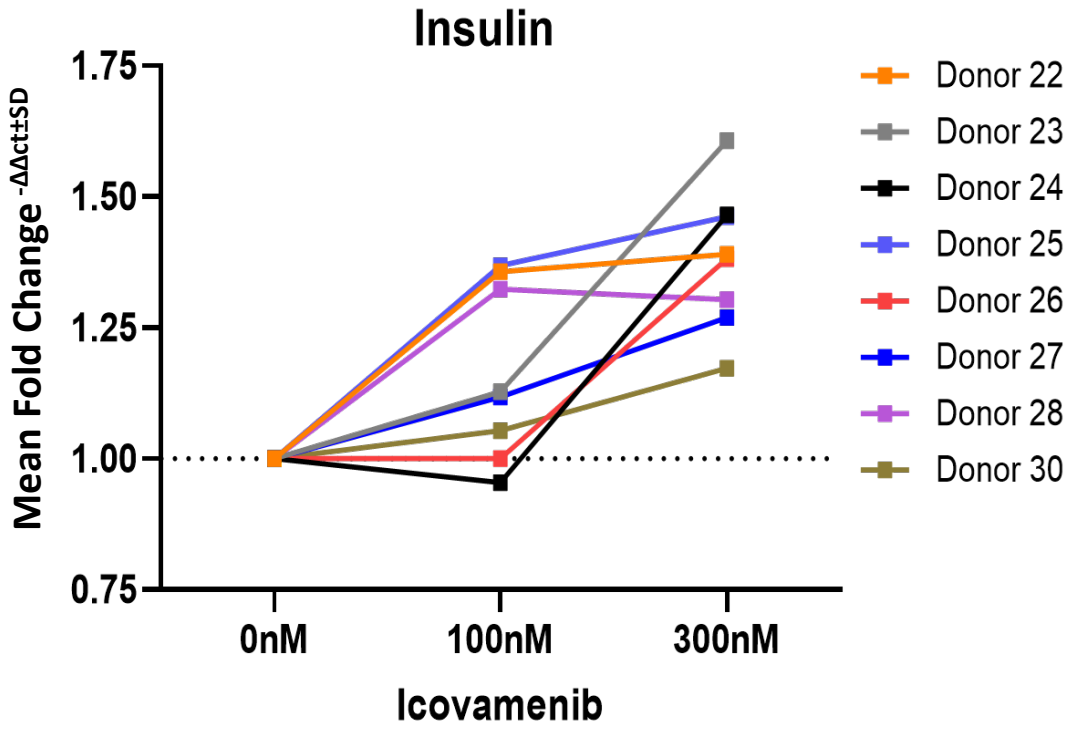
Cadaver derived human islets





Gene expression





Overview of Treatment Emergent Adverse Events (TEAEs) Through 52 Weeks

Parameter	Placebo Combined arms (N=66)	Icovamenib Combined arms (N=201)	Arm A icovamenib (N=67)	Arm B icovamenib (N=67)	Arm C icovamenib (N=67)
Patients with ≥1 TEAE, N (%)	18 (27)	55 (27)	19 (28)	22 (33)	14 (21)
Treatment-Related SAEs, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SAEs*, N (%)	1 (1)	2 (1)	1 (1)	0 (0)	1 (1)
Treatment Discontinuation due to TEAE, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Study Discontinuation due to TEAE, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deaths, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Data are n (%) TEAE = Treatment Emergent Adverse event SAE = Serious Adverse Event

*Arm A had an SAE of atrial fibrillation. Unrelated to study treatment and occurred during the treatment period. Subject required hospitalization and was discharged in 3 days. Subject continued in the study.

*Arm C had an SAE of COVID-19. Unrelated to study treatment and occurred during the treatment period. Subject required hospitalization and was discharged in 3 days. Subject continued in the study.

*Placebo Arm had an SAE of nephrolithiasis. Unrelated to study treatment and occurred during the treatment period. Subject required hospitalization and was discharged in 3 days. Subject continued in the study.

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Treatment Emergent Adverse Events (TEAEs) Occurring in ≥5% in Any Study Arm and TEAEs Reported for ALT and/or AST Elevations

Parameter	Placebo Combined arms (N=66)	icovamenib Combined arms (N=201)	Arm A icovamenib (N=67)	Arm B icovamenib (N=67)	Arm C icovamenib (N=67)
Diarrhea, N (%)	0	7 (3)	4 (6)	2 (3)	1 (1)
Urinary tract infection, N (%)	3 (5)	1 (0)	0	1 (2)	0
Hyperglycemia, N (%)	3 (5)	8 (4)	2 (3)	5 (7)	1 (1)
Headache, N (%)	2 (3)	5 (2)	0	4 (6)	1 (1)
ALT increase, N (%)	0	5 (2)	3 (4)	0	2 (3)
AST increase, N (%)	0	4 (2)	3 (4)	0	1 (1)
Resolution of ALT/AST w/o interruption in study treatment, %	N/A	100	100	100	100

Data are n (%) of TEAE with ≥5% frequency in any arm and ALT or AST increase irrespective of incidence; Safety population
TEAE, treatment-emergent adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase
Diarrhea: In the icovamenib arms, all 7 events were Grade 1.
Nausea: In the icovamenib arms, 6 of 7 events were Grade 1 and 1 event was Grade 2 (Arm B). In the placebo arm, the 1 event was Grade 1.
Hyperglycemia: In the icovamenib arms, 5 of 6 events were Grade 2 and 1 event was Grade 1 (Arm C). In the placebo arm, all 3 events were Grade 2.
Headache: In the icovamenib arms, 3 of the 4 events were Grade 1 and 1 event was Grade 2 (Arm B). In the placebo arm, 2 of the 3 events were Grade 1 and 1 event was Grade 2.
ALT increase: In the icovamenib arms, 3 of the 4 events were Grade 1 and 1 event was Grade 2 (Arm A).
AST increase: In the icovamenib arms, all 3 events were Grade 1.

Icovamenib in T2D: 52-Week Highlights

- **Durable treatment effect in severe insulin-deficient T2D**

  Continued benefit observed in severe insulin-deficient diabetes patients

- **Higher icovamenib exposure (PK) led to improved responses**

  PK analysis shows that greater HbA1c reductions occurred in patients with higher drug exposure

- **Icovamenib increased insulin secretion (C-peptide Index) in severe insulin-deficient T2D**

- **Treatment effect in GLP-1 “failures” continued to improve**

  Demonstrated durable and clinically significant improvements in HbA1c in participants on GLP-1 therapy at baseline

- **Favorable safety profile continued through Week 52**

  Icovamenib was generally well-tolerated, with no adverse-event related discontinuations and no related serious adverse events

COVALENT-111: Potential to Alter the Insulin Treatment Trajectory

COVALENT-111 highlights the potential to restore endogenous insulin production capacity in patients who would otherwise progress to chronic insulin therapy—offering the possibility of short-term oral treatment rather than lifelong injectable management.

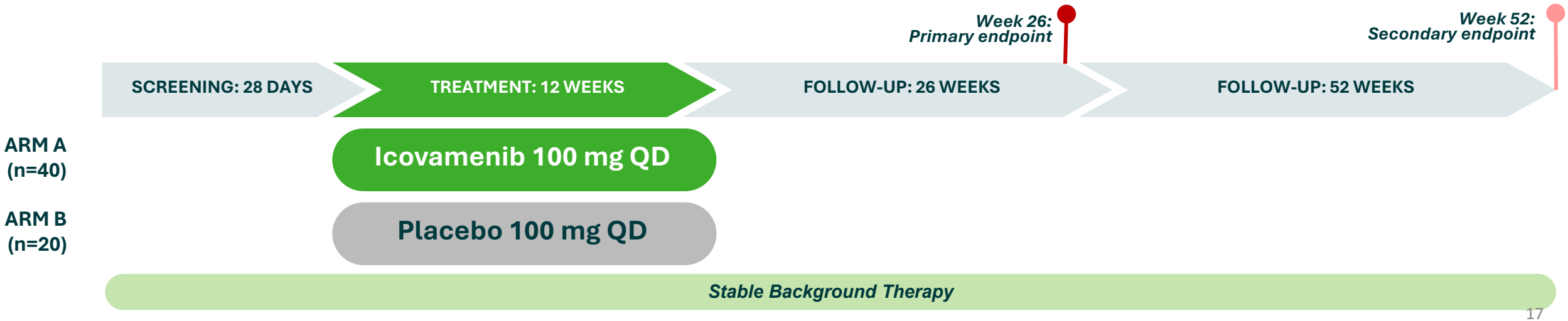
COVALENT-211: A Phase II Trial of Icovamenib in Participants with T2D Who Are Not Achieving Glycemic Targets

Key Inclusion Criteria

Adult participants with T2D treated with 1-3 antidiabetic medications

- HbA1c 7.5 to 10.5%
- BMI ≤ 32 kg/m^2

Background therapy maintained unless rescue required



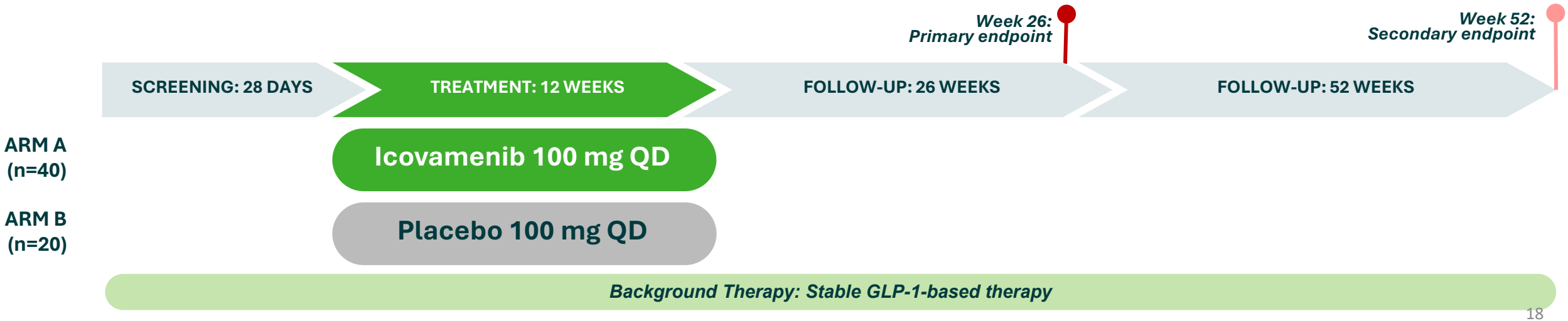
COVALENT-212: A Phase II Trial of Icovamenib in Participants with T2D Mellitus Who Are Not Achieving Glycemic Targets While Using GLP-1-Based Therapy

Key Inclusion Criteria

Adult participants with T2D who are not achieving glycemic targets despite GLP-1-based therapy

- HbA1c ≥ 7.5 and ≤9.5%
- BMI 25 to 40 kg/m^2

Treatment policy estimand; background therapy maintained unless rescue required



ICOVAMENIB

Mechanism of Action of Icovamenib – a Selective and Partial Menin Inhibitor

DUAL EFFECT

BETA CELL QUANTITY & FUNCTION

- Increased beta cell mass and function
- Increased insulin synthesis and secretion

GLP-1 RECEPTOR EXPRESSION

- Increased GLP-1 receptor expression and GLP-1 release; enhanced incretin effect
- Enhanced weight loss with preservation of lean muscle mass in preclinical studies combining icovamenib with a GLP-1RA

Biomea Fusion – BMF-650

BMF-650 (GLP-1 RA)

- **Weight loss**
- **Oral**
- **Small molecule**

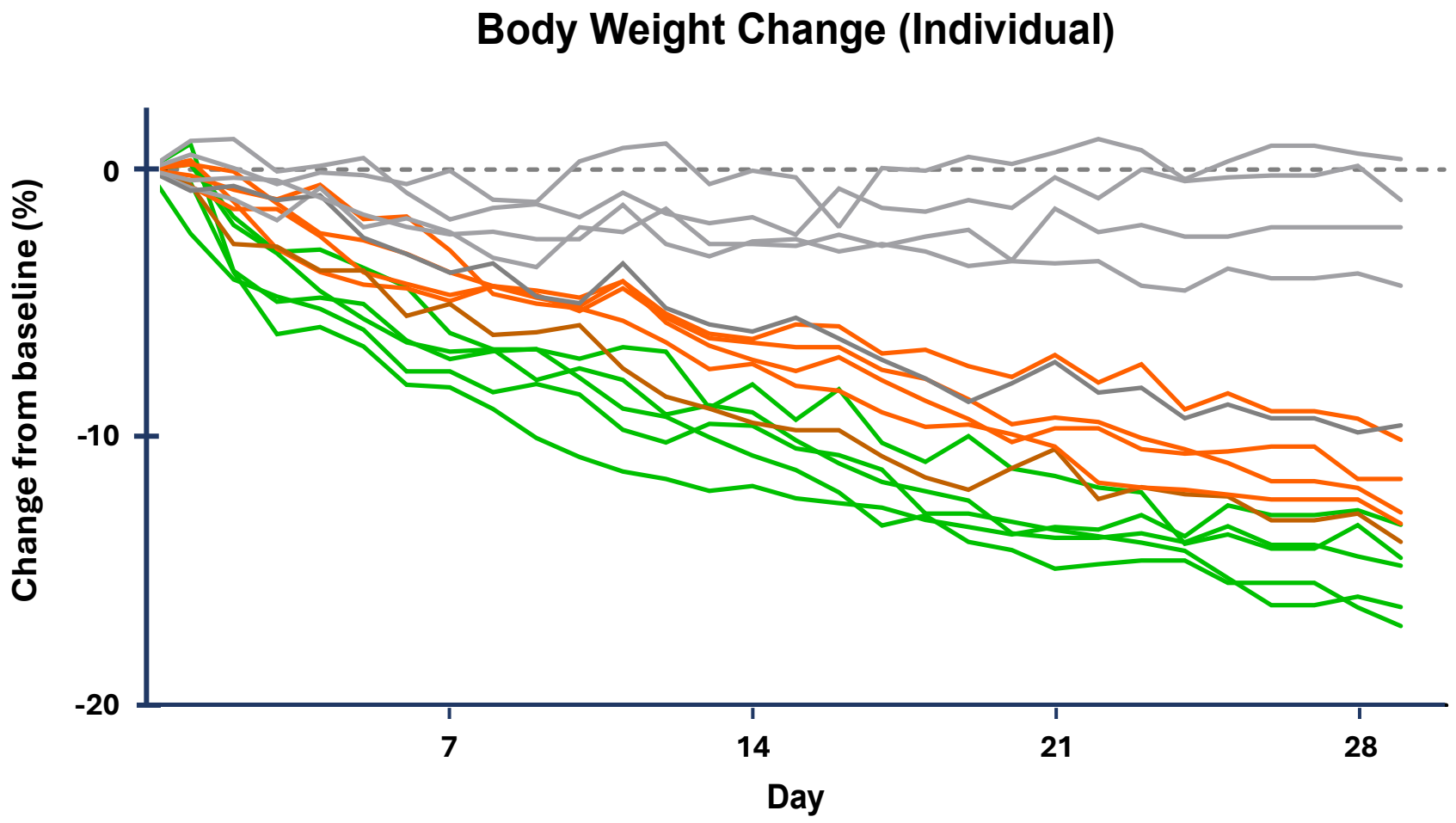
GLP-131 (Phase 1)

Obese (BMI ≥30kg/m^2)

Designed for better bioavailability

>>> More consistent efficacy

Oral BMF-650 Promoted Body Weight Reduction in Obese Cynomolgus Monkeys



Mean reduction in Body Weight (Day 29)

Vehicle	-3.4%
BMF-650 10mg/kg	-12.3%
BMF-650 30mg/kg	-15.2%

(5 animals per dose group)

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BMF-650 Has Demonstrated Favorable Liver Safety to Date

Chugai chemotype / orforglipron:

- 3000+ patients dosed in ATTAIN 1 / 2 studies[1,2]
  No LFT signals for orforglipron
- **BMF-650** is a member of this chemotype

Pfizer chemotype / danuglipron

- Danuglipron and lotiglipron discontinued[3,4]
  TERN-601 discontinued[5]
- Observation of LFTs elevations

- **Daily oral dosing in cynomolgus monkeys (healthy and obese) for up to 6 weeks**
- **No ALT or AST elevations observed across all preclinical studies**
- **First-in-human study ongoing with no ALT or AST elevations observed to date**

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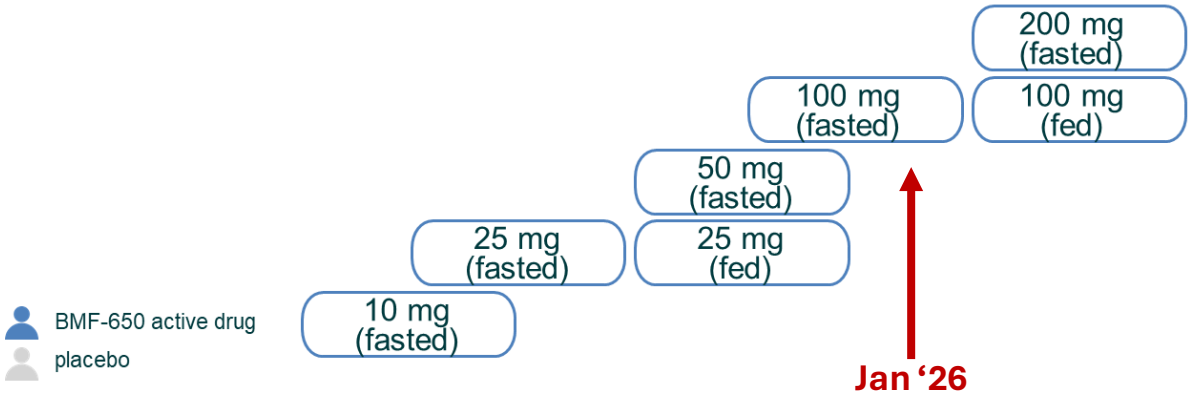
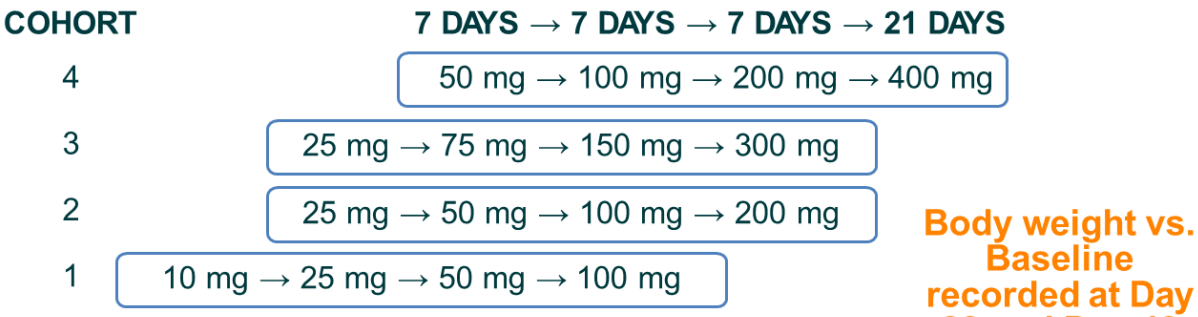
[1]Horn, Lancet, 2026; [2]Knudsen, Cell Chem Biol, 2021; [3]Pfizer press release (danuglipron discontinued, Apr 2025); [4]Pfizer press release (lotiglipron terminated, Jun 2023); [5]Terns Phase 2 topline press release (Oct 2025

GLP-131: A Randomized, Double-blind, Placebo-controlled, FIH Study of an Oral Non-peptide GLP-1 Receptor Agonist

Part 1: single ascending dose (SAD) study | **Part 2** is a multiple ascending dose (MAD) study

	Single Ascending Dose (SAD)	Multiple Ascending Dose (MAD)
Objectives	Safety and tolerability, PK, and food effect	Safety and tolerability, and efficacy (weight-loss)
Eligibility	Healthy overweight or obese patients (BMI 25.0–40.0 kg/m²)	Healthy overweight or obese patients (BMI 30.0–45.0 kg/m²)
Design	N=40 5 cohorts x	N=40 4 cohorts x





Overview of Key Program Activities

ICOVAMENIB

COVALENT 211 (Phase IIB)

- Insulin-deficient T2D (20% of US T2D population)
- First patient enrollment planned in **1Q 2026**
- 26-Week readout expected in **4Q 2026**

COVALENT 212 (Phase II)

- T2D patients not controlled on GLP-1 based medicines (70% of US GLP-1 population)
- First patient enrollment planned in **1Q 2026**
- 26-Week readout in **4Q 2026**

BMF-650

GLP-131 (Phase I)

- Obese, otherwise healthy volunteers
- Currently dosing single ascending dose
- 28-Day weight loss study results expected in **2Q 2026**

Q&A

THANK YOU

(NASDAQ: BMEA)

For questions or inquiries, please reach out to Meichiel Weiss at ir@biomeafusion.com

www.biomeafusion.com

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