

Biomea Fusion Corporate Presentation

Q3 2026



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Transforming diabetes and obesity with novel oral medicines



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Transforming diabetes and obesity with novel oral medicines



Biomea Fusion founded in 2017 (public in 2021; NASDAQ: BMEA)

Clinical-stage company advancing two differentiated metabolic investigative programs

ICOVAMENIB

First-in-class oral small molecule for the treatment of diabetes targeting menin - the natural control switch to beta cell restoration in Type 1 and Type 2 Diabetes

Restores functional beta-cell mass and improve endogenous insulin production

BMF-650

Next-generation oral GLP-1 receptor agonist

Designed for consistent exposure, higher bioavailability and improved tolerability with scalable weight reduction

Investment Thesis

Biomea is building a leading metabolic disease company with two differentiated programs and multiple near-term catalysts

-  First-in-class beta-cell restorative therapy targeting menin in development for diabetes
-  Potential best-in-class Type 1 & 2 diabetes agent
-  Multiple Phase II readouts over the next 12 months
-  Experienced leadership team with a clear vision and execution plan
-  Cash runway through key upcoming value inflection read outs

The Opportunity

Growing market with large unmet need

Diabetes

>38M

People living with diabetes in U.S.¹

>35M

People with T2D in U.S.²

1:3

People in U.S. with T2D using Insulin³

25%

Of U.S. healthcare dollars go to treat those diabetes⁴



Obesity

>190M

People in U.S. are obese or overweight⁵

100M +

People in U.S. are obese⁵

5M+

People in U.S. discontinue GLP-1⁶

Large unmet need

for durable, well-tolerated therapies



Addressing root biology has the potential to address patient outcomes

1. CDC, Natl. Diabetes Stat. Rep., 2022
2. ADA, Standards of Care in Diabetes, Diabetes Care, 2024
3. Li J Diabetes Complications 2012;26(1):17-22

4. CDC Health and Economic Benefits of Diabetes Interventions
5. CDC National Health and Nutrition Examination Survey
6. IQVIA prescription data

Key milestones - overview



Icovamenib in Type 1 Diabetes

PLANNED T1D Investigator Sponsored Study | Phase 2 Study | n=40 | Enrollment anticipated to start 1Q 27

PLANNED T1D | Phase 2 Study | n=36 | Enrollment anticipated to start 1Q 27

T1D
FDA End of Phase 2 Meeting and Phase 3 Initiation



Icovamenib in Obesity

LEICESTER DIABETES CENTER in Obesity | Phase 2 Study | n=64 | Topline data anticipated: end of 27



Icovamenib in Type 2 Diabetes

- Insulin deficient
- GLP-1 uncontrolled

COVALENT-211 in insulin deficient T2D | Phase 2 Study | n=64 | Fully enrolled | Topline data anticipated: 1Q 27

COVALENT-212 in GLP-1 uncontrolled T2D | Phase 2 Study | n=60 | Start: 2Q 26 | Topline data anticipated: 2Q 27

T2D
FDA End of Phase 2 Meeting and Phase 3 Initiation

ICOVAMENIB



BMF-650



BMF-650 Obesity and weight management

GLP-131 in Obesity | Phase I | 28-day weight loss

Current Cash Position
Runway into 2Q 2027

BMF-650 Phase 2
Initiation depending on Phase I results



ICOVAMENIB

First-in-class menin targeting agent in development for the treatment of diabetes - TYPE 1 DIABETES

Opportunity - Type 1 Diabetes

Biomea is aiming to advance icovamenib to be the first fully approved therapy for Type 1 Diabetes patients
New Phase II Study planned for initiation in 4Q 2026



Icovamenib is the first-in-class beta cell restorative therapy targeting menin in development in diabetes



Icovamenib is potentially the best-in-class oral agent addressing diabetes at the root cause level – the depleted pool of beta cells



Preclinical on target evidence of direct impact on beta cells, their proliferation and insulin productivity



Over 500 patients dosed to date with icovamenib, demonstrating with the effective dosing scheme a safety profile comparable to placebo



Phase II Type 1 diabetes study designed with world-renown Type 1 Investigator Team, initiation planned for 4Q 26 with 6 month data expected in 2H 27



Registrational studies targeted for 1H 28 initiation

Type 1 Diabetes - Opportunity

Established market with large unmet need. Patients suffer from loss of beta cells and require the use of exogenous insulin - Type 1 diabetes untreated is deadly.

Type 1 Diabetes in the US and WW

US > 2M WW > 10M

People living with Type 1 diabetes ¹

of approved Agents

one

Teplizumab is approved in Stage 2 of T1D and has an accelerated approval in Stage 3 for children 8-17 years old, contingent on confirmatory evidence of clinical benefit.

Investigational Therapies in Development

Focus primarily on immune modulation and preservation



Immune modulation to slow autoimmune destruction¹



Preserve remaining beta-cell function



Most effective when started shortly after diagnosis²
(<90 days, new onset T1D)

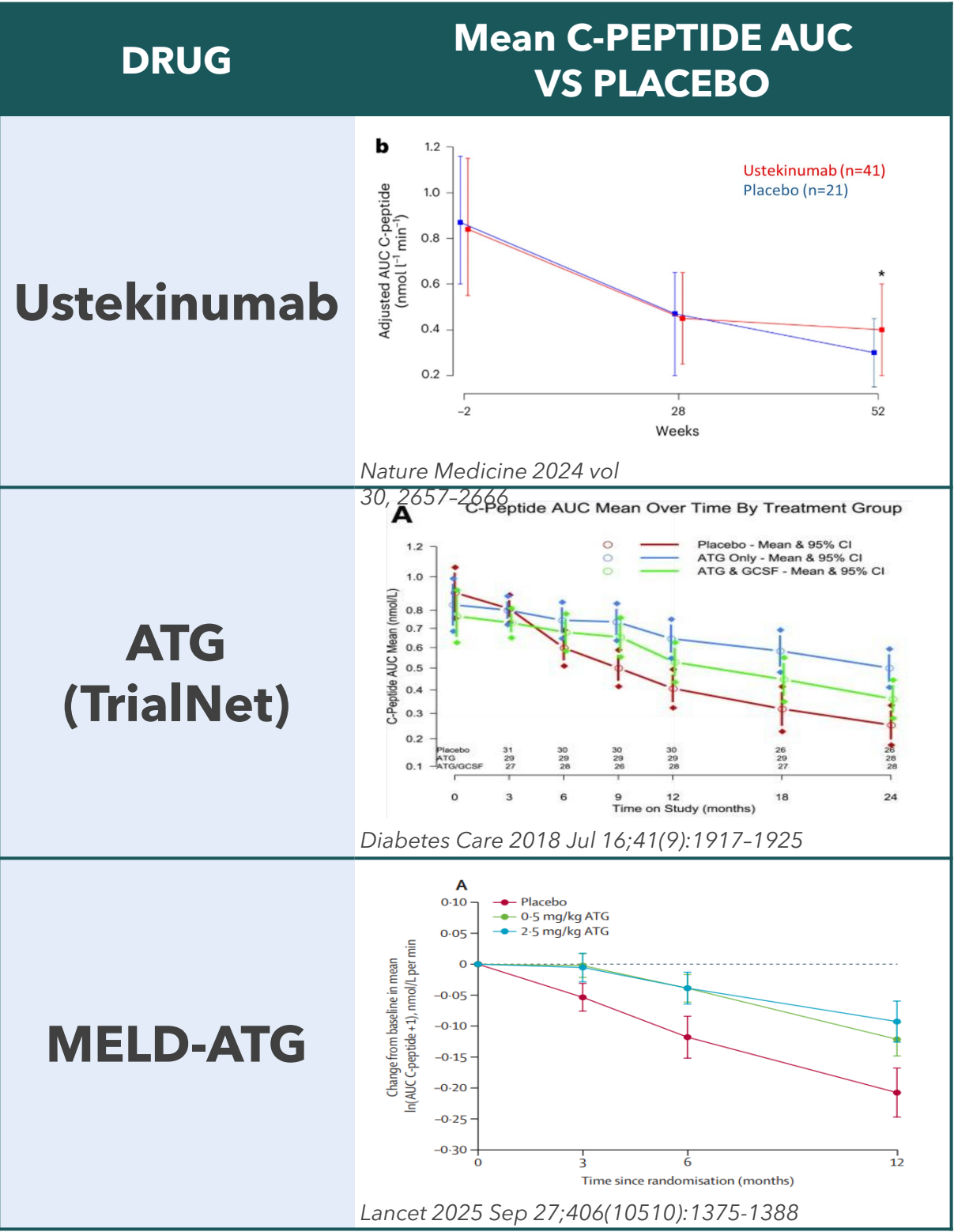
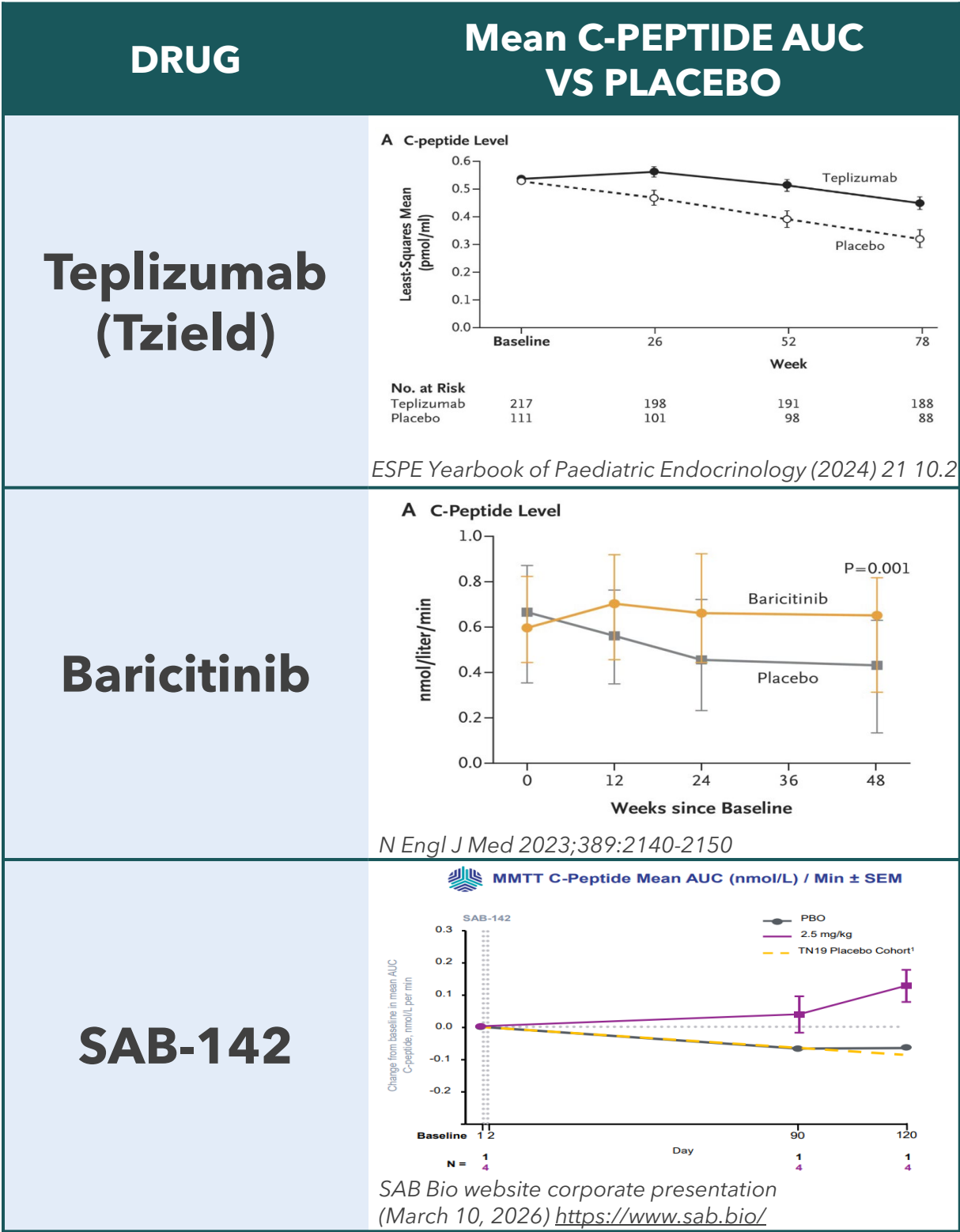
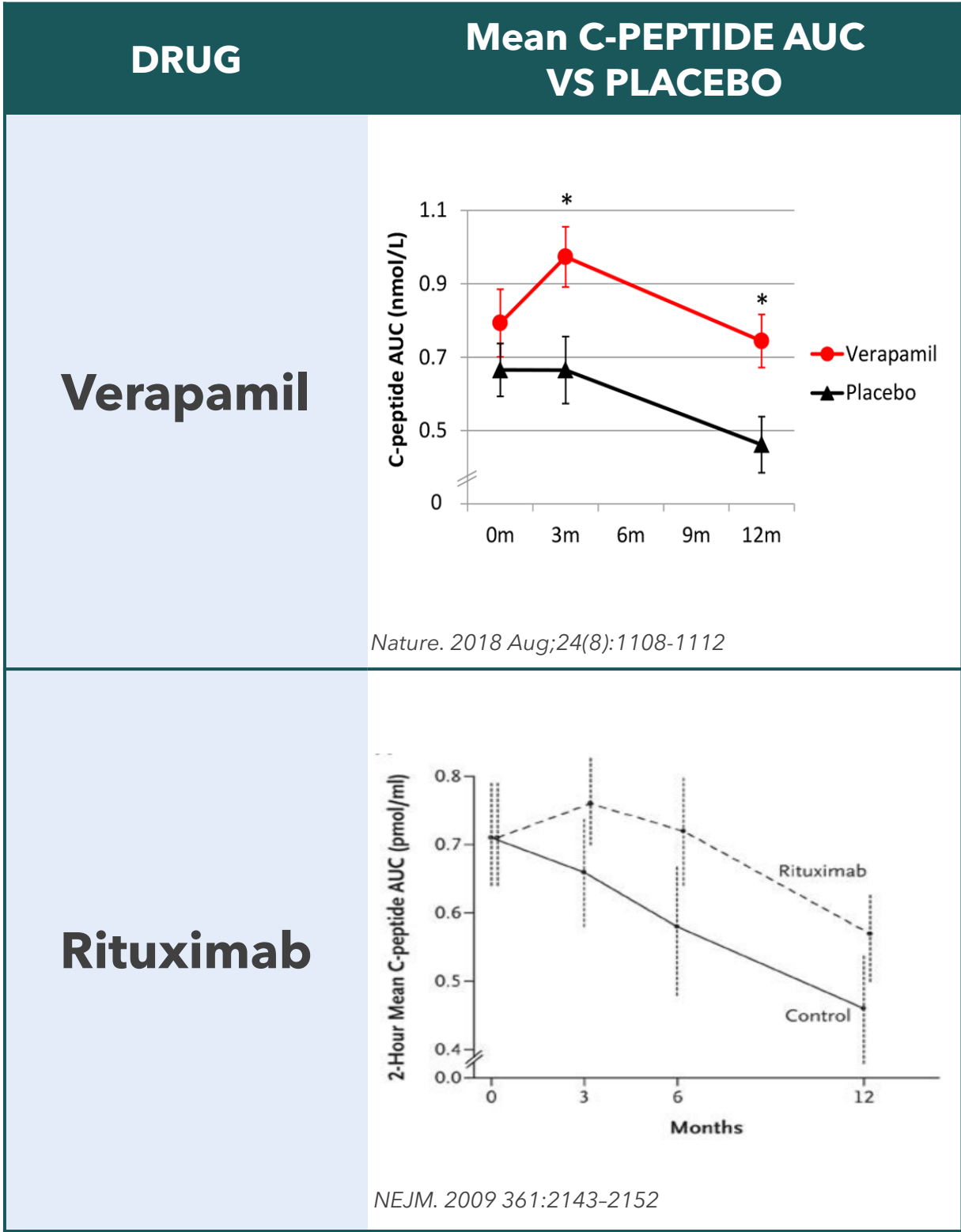


Slows decline in C-peptide over time³

GOAL: Slow disease progression

1. CDC, Natl. Diabetes Stat. Rep., 2022
2. ADA, Standards of Care in Diabetes, Diabetes Care, 2024
3. Li J Diabetes Complications 2012;26(1):17-22

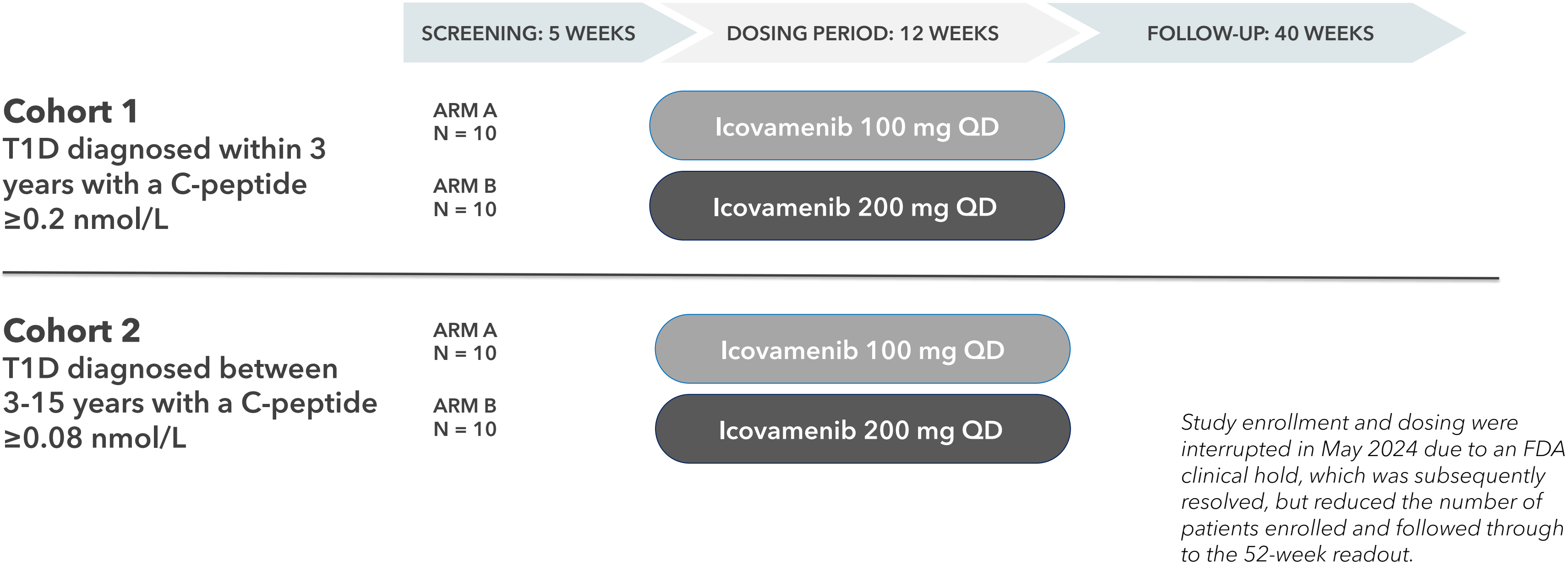
Therapies in development for Type 1 Diabetes aim to slow the disease progression - decline of C-peptide



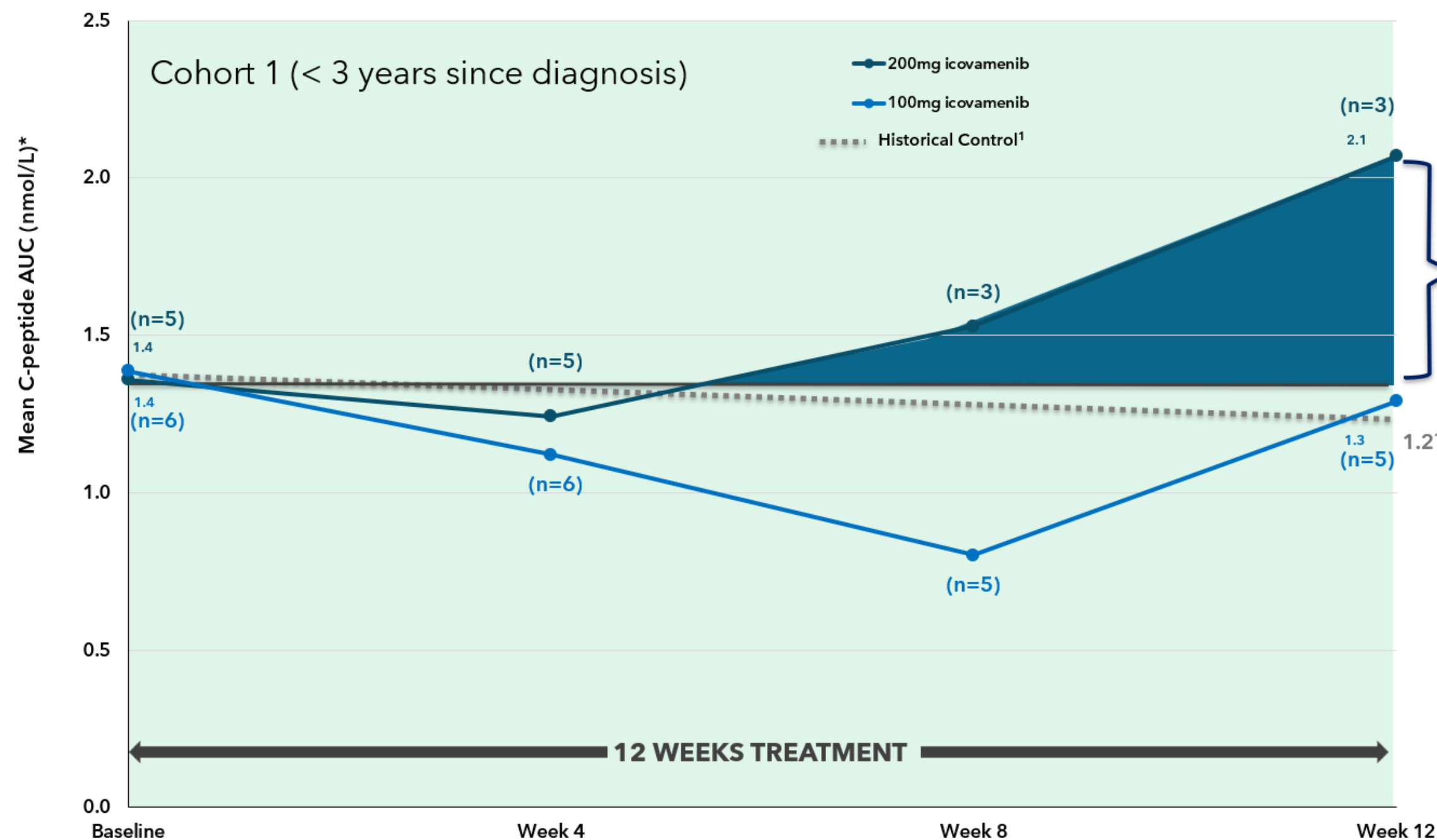
*Ladarixin and Diamyd, both Immune modulating, not mentioned here as they demonstrated no meaningful difference compared to placebo

All-comers Study Covalent-112 - completed

COVALENT-112 (NCT06152042) was a Phase 2 trial designed to examine beta cell function (as measured by C-peptide change and the change of exogenous insulin usage) and glucose and lipid metabolism in participants with T1D treated with standard of care insulin and icovamenib.



Compelling Signal of Beta Cell Restoration in T1D with Icovamenib



- 52% Mean increase in C-Peptide AUC* at Week 12
- Durable effect through Week 52 after only 12 weeks of dosing
- Greatest response in patients ≤ 3 years since diagnosis
- No Systemic immune activation
- Favorable safety profile through 52 weeks

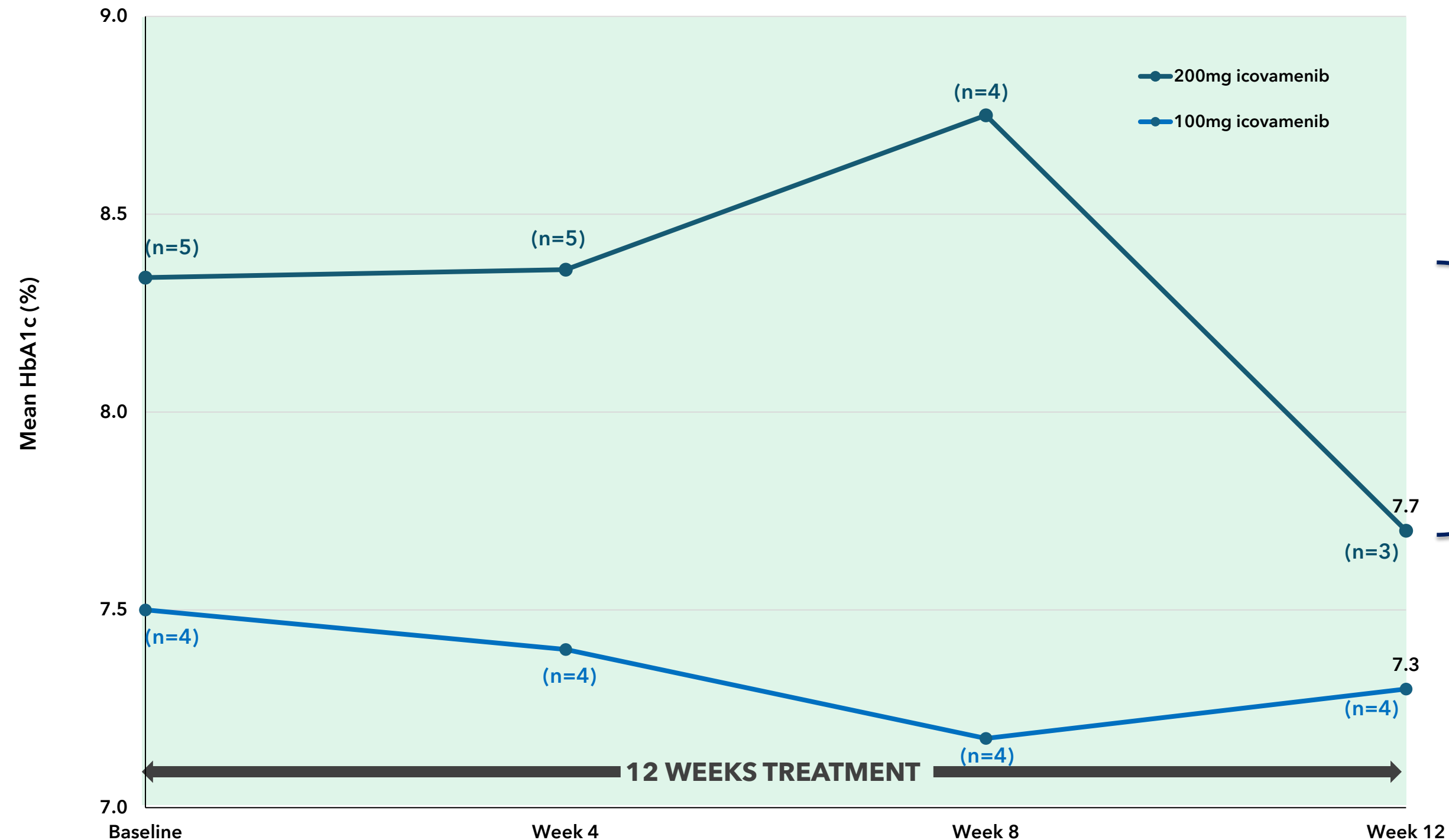
Data represents post-hoc analysis of patients who received per statistical analysis plan, 80% of planned doses

¹ Historical control in T1D patients (n=1549) C-peptide declining over first 7 years at 47% yearly. *Diabetes Care*. 2018 Jun 7;41(7):1486-1492

* 4-hour Mixed Meal Tolerance Test (MMTT)

Frias, J. (ADA) *Diabetes* 2026; 75 (Supplement_1): 2858-LB.

0.6% mean reduction in HbA1c during the 12 weeks treatment period of icovamenib



0.6%
reduction in
mean HbA1c
from baseline

Cytokine profiling of cohort 1 (<3 years since T1D diagnosis) participants receiving 200mg icovamenib

	Week 12			Week 26			Week 52		
	pg/mL	change	status	pg/mL	change	status	pg/mL	change	status
IL-1β	1.07	0.40	Non-Inflammatory	1.00	0.27	Non-Inflammatory	0.70	-0.27	Non-Inflammatory
IL-2	3.43	-0.83	Non-Inflammatory	3.57	-1.20	Non-Inflammatory	1.20	-3.23	Non-Inflammatory
IL-6	3.27	0.70	Non-Inflammatory	0.53	-1.70	Non-Inflammatory	0.53	-1.70	Non-Inflammatory
IL-8	6.57	0.77	Non-Inflammatory	7.17	-0.07	Non-Inflammatory	5.37	-1.18	Non-Inflammatory
IL-10	1.30	-0.03	Non-Inflammatory	1.33	0.00	Non-Inflammatory	1.30	-0.03	Non-Inflammatory
IFN-γ	-	-	Non-Inflammatory	-	-	Non-Inflammatory	-	-	Non-Inflammatory
TNF-α	7.53	-0.17	Non-Inflammatory	7.73	-1.35	Non-Inflammatory	4.07	-5.33	Non-Inflammatory

Mean values were assessed for all patients for each cytokine (n=3) relative to baseline.

- All cytokines remained classified as Non-Inflammatory from baseline through Week 52, indicating no evidence of systemic immune activation in participants receiving 200 mg icovamenib
- Small Week 12 increases in IL-1β, IL-6, and IL-8 were transient and not associated with increases in IL-2 or TNF-α
- By Week 52, most pro-inflammatory cytokines were stable or decreased from baseline
- **The increase in C-peptide was not accompanied by a measurable systemic inflammatory cytokine response but rather led to a stabilization and mild reduction of inflammatory markers over time**

Frias, J. (ADA) Diabetes 2026; 75 (Supplement_1): 2858-LB.

Favorable 52-week safety profile

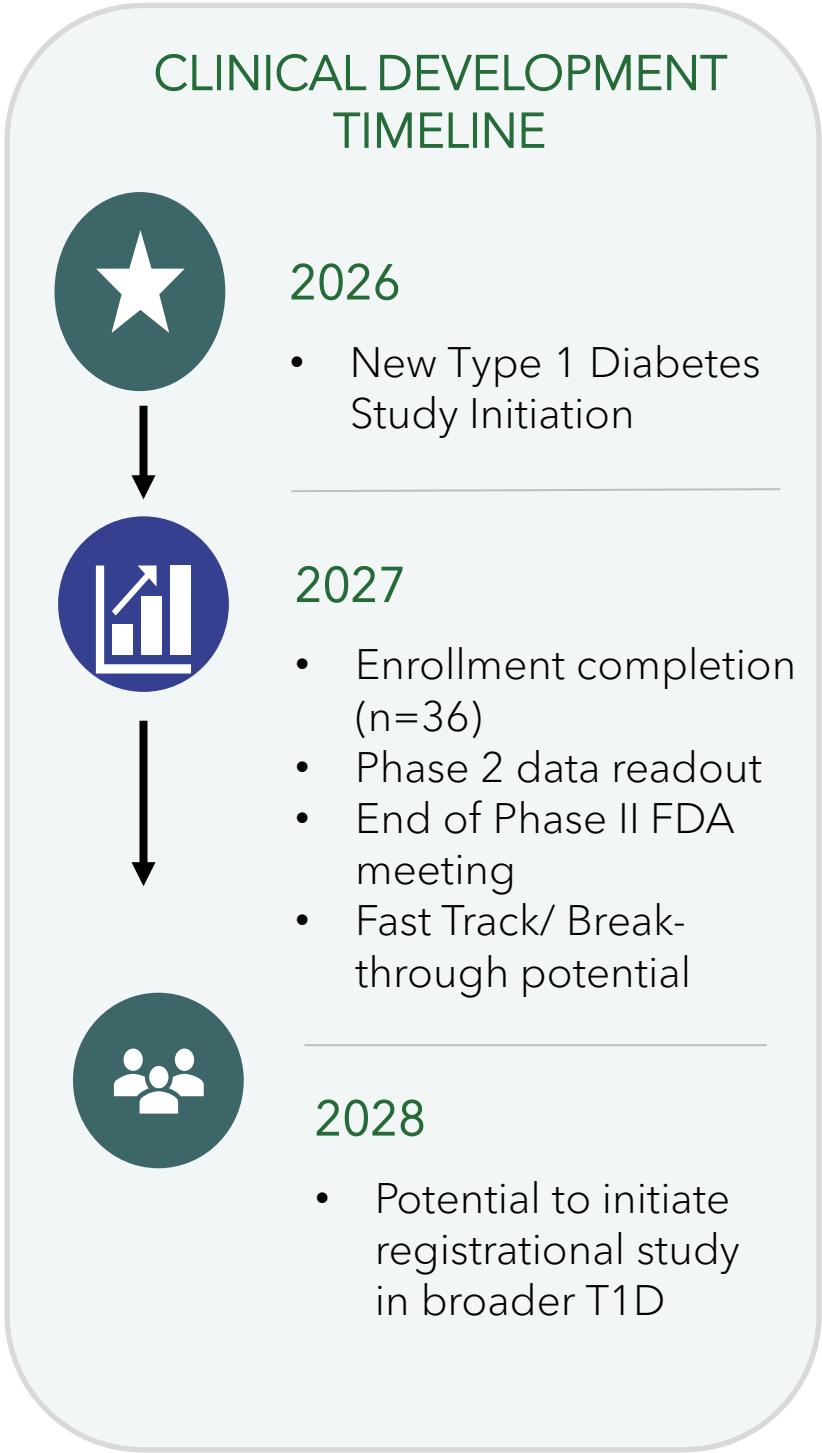
	Cohort 1			Cohort 2		
	Arm A 100 mg QD (N = 8)	Arm B 200 mg QD (N = 9)	Cohort 1 Total (N = 17)	Arm A 100 mg QD (N = 9)	Arm B 200 mg QD (N = 10)	Cohort 2 Total (N = 19)
Patients with ≥ 1 TEAE, N (%)	3 (38)	0 (0)	3 (18)	1 (11)	3 (30)	4 (21)
Treatment-Related SAEs, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SAEs*, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Treatment Discontinuation due to TEAE, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Study Discontinuation due to TEAE, N (%)	0	0	0	0	0	0
Deaths, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Diarrhea, N (%)	1 (13)	0	1 (6)	1 (11)	0	1 (5)
Nausea, N (%)	1 (13)	1 (11)	2 (12)	1 (11)	1 (10)	2 (11)
Hyperglycemia, N (%)	0	0	0	0	1 (10)	1 (5)
Headache, N (%)	1 (13)	0	1 (6)	0	1 (10)	1 (5)
AST/ALT increase, N (%)	3 (38)	2 (22)	5 (29)	1 (11)	7 (70)	8 (42)
Resolution of ALT/AST w/o interruption in study treatment, %	100	100	100	100	80	90

Potential to Expand the Treatable Population in Type 1 Diabetes

Approved Therapy in T1D TEPLIZUMAB (Tzield®)	Key Characterization	ICOVAMENIB
Newly diagnosed Stage 3 T1D	 Eligible Population	Newly diagnosed and established T1D with residual beta cell function
0-90 days from diagnosis	 Time From Diagnosis	0-3+ years demonstrated clinically
Pediatric only (8 to 17 years)	 Age	Adult T1D patients at first with pediatric to follow in development
Immune modulation	 Mechanism of Action	Beta cell restoration / preservation
Two 12-day infusion 26 weeks apart	 Treatment	Oral, once daily
Delay insulin dependence	 Goal	Restore endogenous insulin secretion and preserve beta cell function

A SUBSTANTIALLY LARGER TREATABLE PATIENT POPULATION

Icovamenib potentially expands the treatment window and the patient population by more than 10-fold

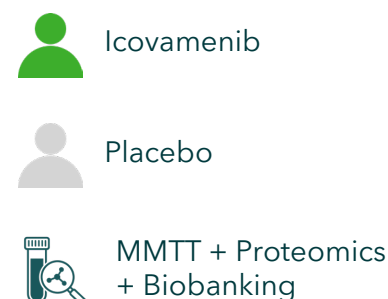
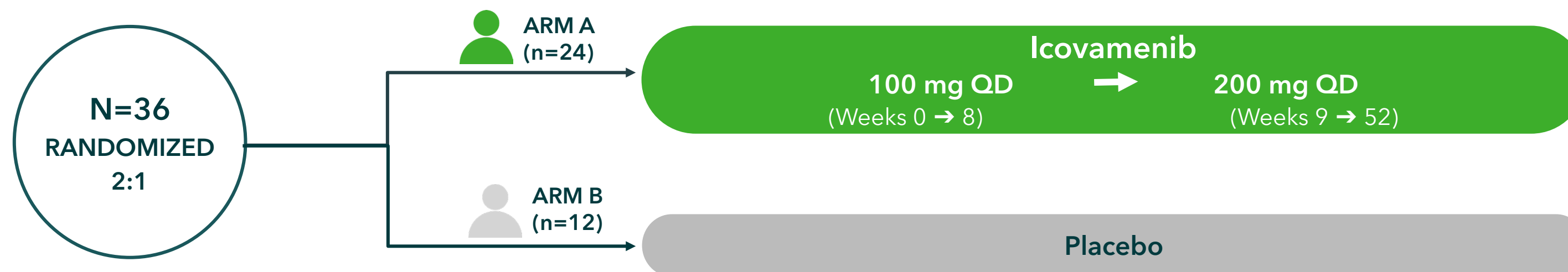


ICOVAMENIB in TYPE 1 DIABETES

Planned Biomea sponsored T1D study *

Inclusion Criteria

- Adult participants with T1D with a C-peptide ≥ 0.2 nmol/L

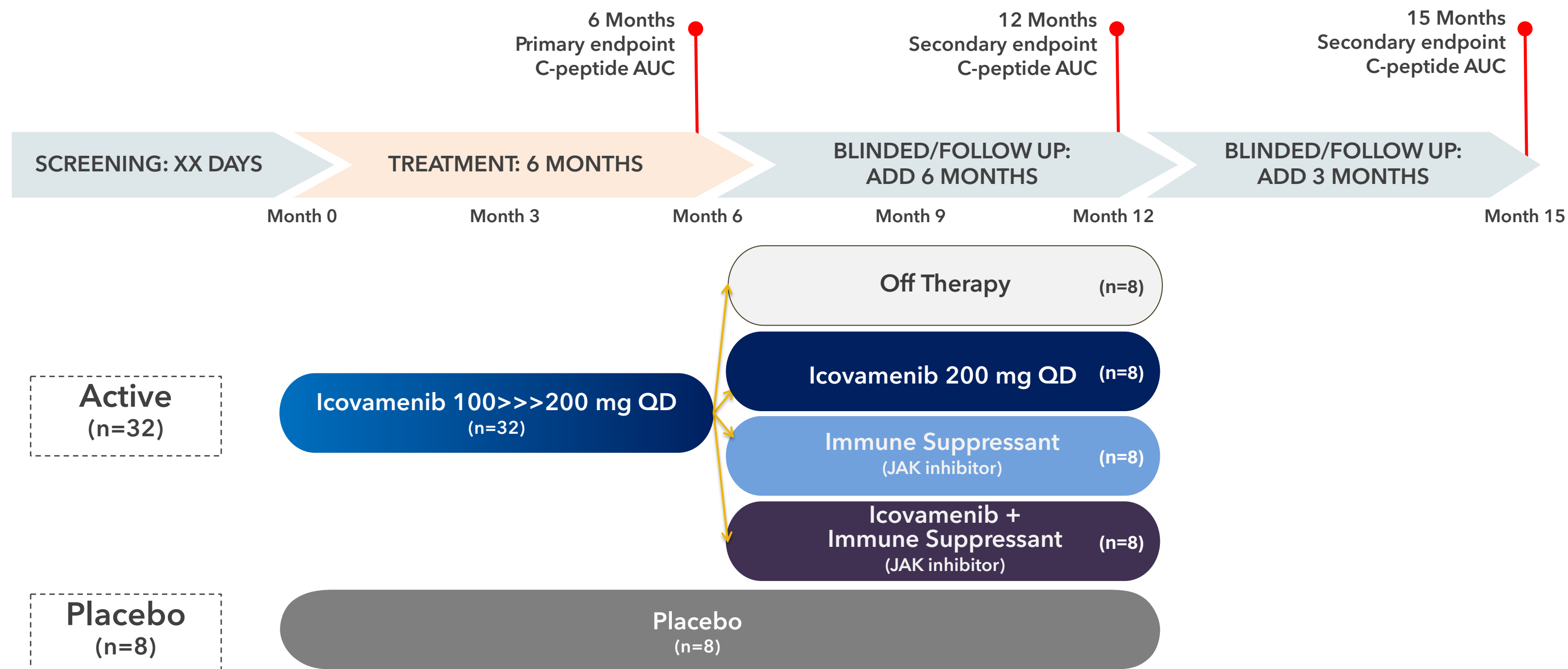


*Subject to regulatory and investigator alignment, and feedback from applicable health authorities.

Planned investigator sponsored phase II trial *

Inclusion Criteria

- Adult participants with T1D diagnosed within 3 years with a C-peptide ≥ 0.2 nmol/L



*Subject to regulatory and investigator alignment, and feedback from applicable health authorities.

Planned study investigators *

Primary Investigator

Peter Gottlieb, MD

Professor of Pediatrics and Medicine | Barbara Davis Center, University of Colorado

- Professor of Pediatrics and Medicine and holds the Orr Family Endowed Chair in Adult Diabetes at the Barbara Davis Center, one of the world's leading centers for Type 1 diabetes research and clinical care.
- Long-standing member of Type 1 Diabetes TrialNet and chairs its Collaborative Mechanistic Studies Panel, helping drive pivotal immunotherapy trials across all stages of T1D.
- With 190+ publications, his work focuses on T- and B-cell-driven autoimmunity.



Sub-Investigators

Jason Gaglia, MD, MMSc

Ass. Professor | Joslin Diabetes Center, Harvard Medical School

World's leading diabetes center (36,000 patients annually, 150 MDs/PhDs)



David Baidal, MD

Ass. Professor | Diabetes Research Institute, University of Miami Miller School of Medicine



Ralph A. DeFronzo, MD

Professor and Chief of the Diabetes Division | UT Health of San Antonio



KOL perspectives across clinical significance, biology, and future development in T1D

“

Efforts to intervene against type 1 diabetes (T1D) have historically focused on preserving remaining insulin secretion in people just diagnosed with T1D. These icovamenib data are unique in showing increased C-peptide-reflected insulin secretion in patients with established T1D during dosing and persistence of this effect after treatment was stopped. In people with established T1D, endogenous insulin secretion progressively declines to very low levels. Any evidence of improvement in endogenous insulin secretion—even among a few T1D individuals—is unprecedented and of immense biologic and clinical significance. These findings warrant rigorous and longer-term evaluation.



G. Alexander “Zan” Fleming, MD

FOUNDER & EXECUTIVE CHAIRMAN, KINEXUM
FORMER FDA SENIOR MEDICAL OFFICER AND
DIVISION LEADER FOR METABOLIC & ENDOCRINE
DRUGS, INVOLVED IN THE REVIEW OF LANDMARK
DIABETES AND METABOLIC THERAPIES
INCLUDING METFORMIN, THE FIRST RAPID-
ACTING INSULIN ANALOGS, EARLY STATINS, AND
PPAR AGONISTS

“

The new data presented today with icovamenib in patients with type 1 diabetes suggest a potential new therapeutic avenue in a disease where fundamental unmet need has long persisted. To date, approved therapies have not directly addressed the progressive loss of functional beta cells that underlies diabetes. Biomea has made critical progress in identifying and characterizing this molecule, which has demonstrated the ability to reduce menin protein levels and activate pathways associated with beta cell function. Today's icovamenib type 1 data further validates and deepens our understanding of icovamenib's mechanism of action. Congratulations to the Biomea team on reaching this important therapeutic milestone.



Rohit Kulkarni, MD, PhD

PROFESSOR OF MEDICINE, HARVARD MEDICAL
SCHOOL | SENIOR INVESTIGATOR & SECTION CO-
HEAD (ISLET CELL & REGENERATIVE BIOLOGY),
JOSLIN DIABETES CENTER

“

What stands out to me in the icovamenib diabetes data is not only the emerging signal of biological activity, but also the safety profile observed to date with using icovamenib in diabetes studies. That combination is important, because safety ultimately determines whether rational combination strategies can be explored as the program moves forward. Looking ahead, future studies will be critical in determining whether the improvements observed in beta cell function of these Type 1 diabetes patients can be maintained over time, particularly in the presence of ongoing immune activity. It will also be important to understand whether combination approaches—including immunomodulatory therapies—are needed and can further enhance or stabilize the observed effects. These are key questions that will inform the long term clinical potential of this approach.



David Baidal, MD

ASSISTANT PROFESSOR DIABETES RESEARCH
INSTITUTE, UNIVERSITY OF MIAMI MILLER
SCHOOL OF MEDICINE

KOL perspectives across clinical significance, biology, and future development in T1D

“

The icovamenib data in Type 1 diabetes naturally makes us pause and reflect on what it could ultimately mean for people living with Type 1 diabetes. While these early findings require confirmation, they suggest a different way of thinking about treatment, one that extends beyond glucose management and begins to engage underlying disease biology. For younger individuals in particular, the possibility of preserving or improving endogenous beta cell function over time could have meaningful implications for lifelong disease burden. Results like these invite consideration of how the treatment landscape in Type 1 diabetes may evolve if such approaches prove durable and safe.



Alice Cheng, MD

ENDOCRINOLOGIST, ASSOCIATE PROFESSOR OF
MEDICINE UNIVERSITY OF TORONTO

“

The icovamenib data in type 1 diabetes are encouraging, this is particularly interesting as icovamenib targets a pathway that has not been meaningfully explored in this disease. Despite advances in insulin delivery and glucose monitoring, disease-modifying options remain limited for patients. These findings support the need for focused, proof-of-concept studies in well-characterized patient populations to better understand this signal, its durability, and the underlying biology. An important next step will be examining the interplay between beta cell effects and the autoimmunity inherent in type 1 diabetes, and whether combination approaches with immunomodulatory therapies could further enhance or stabilize these beta cell effects.



Jason Gaglia, MD, MMSc

ASSISTANT PROFESSOR OF MEDICINE, HARVARD
MEDICAL SCHOOL | STAFF PHYSICIAN, JOSLIN
DIABETES CENTER – ONE OF THE WORLD'S
LEADING DIABETES CENTERS

“

While insulin therapy is life saving for people with Type 1 diabetes, chronic exogenous insulin use is not without consequence. Over time, it is associated with well recognized iatrogenic risks, including hypoglycemia, diabetic ketoacidosis, weight gain, lipohypertrophy, and increased cardiovascular burden. Targeting menin with icovamenib represents a fundamentally new therapeutic approach in diabetes. Rather than simply replacing insulin, it seeks to improve endogenous beta cell function. The early results we are seeing in Type 1 diabetes are highly encouraging. I am excited to explore longer dosing periods to fully assess the potential of enabling patients to regain their own beta cell-mediated glucose control which is something no current therapy has been able to achieve. If this approach is confirmed, this could represent a meaningful step towards allowing patients to live their daily lives with greater physiological stability and far less constant fear of their disease.



Ralph DeFronzo, MD

ENDOCRINOLOGIST, PROFESSOR OF MEDICINE
UTHSCSA



ICOVAMENIB

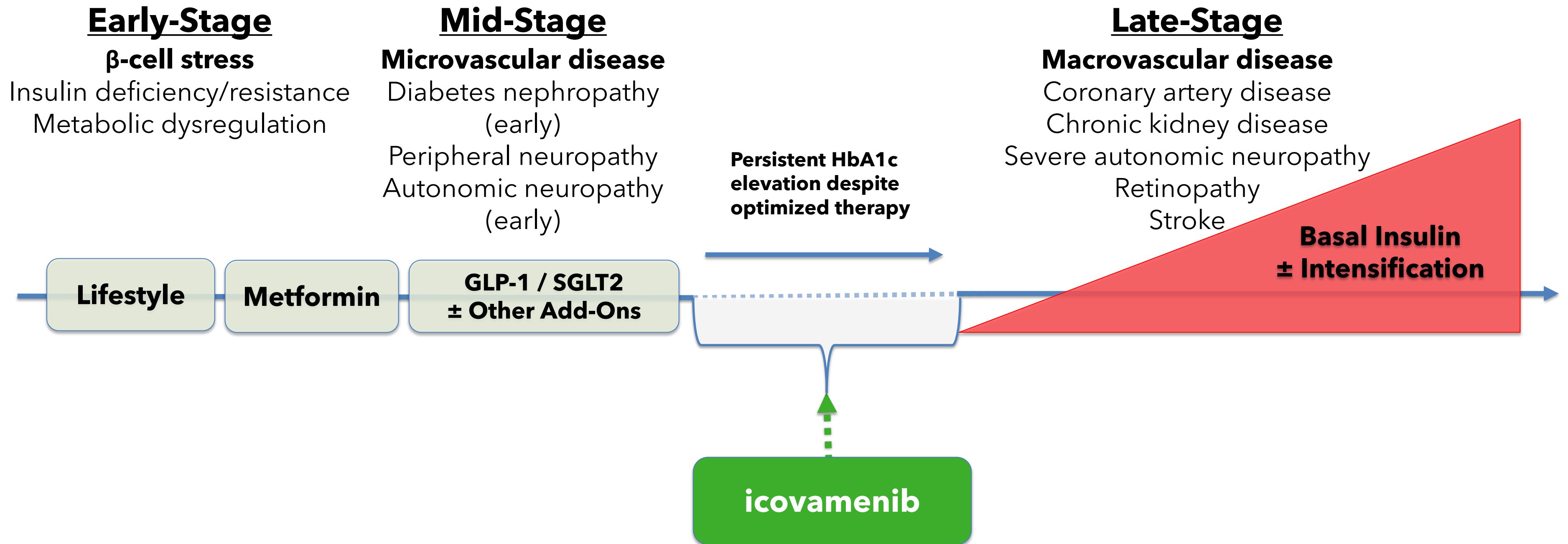
First-in-class menin targeting agent in development for the treatment of diabetes - TYPE 2 DIABETES

Opportunity - Type 2 Diabetes

Biomea is aiming to be the first approved beta cell restorative agent targeting menin in Type 2 Diabetes

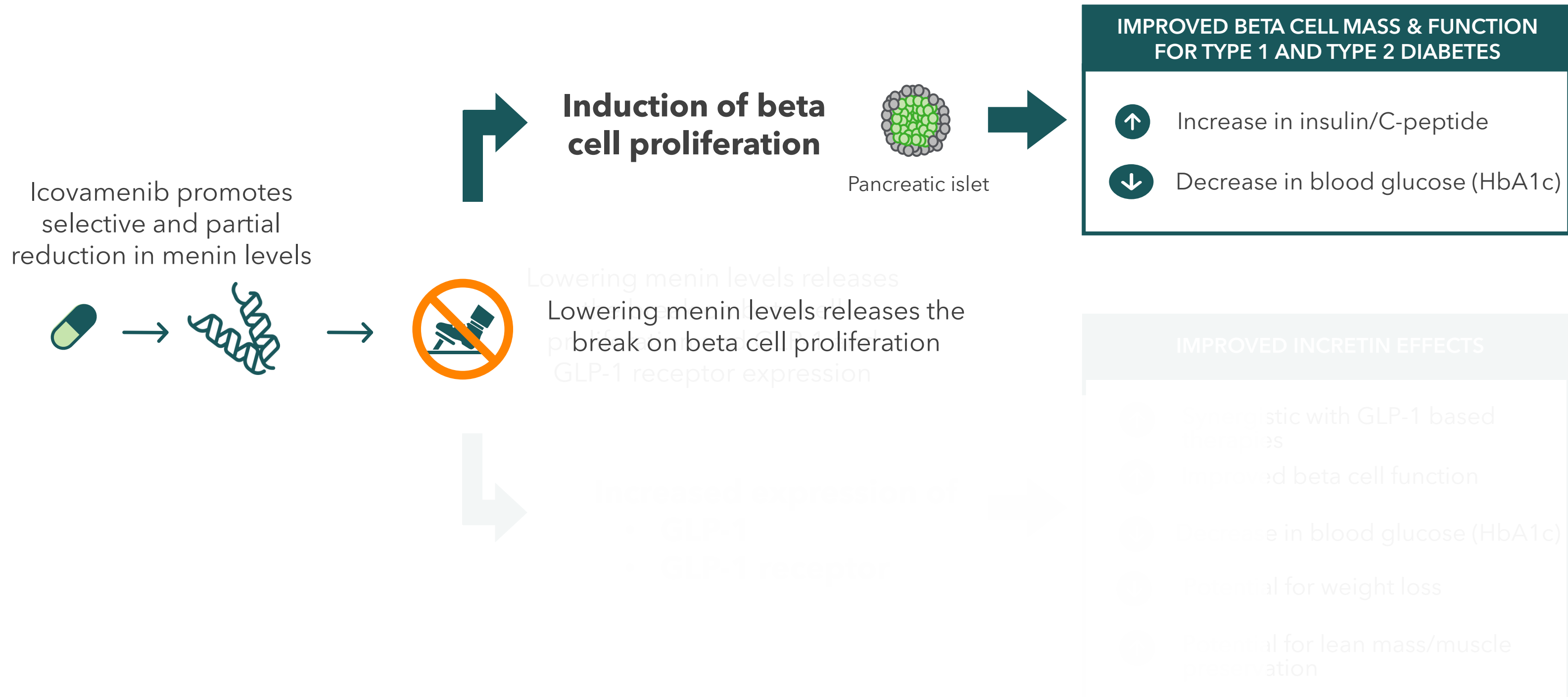
-  Icovamenib is the first-in-class beta cell restorative therapy in development in diabetes
-  Icovamenib is potentially the best-in-class oral agent addressing diabetes at the root cause level – the depleted pool of beta cells
-  Preclinical on target evidence of direct impact on beta cells, their proliferation and insulin productivity
-  Over 500 patients dosed to date with icovamenib, demonstrating at the effective dosing scheme a safety profile that mirrors placebo
-  Two ongoing Phase II Type 2 diabetes study reading out in 1H 27
-  Registrational studies targeted for 1H 28 initiation

Restoring beta-cell health to delay insulin dependence and reduce complications and disease burden



*In the U.S., >50% of patients with diabetes remain above HbA1c targets $\geq 7\%$ ¹
Depending on the GLP-1 RA agent, 15-45% do not achieve HbA1c < 7% in clinical trials²*

Icovamenib's mechanism of action



Baseline demographics & characteristics

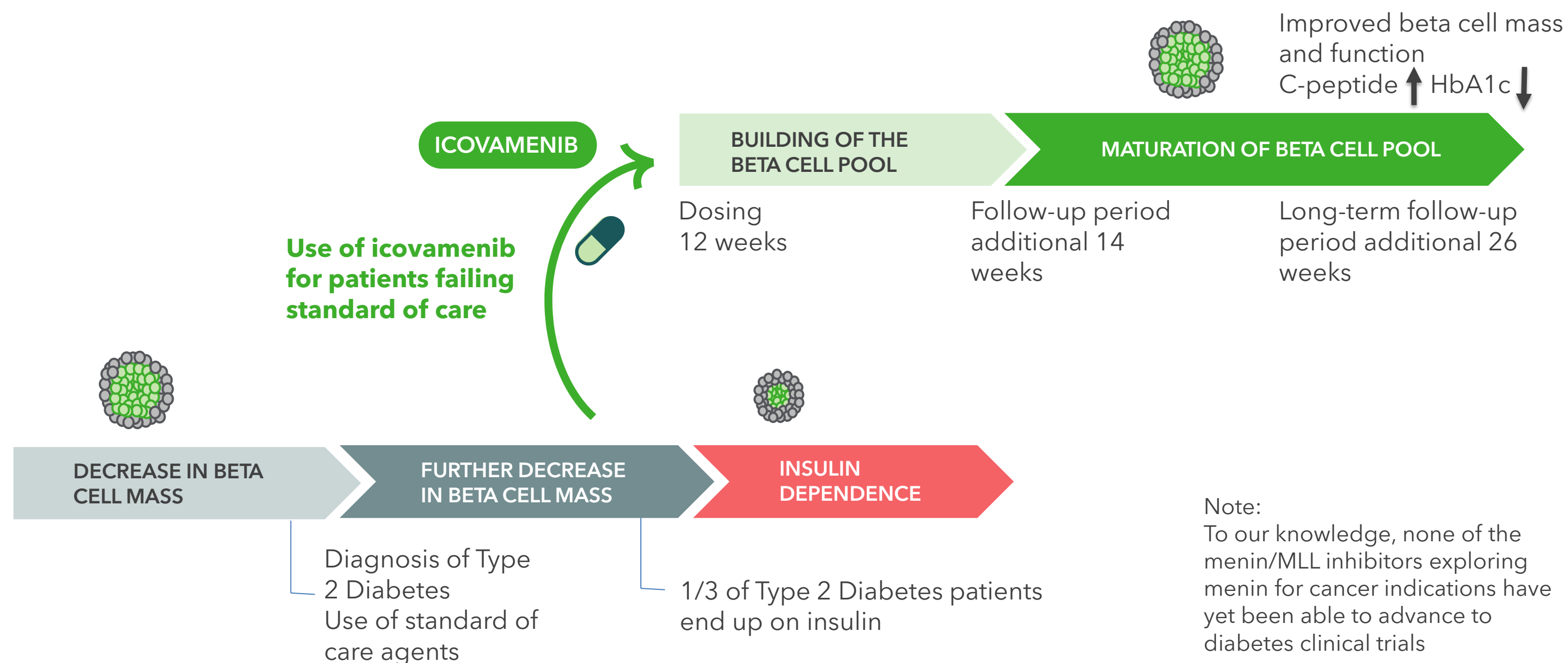
Per Protocol Population* on 1 or More Antihyperglycemic Agents at Baseline (N=163)

Parameter Mean (SD) or %	Arm A icovamenib (8 wks 100mg QD) (N=45)	Arm B icovamenib (12 wks 100 mg QD) (N=36)	Arm C icovamenib (8 wks 100 mg QD then 4 wks of 100 mg BID) (N=33)	Combined Arms icovamenib (N=114)	Combined Arms placebo (N=49)
Age (yr)	55 (7)	56 (6)	51 (10)	54 (8)	55 (7)
Duration of T2D Diagnosis (yr)	4.3 (1.8)	4.7 (1.8)	4.2 (2.2)	4.4 (1.9)	4.3 (2.0)
Sex (% Female)	(31)	(56)	(36)	(40)	(43)
HbA1c % (SD)	8.3 (1.1)	8.3 (1.0)	8.0 (0.8)	8.2 (1.0)	8.3 (1.0)
Fasting C-peptide (ng/mL)	3.4 (1.2)	3.8 (1.5)	3.7 (1.8)	3.6 (1.5)	3.5 (1.4)
BMI (kg/m ²)	30.9 (4.7)	32.7 (4.5)	32.4 (4.9)	31.9 (4.7)	32.6 (4.2)
BMI <30 kg/m ² (%)	(49)	(22)	(30)	(35)	(27)
BMI ≥30 kg/m ² (%)	(51)	(75)	(70)	(64)	(73)
Number of T2D Medications, n (%)					
1	39 (87)	23 (64)	23 (70)	85 (75)	41 (84)
2	4 (9)	11 (31)	7 (21)	22 (19)	6 (12)
3	2 (4)	2 (6)	3 (9)	7 (6)	2 (4)

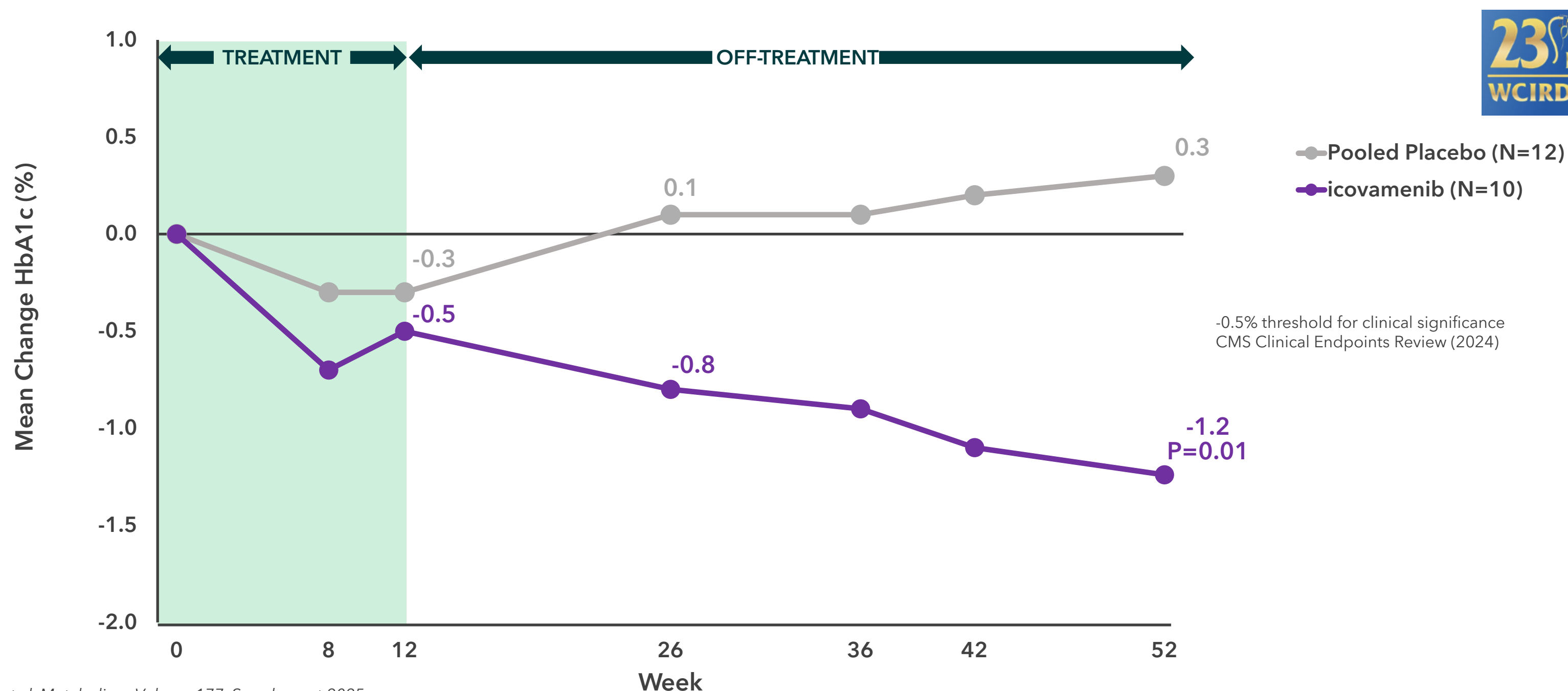
Frias, et al. Metabolism, Volume 177, Supplement,2025

*Per the COVALENT-111 Protocol the population analyzed includes only subjects who received ≥80% of their planned dosing. A clinical hold interrupted the dosing. Patients were also excluded if they had significant protocol deviation.

Icovamenib increased beta cell quantity, function & GLP-1 receptor expression following a short treatment period



12 weeks of dosing (arms B&C) delivered lasting benefit through 52 weeks for severe insulin-deficient diabetes patients



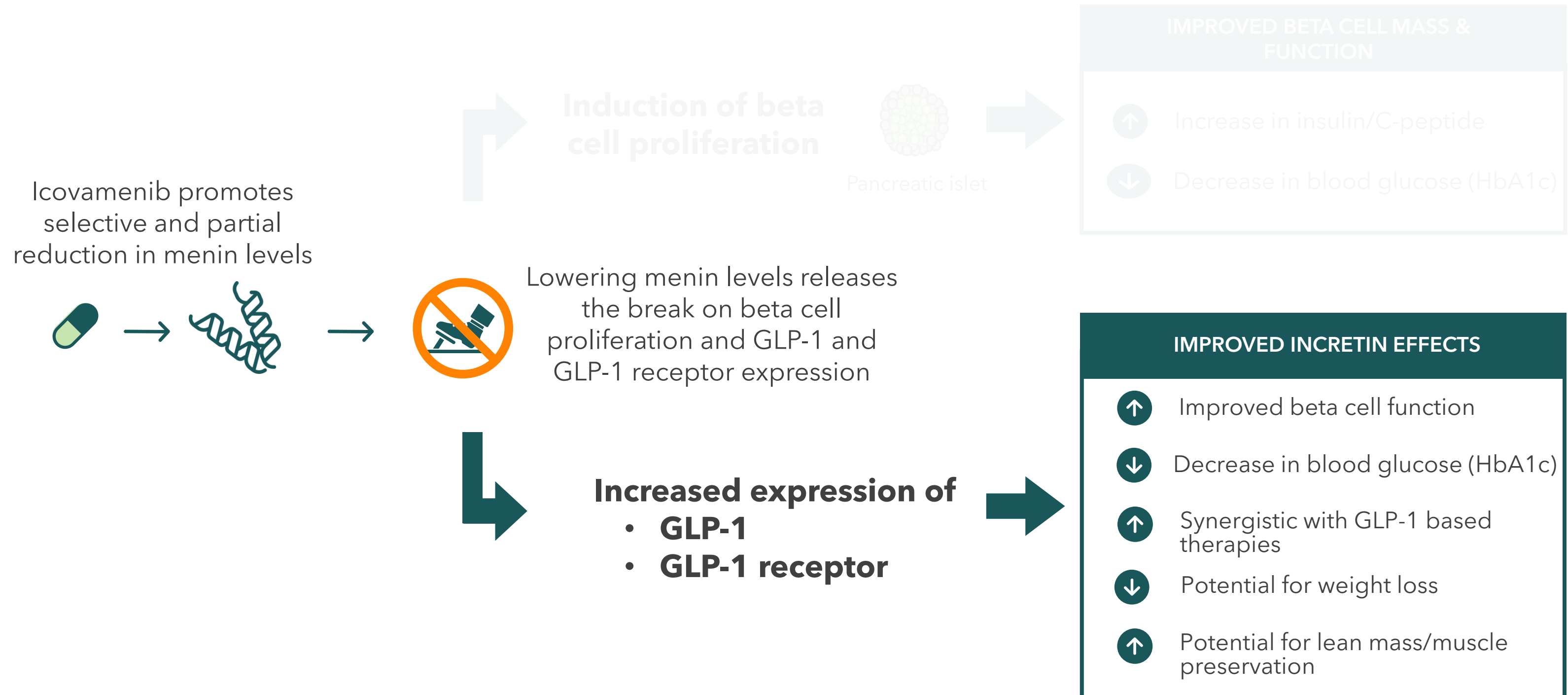
Frias, et al. Metabolism, Volume 177, Supplement, 2025

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

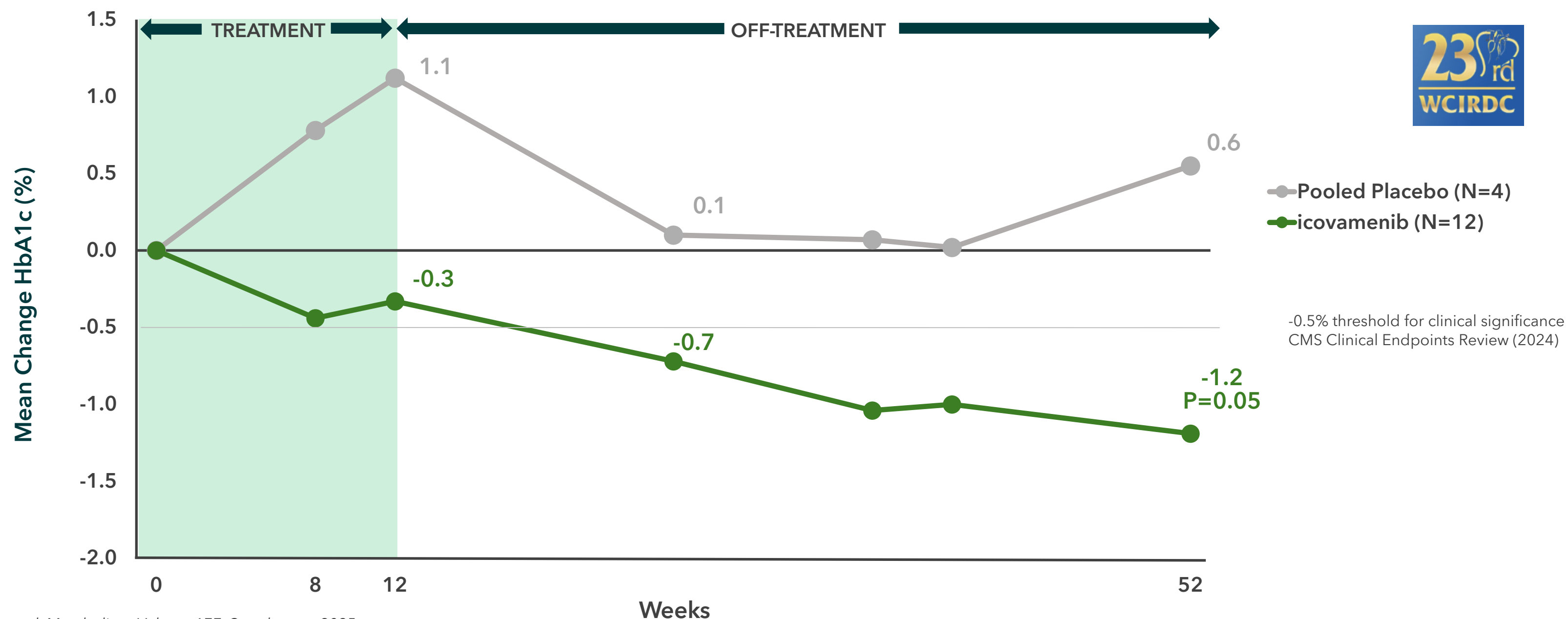
Icovamenib increased insulin secretion as measured by C-peptide index in severe insulin-deficient patients (arms B&C)



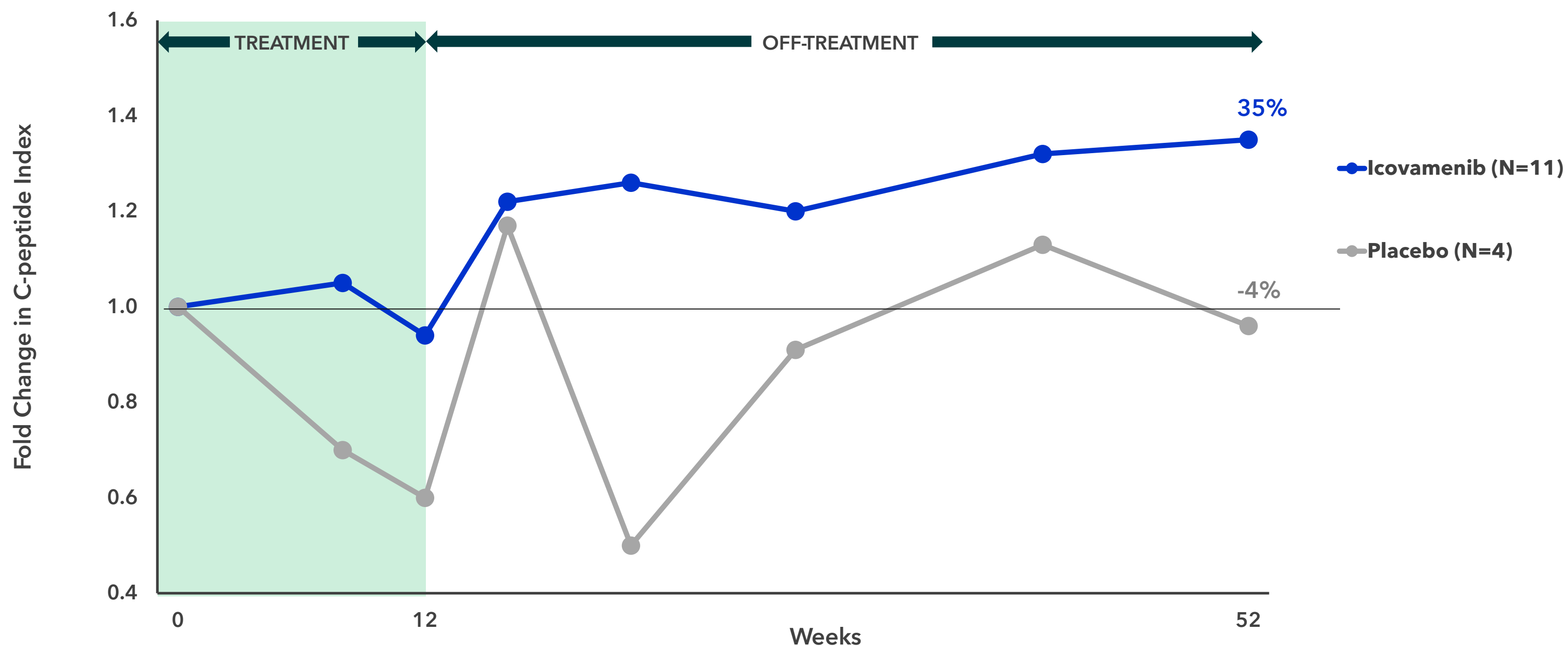
Icovamenib's mechanism of action



Patients on a GLP-1 based therapy at enrollment showed durable & clinically meaningful response in reduction of blood sugar (HbA1c)



Icovamenib increased insulin secretion as measured by C-peptide index in GLP-1 RA treated patients - 9 months post last dose



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

Favorable 52-week safety profile



Parameter	Arm A icovamenib (N=67)	Arm B icovamenib (N=67)	Arm C icovamenib (N=67)	Combined Arms icovamenib (N=201)	Combined Arms placebo (N=66)
Patients with ≥ 1 TEAE, N (%)	19 (28)	22 (33)	14 (21)	55 (27)	18 (27)
Treatment-Related SAEs, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SAEs*, N (%)	1 (1)	0 (0)	1 (1)	2 (1)	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)
ALT increase, N (%)	3 (4)	0	2 (3)	5 (3)	0
AST increase, N (%)	3 (4)	0	1 (1)	4 (2)	0
Resolution of ALT/AST w/o treatment interruption (%)	100	100	100	100	N/A
Deaths, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Frias, et al. Metabolism, Volume 177, Supplement, 2025

Data are n (%) TEAE = Treatment Emergent Adverse event. SAE = Serious Adverse Event. Data are n (%) of TEAE with $\geq 5\%$ frequency in any arm. ALT (alanine aminotransferase) or AST (aspartate aminotransferase) increase irrespective of incidence %.

*Arm A had an SAE of atrial fibrillation, unrelated to study treatment and occurred during the treatment period.

*Arm C had an SAE of COVID-19. Unrelated to study treatment and occurred during the treatment period.

*Placebo Arm had an SAE of nephrolithiasis. Unrelated to study treatment and occurred during the treatment period.

ALT increase: In the icovamenib arms, 4 of the 5 events were Grade 1 and 1 event was Grade 2.

AST increase: In the icovamenib arms, all 4 events were Grade 1.

All incidences of ALT and AST elevations resolved without interruption.

Note:

In AML studies icovamenib demonstrated a well-tolerated safety profile across all dose levels, with up to 500 mg QD / 325 mg BID, and dose durations extending over 1 year

Short treatment with icovamenib delivered HbA1c reductions comparable to chronic injectable & oral standards of care

Comparing icovamenib to currently approved type 2 diabetes agents with chronic dosing

THERAPY	DOSING REGIMEN	ADMINISTRATION ROUTE	OBSERVATION PERIOD	MEAN HbA1c REDUCTION (PLACEBO ADJ. %)
Ozempic (GLP-1 Agonist)	Chronic dosing	Injectable	Week 52 (SUSTAIN 8)	-1.5 (1mg)
Mounjaro (GLP-1/GIP Agonist)	Chronic dosing	Injectable	Week 40 (SURPASS 1)	-1.9 (5mg) -2.1 (15 mg)
Jardiance (SGLT2 Inhibitor)	Chronic dosing	Oral	Week 52 (Extension study)	-0.6 (10mg) -0.6 (25mg)
Januvia (DPP4 Inhibitor)	Chronic dosing	Oral	Week 52 (Sitagliptin)	-0.5 (100mg)
Ozempic FDA Label; Mounjaro FDA Label; Jardiance FDA Label; Januvia FDA Label				
Icovamenib (menin inhibitor)	12 weeks dosing	Oral	Week 52 (COVALENT-111)	-1.5% to -1.8%* (100 mg)

*Icovamenib data are from a Phase II study in selected populations: insulin deficient diabetes patients and GLP-1 inadequate responders.
Disclaimer: The data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences.
The values shown in the cross-study comparisons are directional and may not be directly comparable.

Optimal dose, dose-duration, target population identified for phase IIb program

Phase IIa key derisking-insights:

- ✓ Optimal dose selected, 100 mg
- ✓ Food Effect Study confirmed optimal PK exposure of icovamenib within 30 minutes after a meal
- ✓ 12-week treatment observed to drive durable and lasting effects, no chronic treatment required
- ✓ Strong clinical activity in insulin-deficient and GLP-1 inadequate responder populations
- ✓ Treatment-emergent AEs comparable to placebo

COVALENT-211

Phase II trial in type 2 insulin deficient diabetes patients failing standard of care

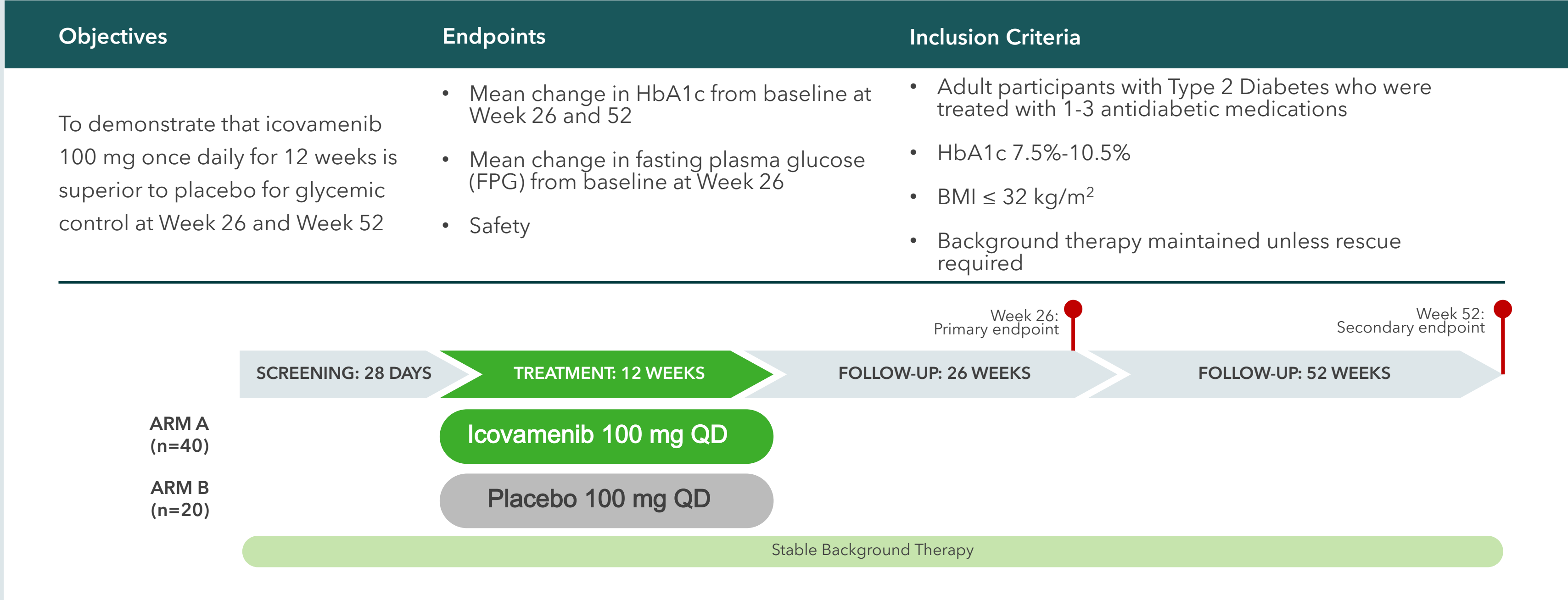
- Adult participants with T2D who were treated with 1-3 antidiabetic medications
- HbA1c 7.5%-10.5% and BMI ≤ 32 kg/m²
- Background therapy maintained unless rescue required

COVALENT-212

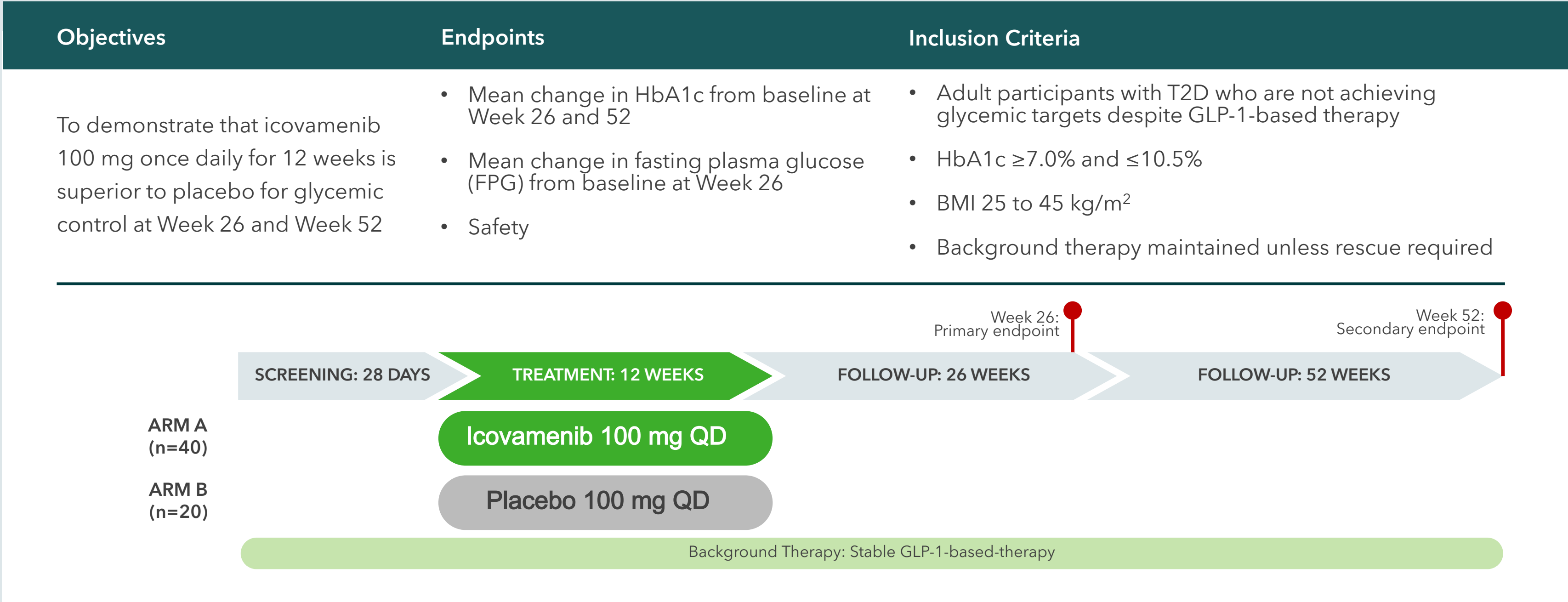
Phase II trial in type 2 diabetes patients failing standard of care while on a GLP-1 RA

- Adult participants with T2D who are not achieving glycemic targets despite GLP-1-based therapy
- HbA1c $\geq 7.0\%$ and $\leq 10.5\%$ and BMI 25 to 45 kg/m²
- Background therapy maintained unless rescue required

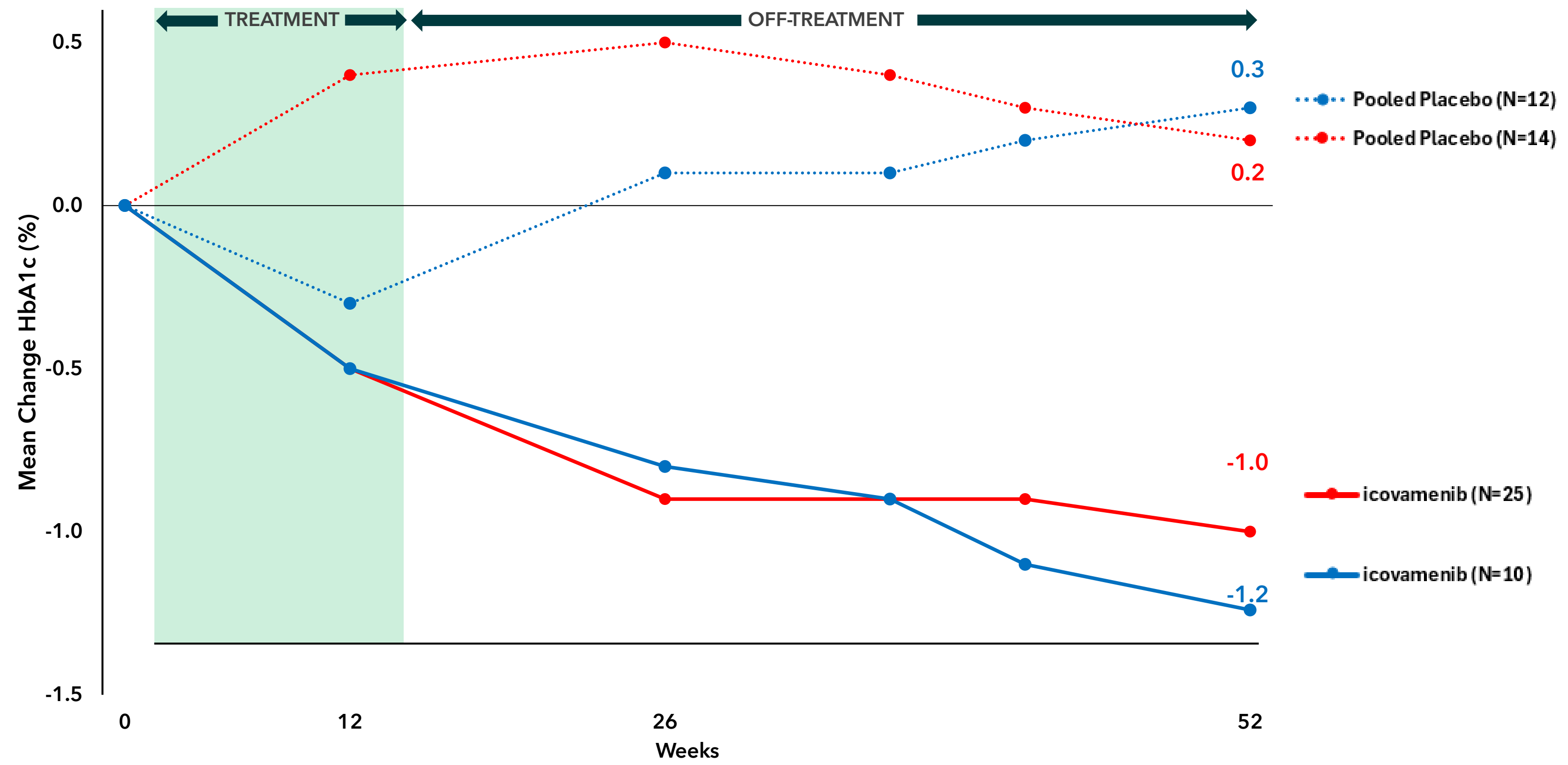
A Phase II trial of icovamenib in T2D insulin deficient participants who are not achieving glycemic targets



Phase II trial of icovamenib in participants with T2D who are not achieving glycemic targets while using GLP-1-based therapy



Applying enrollment criteria of COVALENT-211 (red) vs published results in SIDDs dosed in COVALENT-111 (blue)





ICOVAMENIB

First-in-class menin targeting agent in development for the treatment of diabetes - PRECLINICAL RESULTS

Menin is naturally inhibited during pregnancy and breastfeeding

- allowing for adaptive beta cell mass increase & reduced diabetes risk

- 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.

First in a 2005 paper in Proceedings of the National Academy of Sciences (PNAS) by Satyajit K. Karnik et al. titled "**Menin regulates pancreatic islet growth** by promoting histone methylation and expression of genes encoding p27^{Kip1} and p18^{INK4c}"

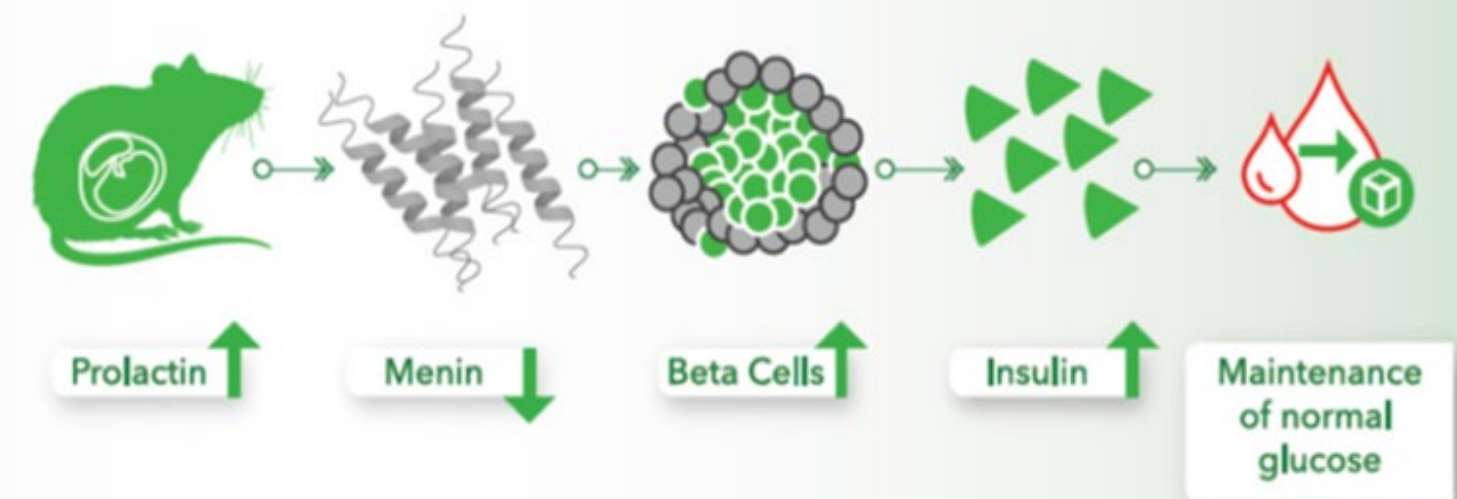
- Icovamenib has been shown to directly inhibit menin, aiming to pharmacologically replicate a naturally occurring, validated biologic process



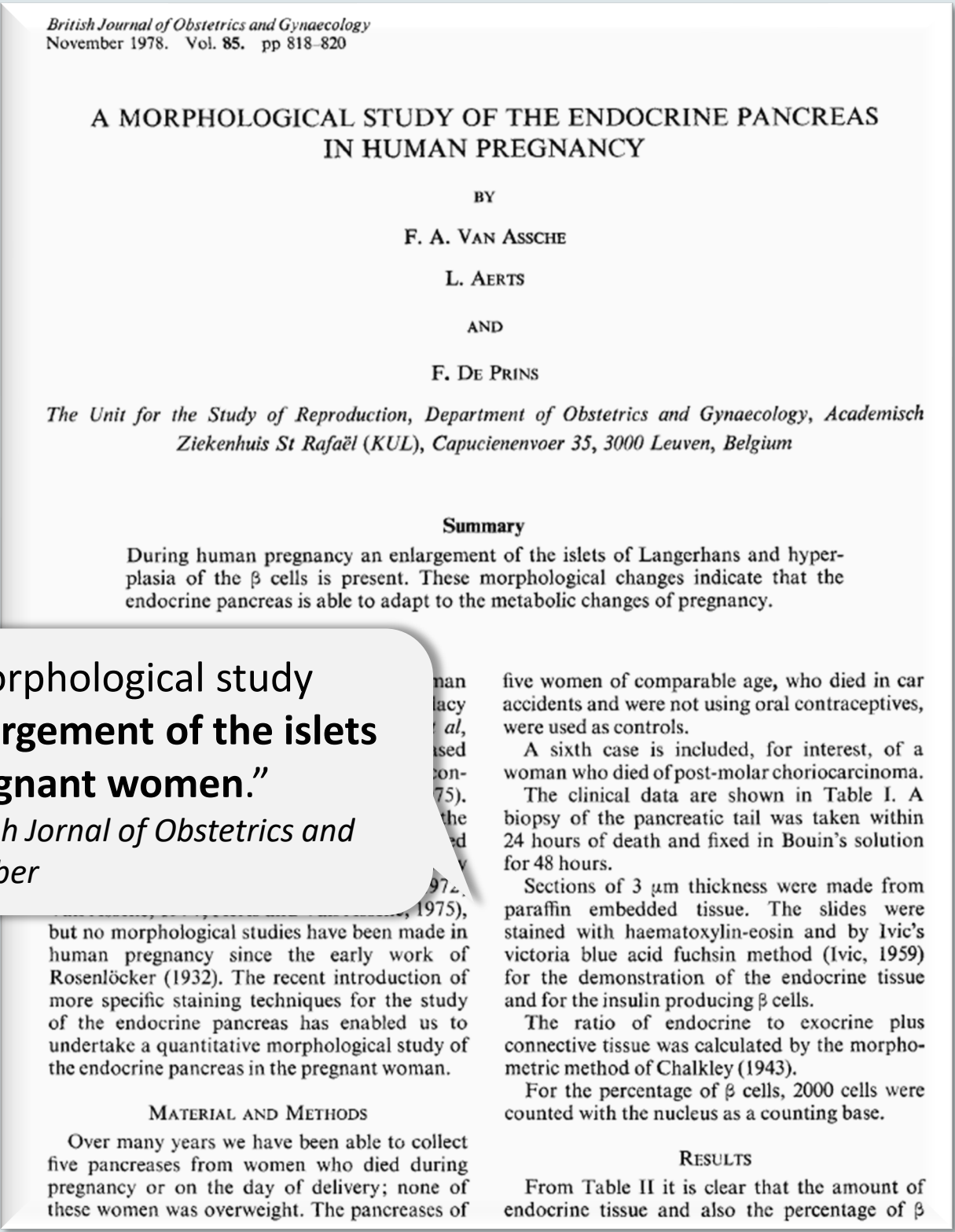
Menin Controls Growth of Pancreatic β -Cells in Pregnant Mice and Promotes Gestational Diabetes Mellitus

Satyajit K. Karnik,¹ Hainan Chen,^{1*} Graeme W. McLean,^{1*} Jeremy J. Heit,^{1*} Xueying Gu,¹ Andrew Y. Zhang,¹ Magali Fontaine,² Michael H. Yen,^{1,3} Seung K. Kim^{1,3†}

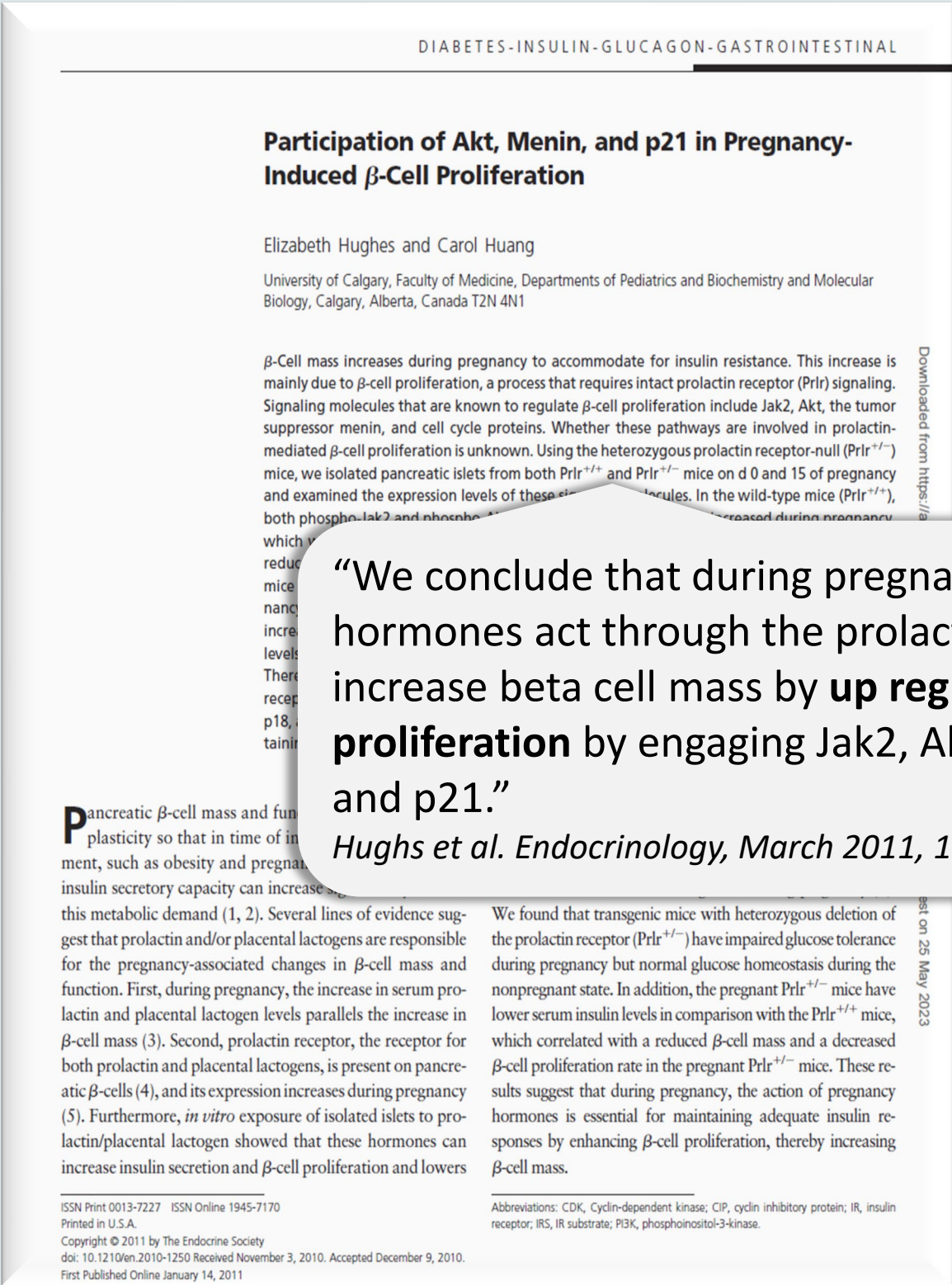
Karnik SK, et al. Science. 2007;318:806-809



Beta Cells Proliferation During Pregnancy



“This quantitative morphological study shows a **marked enlargement of the islets of Langerhans in pregnant women.**”
F. A. Van Assche et al. British Journal of Obstetrics and Gynaecology, 1978 November



Beta Cells Proliferation in Obesity

Pancreatic β -Cell Proliferation in Obesity^{1,2}

Amelia K. Linnemann,³ Mieke Baan,^{3,4} and Dawn Belt Davis^{3,5*}

³Division of Endocrinology, Department of Medicine, and ⁴School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI; and ⁵William S. Middleton Memorial Veterans Hospital, Madison, Wisconsin

ABSTRACT

Because obesity rates have increased dramatically over the past 3 decades, type 2 diabetes has become increasingly prevalent as well. Type 2 diabetes is associated with decreased pancreatic β -cell mass and function, resulting in inadequate insulin production. Conversely, in nondiabetic obesity, an expansion in β -cell mass occurs to provide sufficient insulin and to prevent hyperglycemia. This expansion is at least in part due to β -cell proliferation. This review focuses on the mechanisms regulating obesity-induced β -cell proliferation in humans and mice. Many factors have potential roles in the regulation of obesity-driven β -cell proliferation, including nutrients, insulin, incretins, hepatocyte growth factor, and recently identified liver-derived secreted factors. Much is still unknown about the regulation of β -cell replication, especially in humans. The extracellular signals that activate proliferative pathways in obesity, the relative importance of each of these pathways, and the extent of cross-talk between these pathways are important areas of future study. *Adv. Nutr.* 5: 278–288, 2014.

Introduction

The rates of obesity worldwide continue to climb because of numerous social, environmental, and perhaps even genetic factors. In the United States, >35% of adults are obese (1). Along with obesity has come increasing prevalence of type 2 diabetes. Notably, however, only 11.3% of adults are estimated to have diagnosed or undiagnosed diabetes (2). These statistics reveal

that secondary factors other than obesity are important for diabetes to develop; the 2 a sity is associated with periphe of the pathophysiology of type hyperglycemia there must be sulin to meet this increased de to the pancreatic β -cell, where to circulating nutrients and o

Pancreatic β -cells are found small clusters of endocrine the total pancreatic mass. Th ple cell types, including in gon-producing α -cells, and types producing somatostat ghrelin. The amount of in

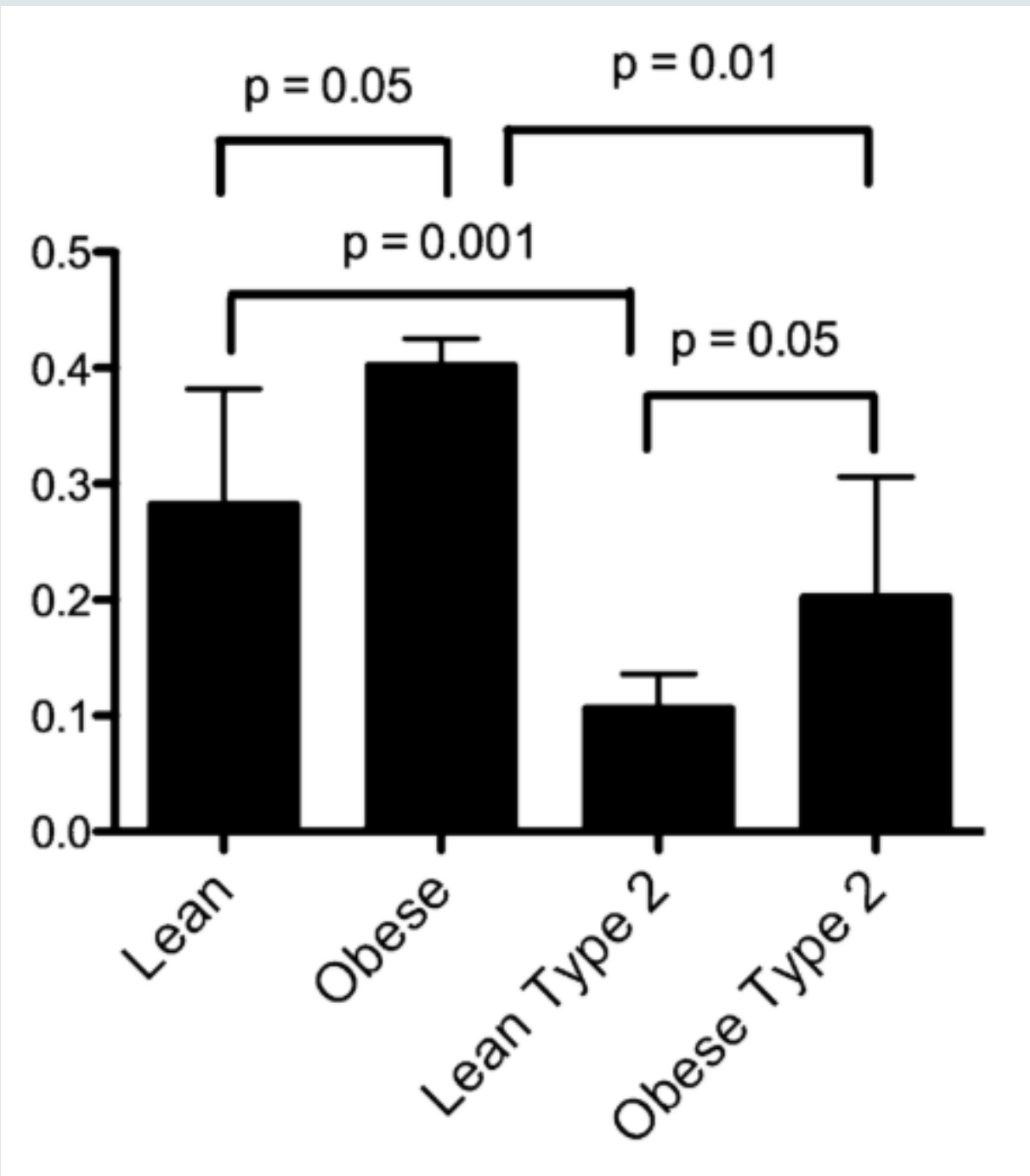
metabolic demand is dependent on numerous factors, including proper sensing of nutrient and hormonal signals, adequate insulin synthesis and secretion, and the overall number of functional β -cells. Although all of these factors are important, this review will focus on the regulation of β -cell number. The number of β -cells in a pancreas can be determined by using histologic analysis. To-

“In nondiabetic obesity, an expansion in beta cell mass occurs to provide sufficient insulin and to prevent hyperglycemia. This expansion is at least in part due to beta cell proliferation.

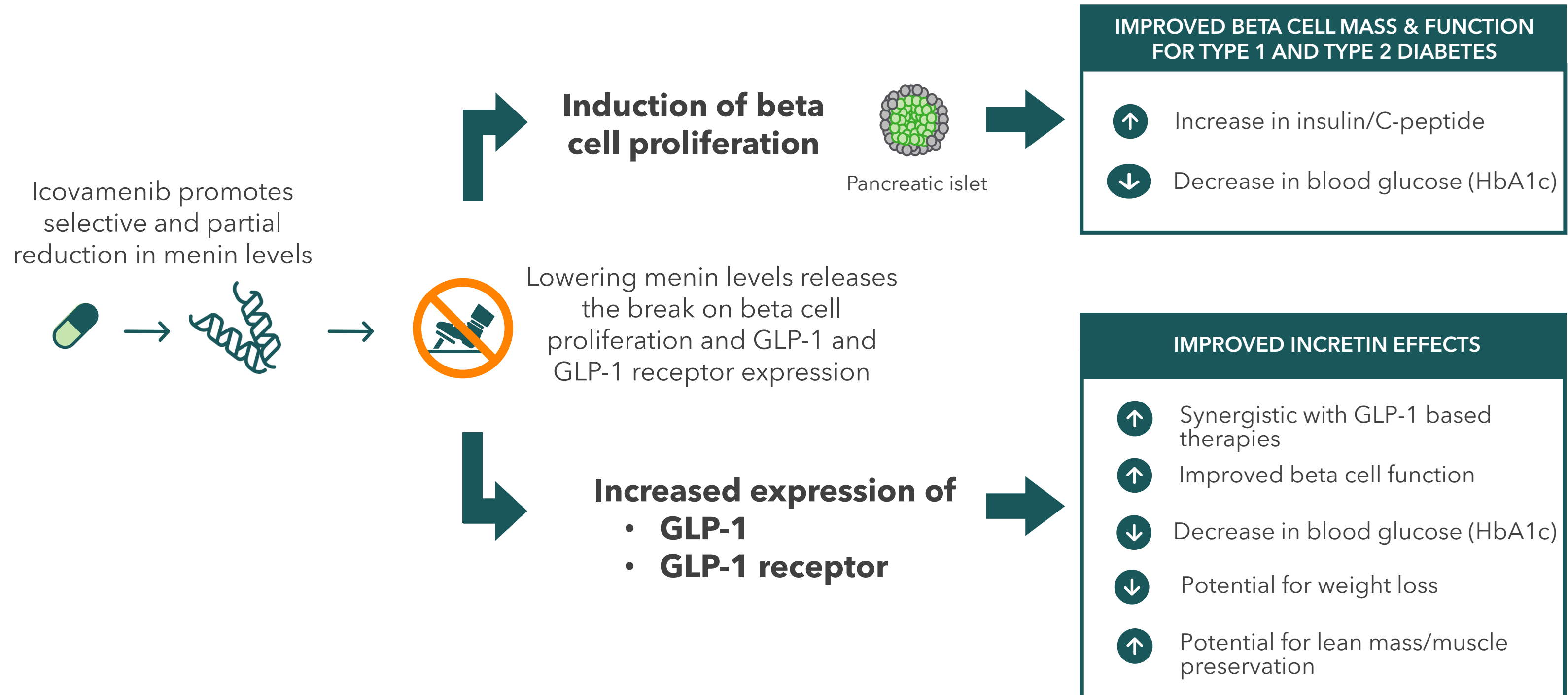
Linnmann et al. American Society for Nutrition. *Adv. Nutr.* 5: 278–288, 2014

¹D.B.D. is supported by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) DK083442. M.B. is supported by the National Service Award Institutional Training Grant T32 RR023916/OD010423 from the National Center for Research Resources. The William S. Middleton Memorial Veterans Hospital provided resources and use of facilities. The contents of this manuscript do not necessarily represent the views of the Department of Veterans Affairs or the U.S. Government. ² Author disclosures: A. K. Linnemann, M. Baan, and D. B. Davis, no conflicts of interest. * To whom correspondence should be addressed. E-mail: dbd@medicine.wisc.edu.

Insulin Positive Beta-Cell Volume (ml)



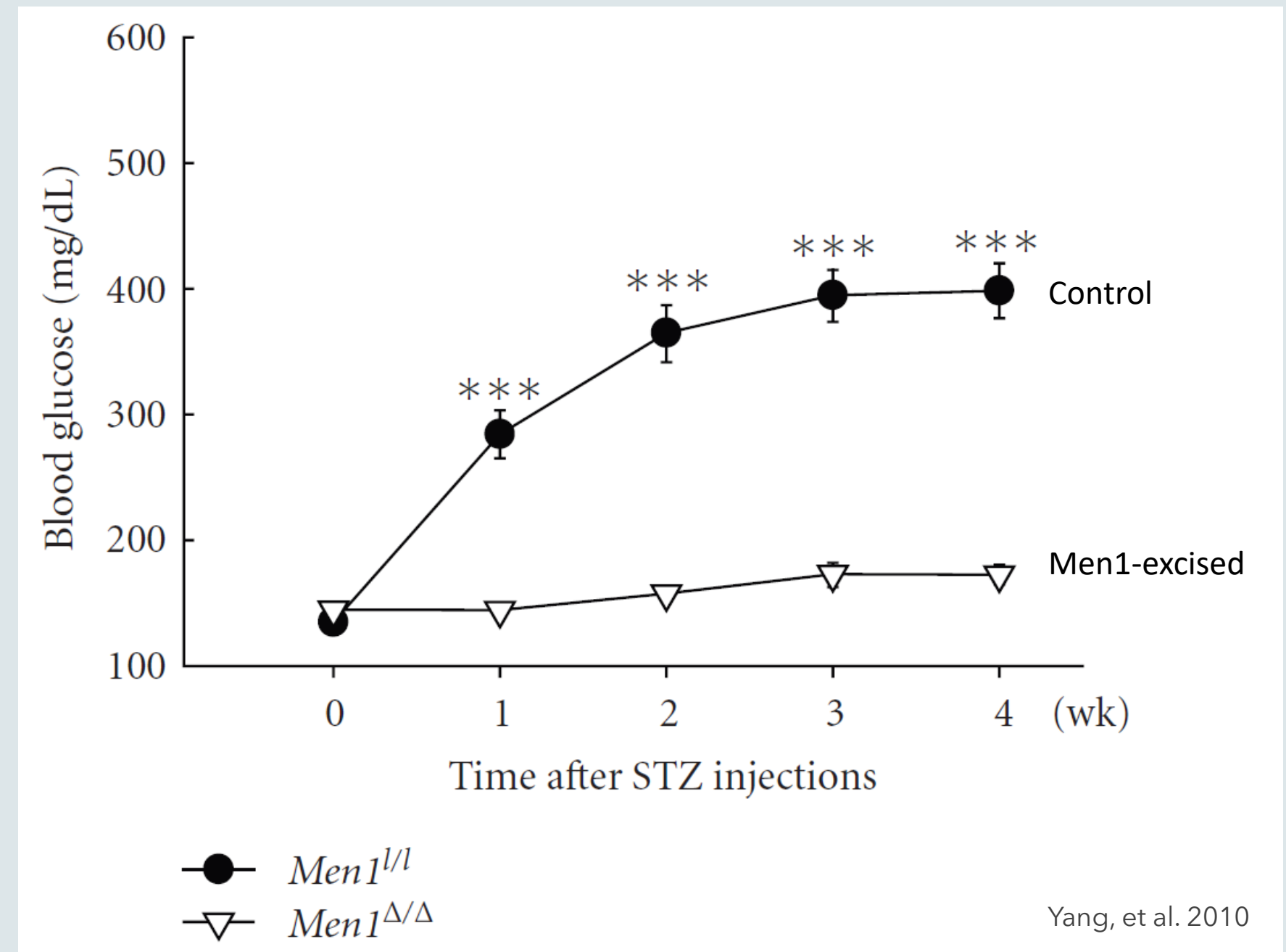
Icovamenib's mechanism of action



Potential for menin inhibition demonstrated by beta cell ablation diabetes model in MEN1-excised mice

MEN1 excision prevents development of STZ-induced hyperglycemia

- Menin is a scaffold protein, encoded by the gene MEN1, that has been recognized for its role in Type 2 Diabetes Mellitus (T2DM) as a key regulator of beta-cell proliferation.
- Men1 knockout mice demonstrate increased beta-cell mass generation (Yang et al., 2010) and menin inhibition has previously been shown to improve glycemic control in high fat induced diabetic mice (Ma et al., 2021).
- Men1-excised mice do not develop hyperglycemia in a Streptozotocin-(STZ) induced rat model, which is a model for impaired beta-cell function and insulin production, demonstrating the role of menin in glycemic control.

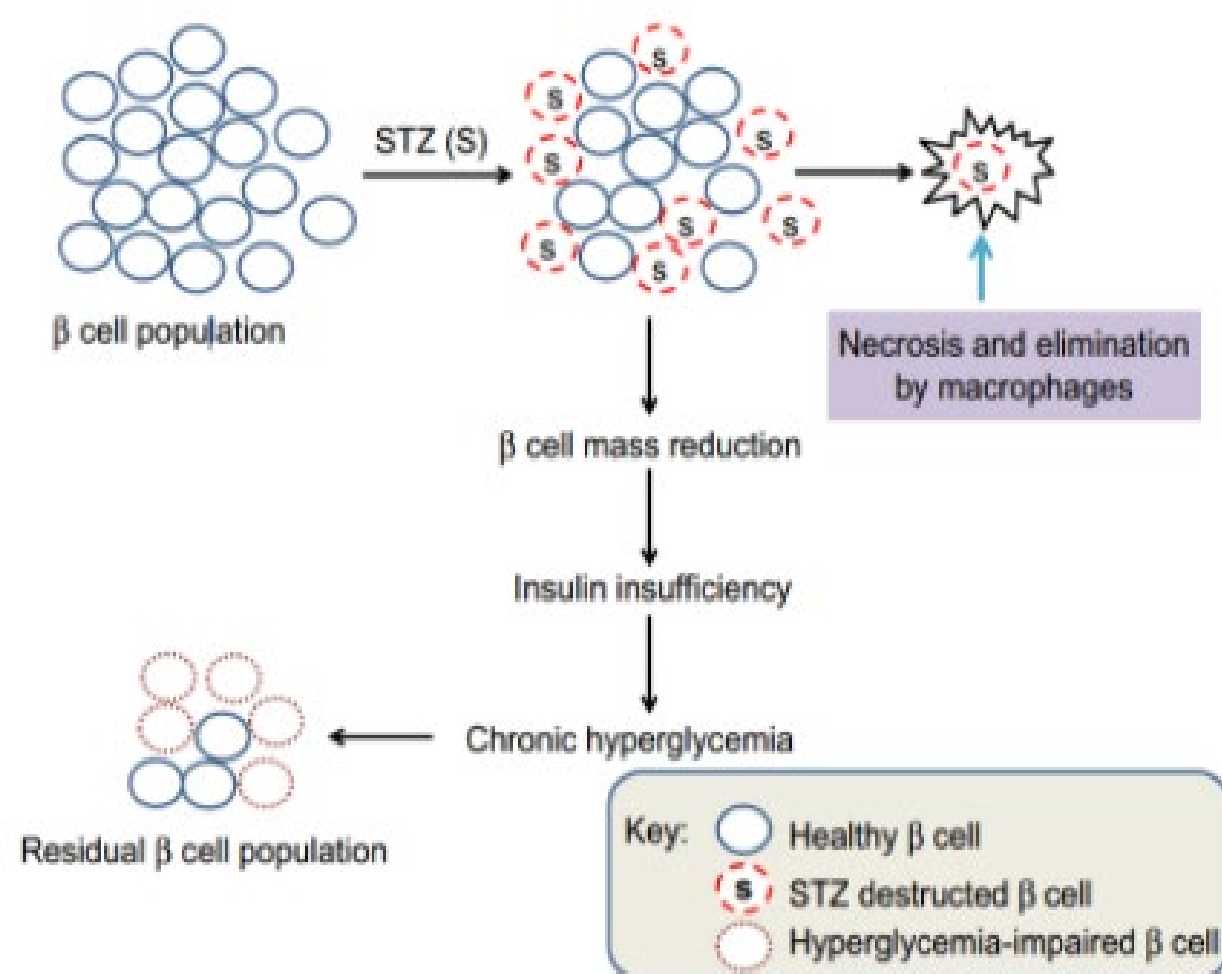


Men1-excised mice did not develop hyperglycemia in the STZ model, which was observed in the control group

Icovamenib significantly reduced blood glucose in STZ rats (a model in which only insulin decreases blood glucose levels)

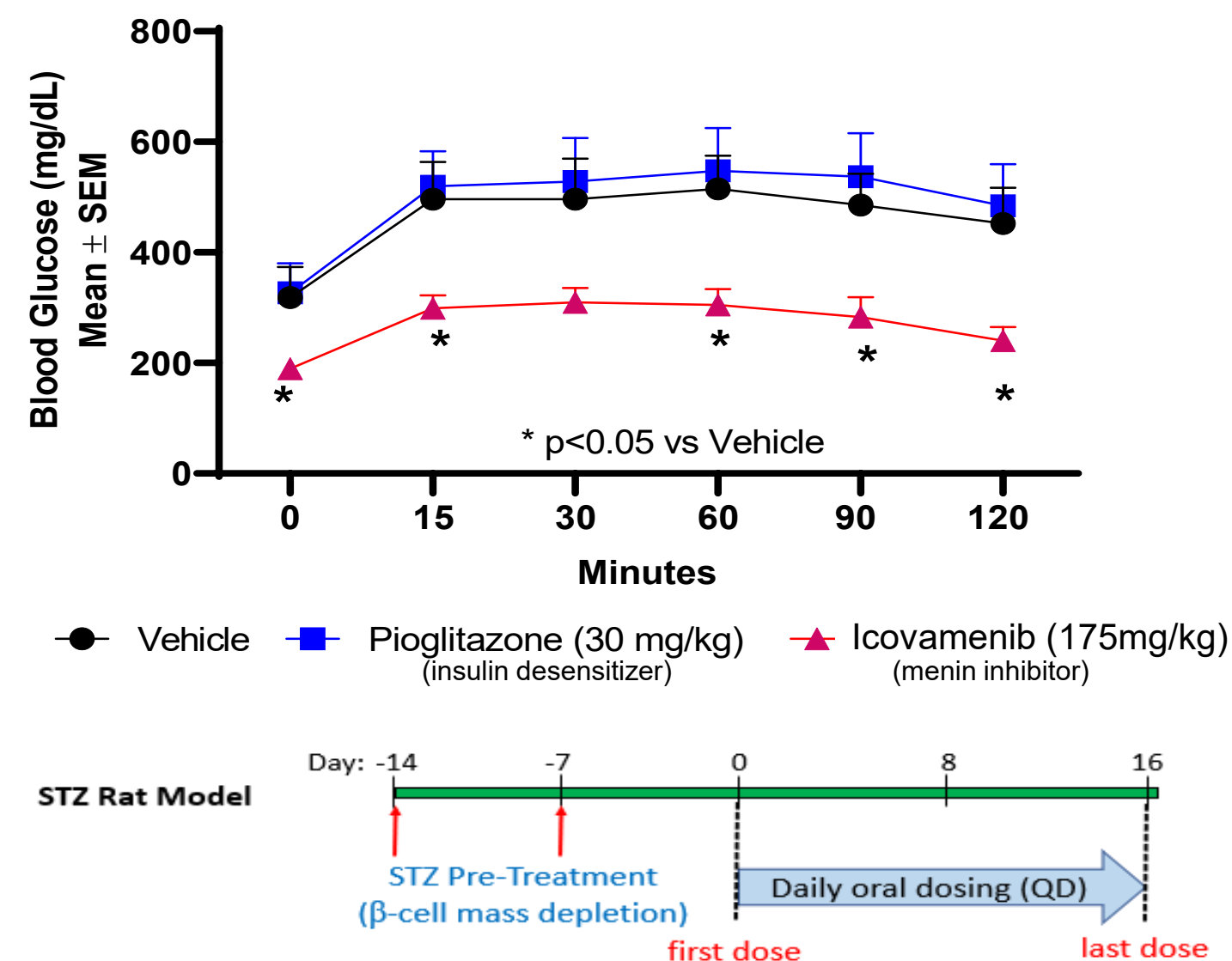


STZ TREATMENT TYPICALLY RESULTS IN ~50% BETA CELL LOSS



STZ=Streptozotocin, an antibiotic that produces pancreatic islet beta cell destruction and is widely used experimentally to produce a model in diabetes

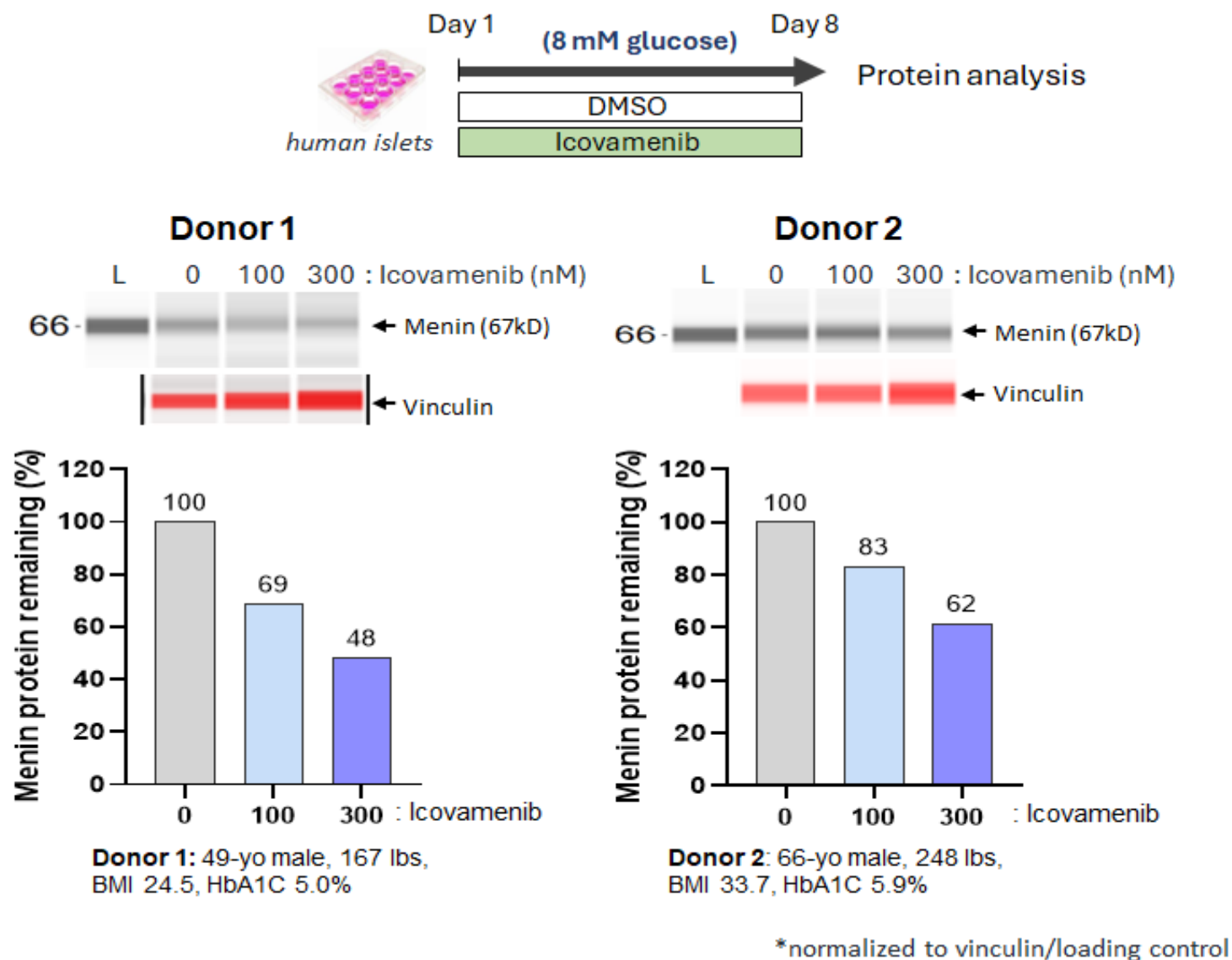
ORAL GLUCOSE TOLERANCE TEST (DAY 17)



Butler, et al. (EASD) Diabetologia 65 (Suppl 1), 1-469 (2022) presentation #197

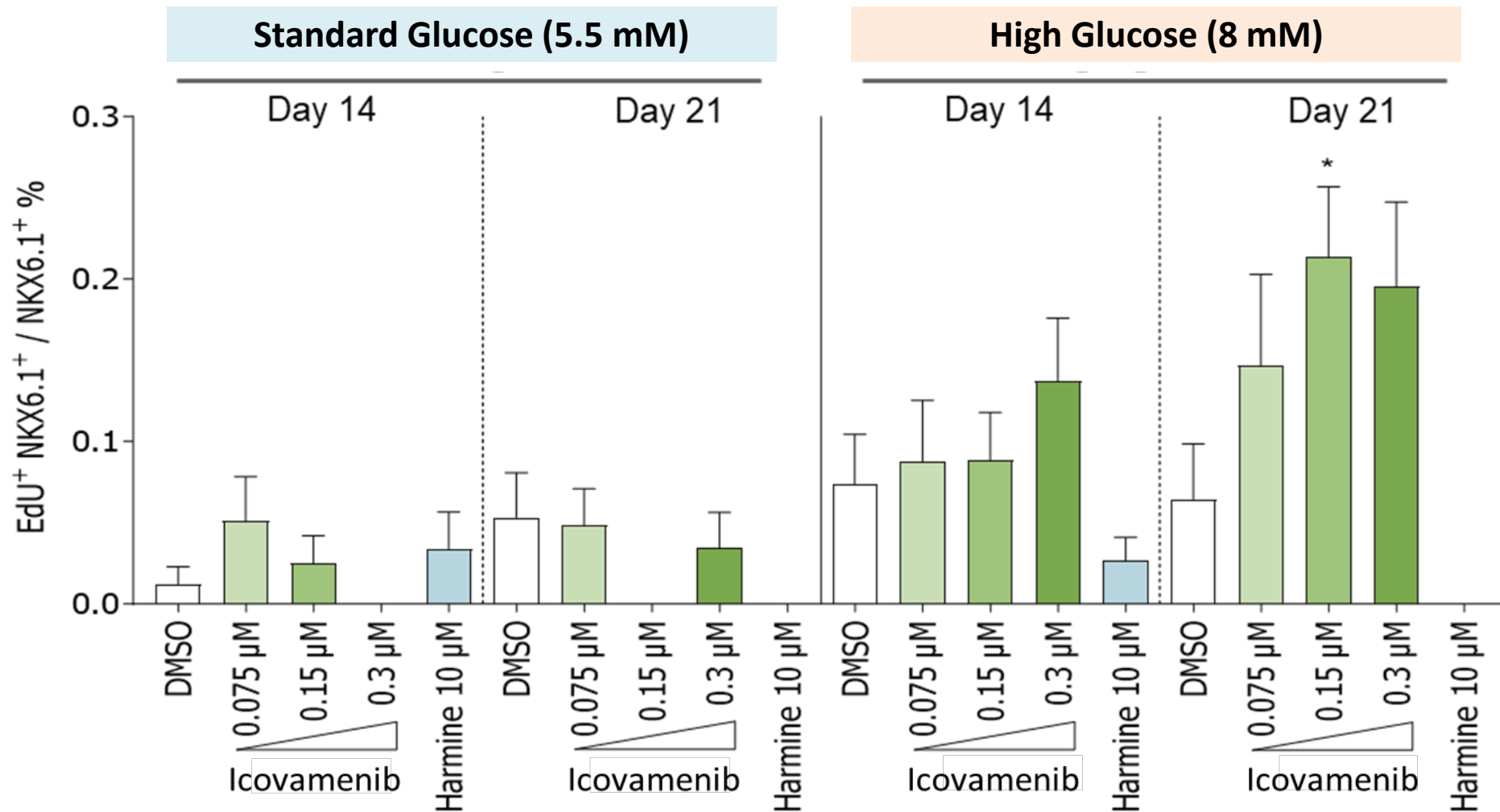
Icovamenib downregulated menin protein levels & promoted beta cell proliferation in ex vivo human islet cultures

MENIN LEVELS DOWNREGULATED



Somanath, et al. (EASD) Diabetologia 68 (Suppl 1), 1-754 (2025). Oral presentation #66

ICOVAMENIB CONDITIONALLY PROMOTED BETA CELL PROLIFERATION ONLY UNDER HYPERGLYCEMIC CONDITIONS

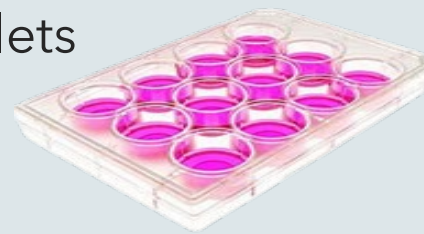


Frias, et al. (WCIRDC) Metabolism, Vol153, Supplement, 2023, #88

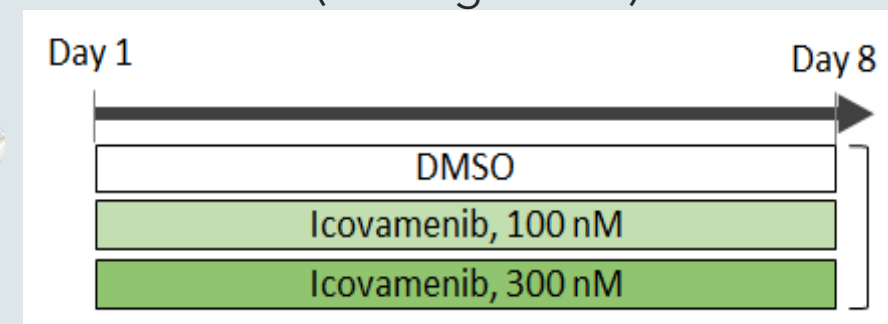
Icovamenib enhanced GLP-1 receptor & insulin expression in human islets



Cadaver derived human islets

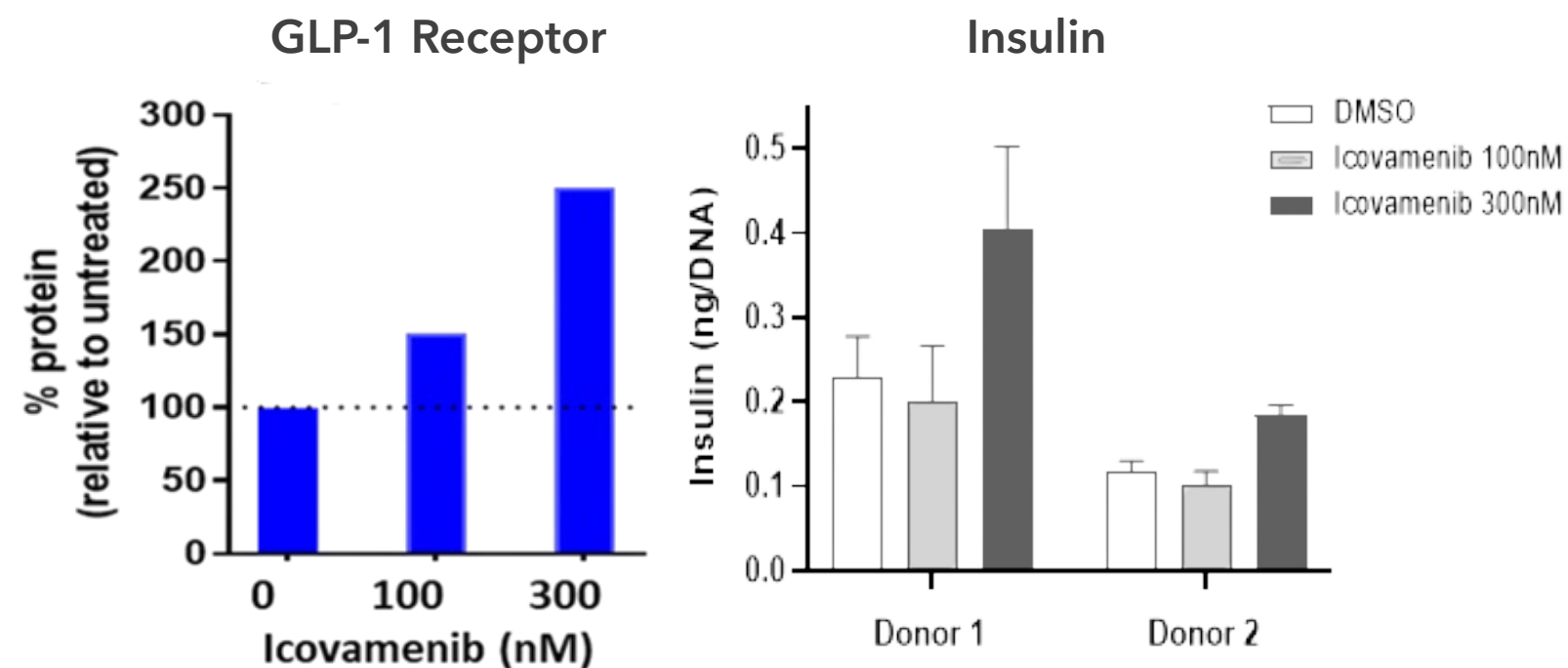


Culture 7 days under glucotox conditions (8mM glucose)

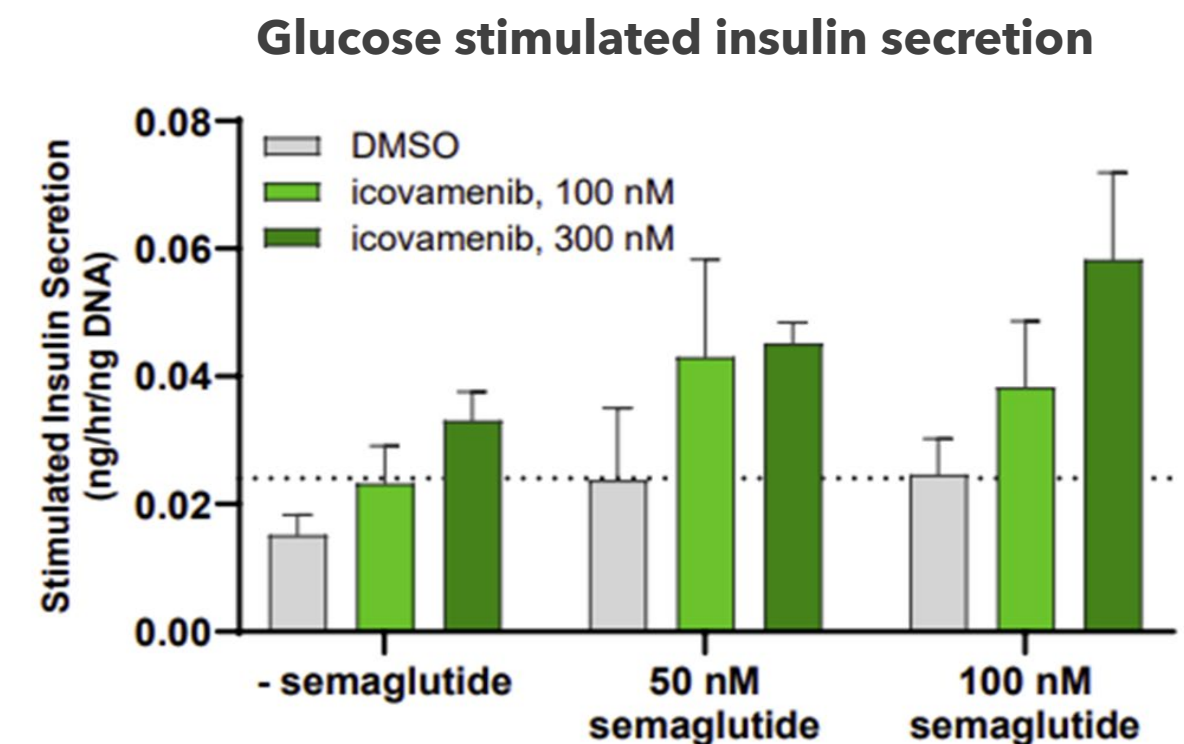


- Gene expression & Protein analysis
- Glucose Stimulated Insulin Secretion +/- Semaglutide

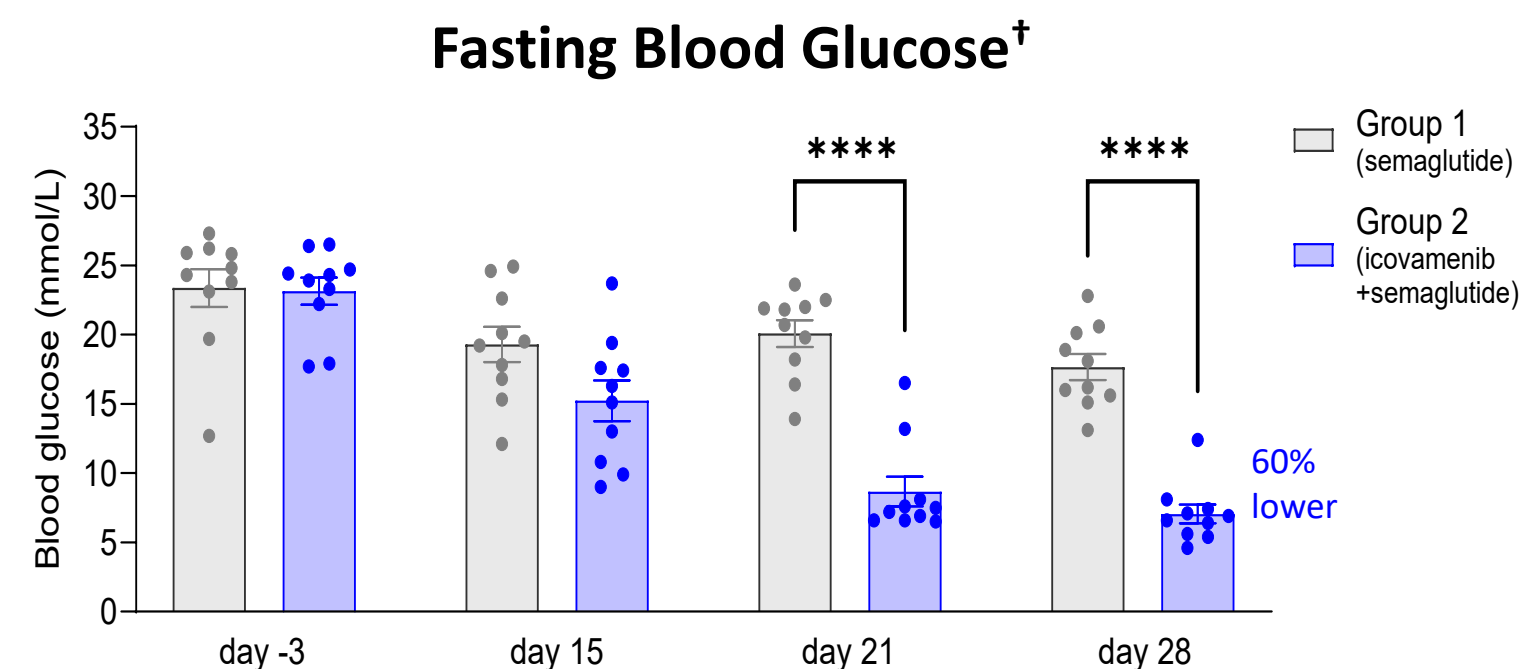
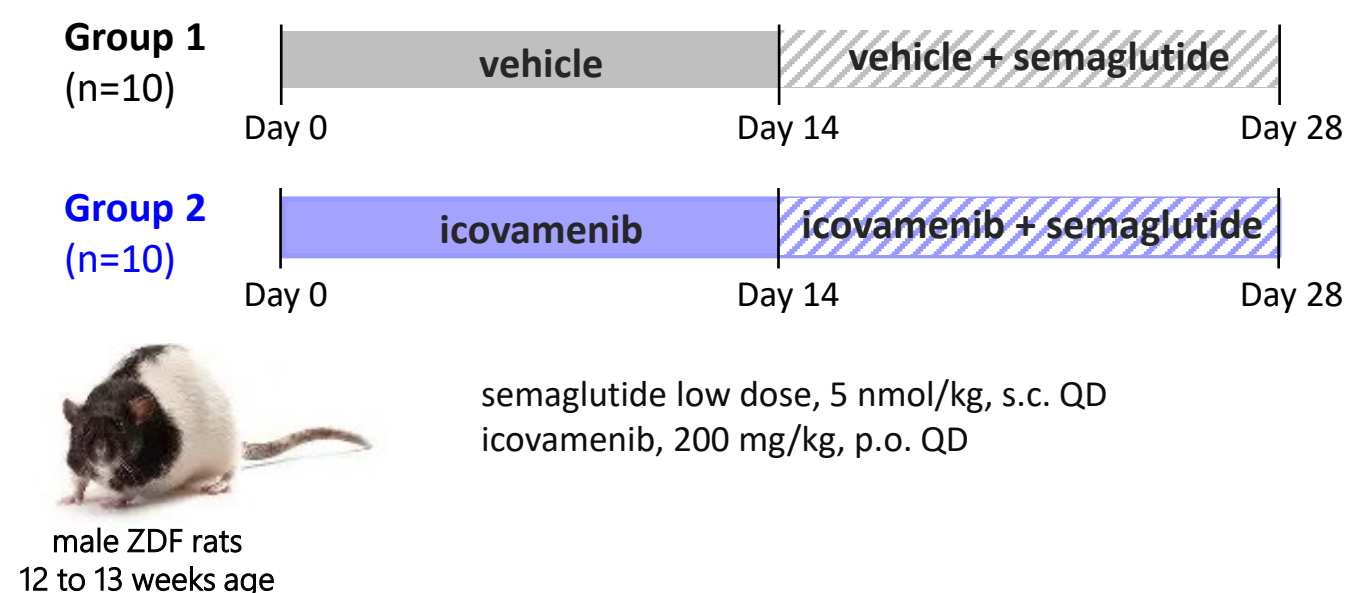
ICOVAMENIB INCREASED GLP-1 RECEPTOR AND INSULIN PROTEIN LEVELS



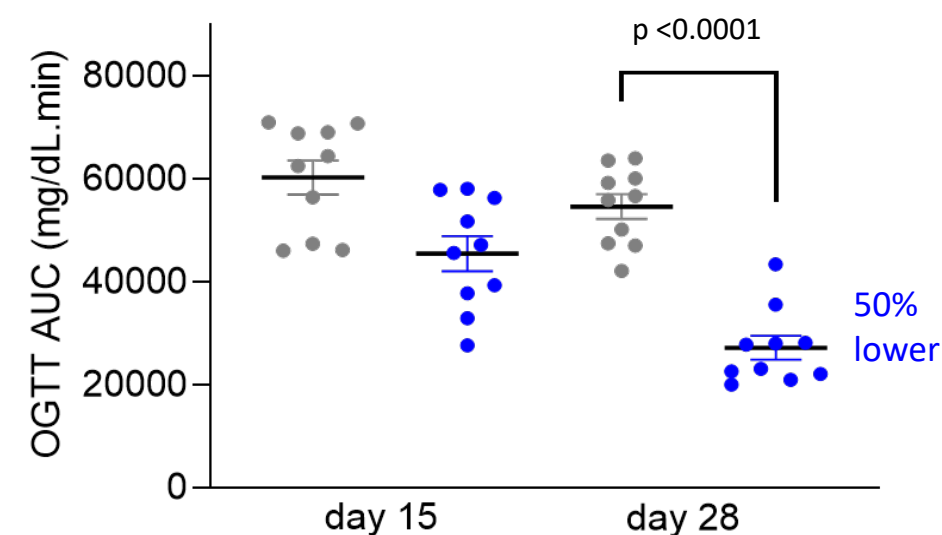
ICOVAMENIB ENHANCES THE RESPONSIVENESS OF HUMAN ISLETS TO GLP-1 RECEPTOR AGONISTS



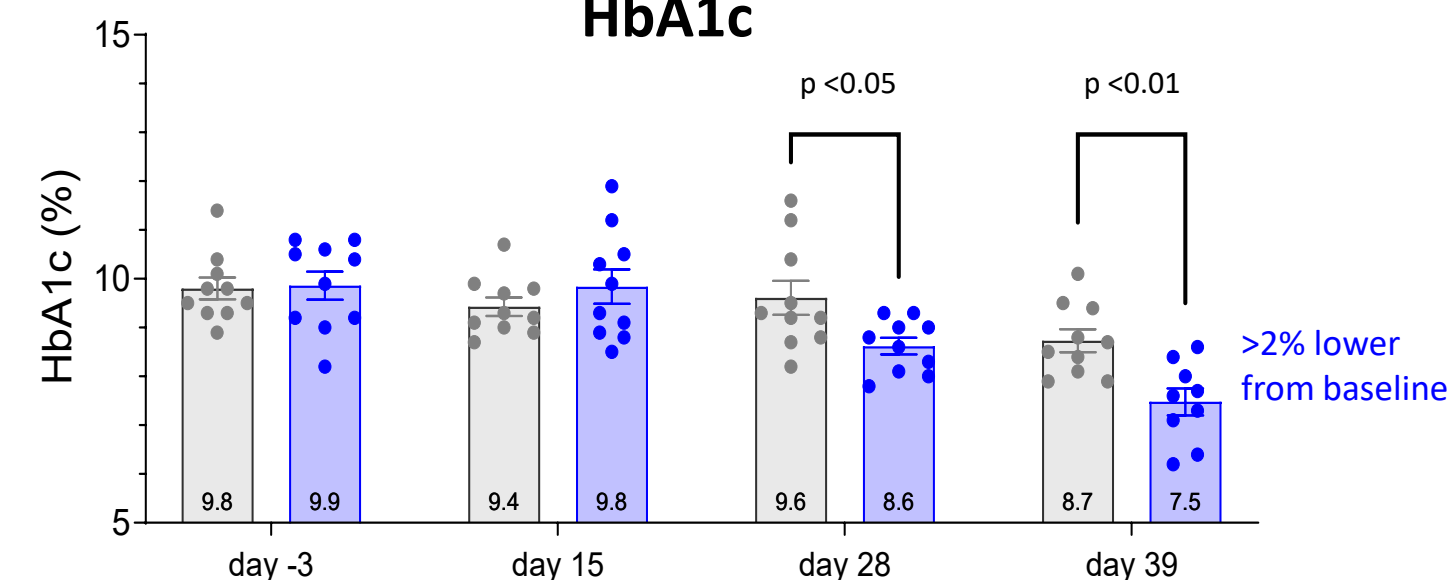
Combination treatment of icovamenib & low-dose semaglutide improved glycemic control in ZDF rats



Glucose AUC during Oral Glucose Tolerance Test



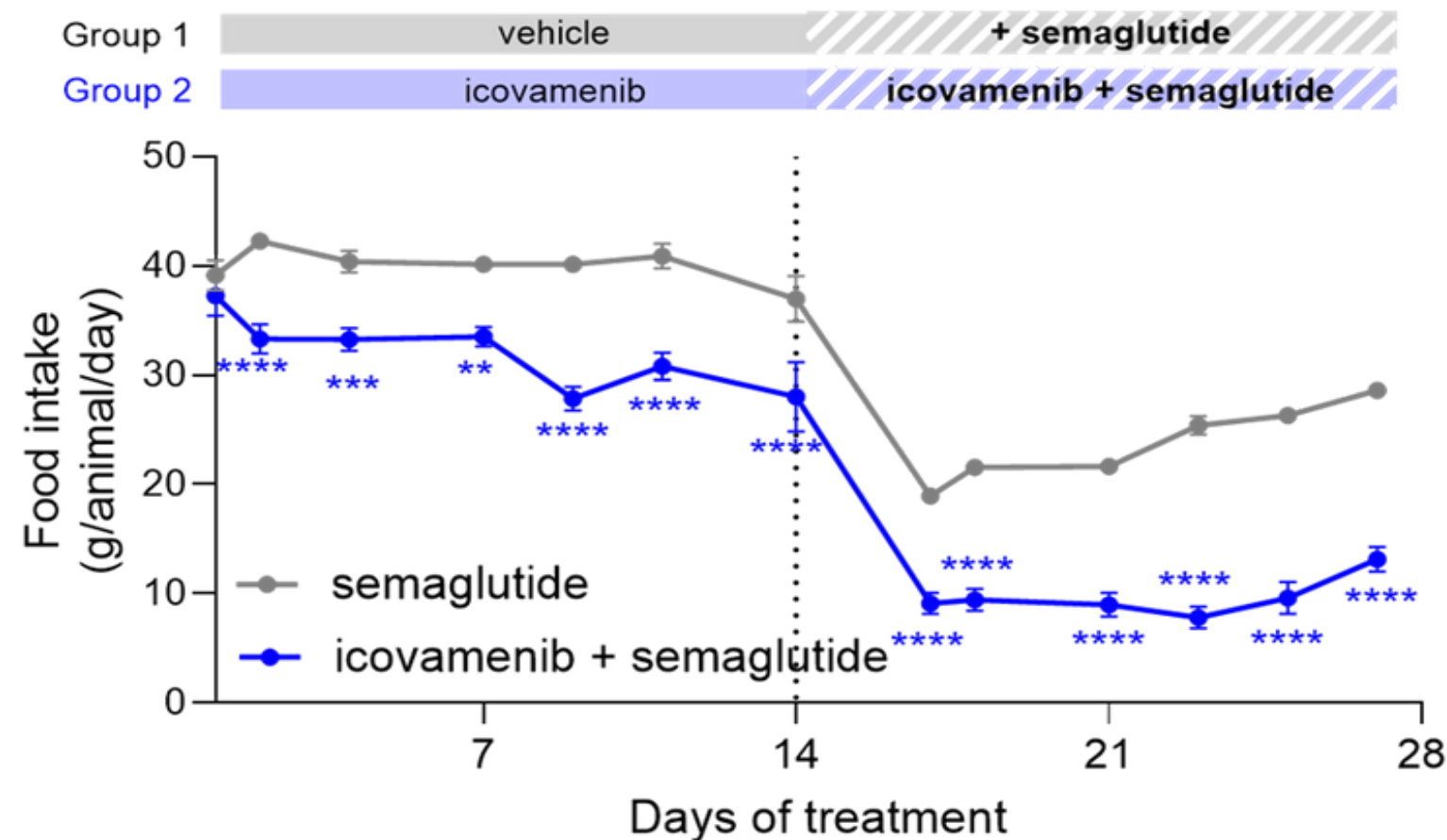
HbA1c



Plots represent mean $\pm$ SEM
Dots represent data for individual animal
[†] 6hr fasting on days -3 and 21, overnight fasting on days 15 and 28.

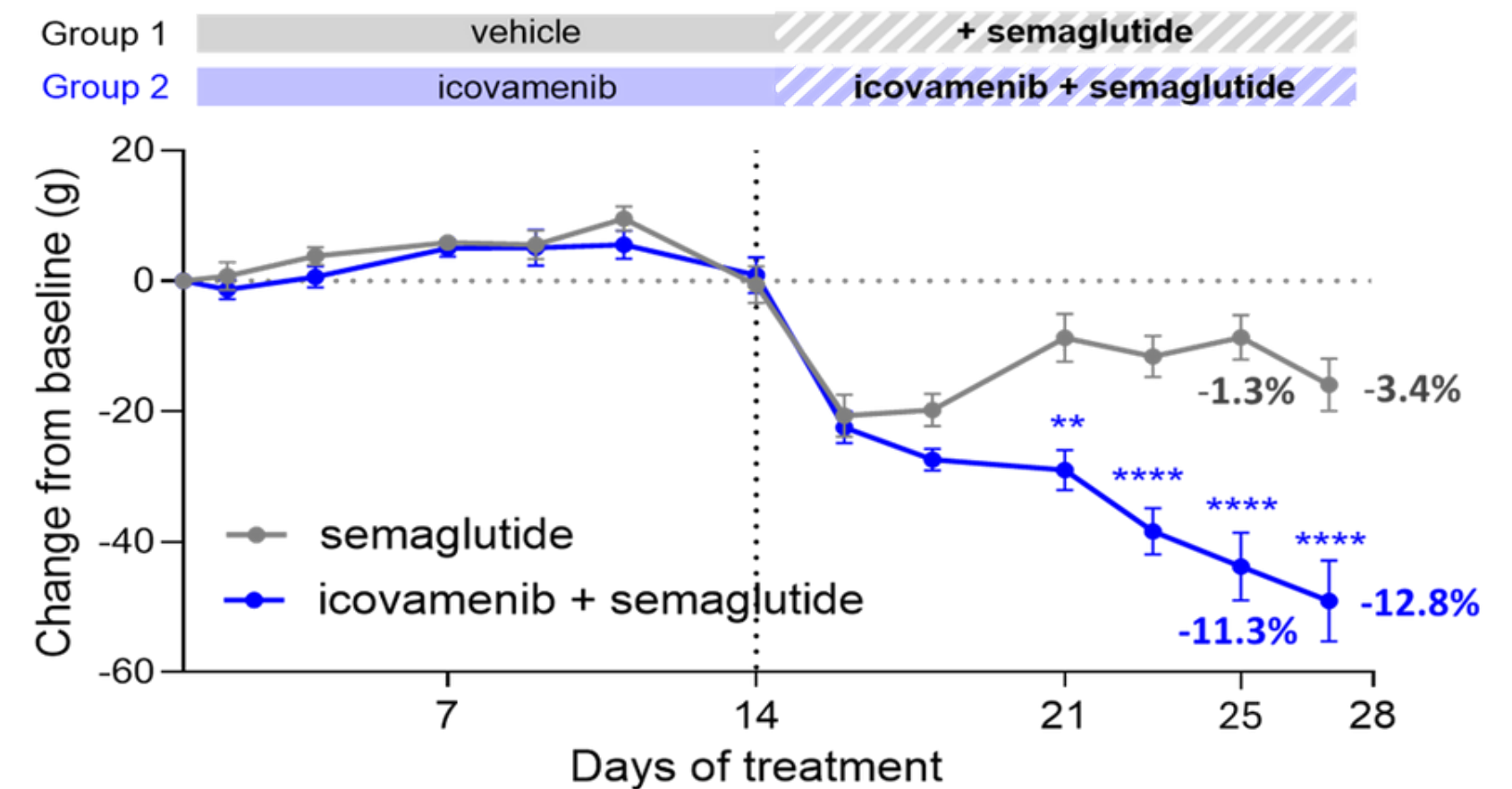
Combination Treatment of Icovamenib & Low-dose Semaglutide Reduces Food Intake & Body Weight

APPETITE SUPPRESSION



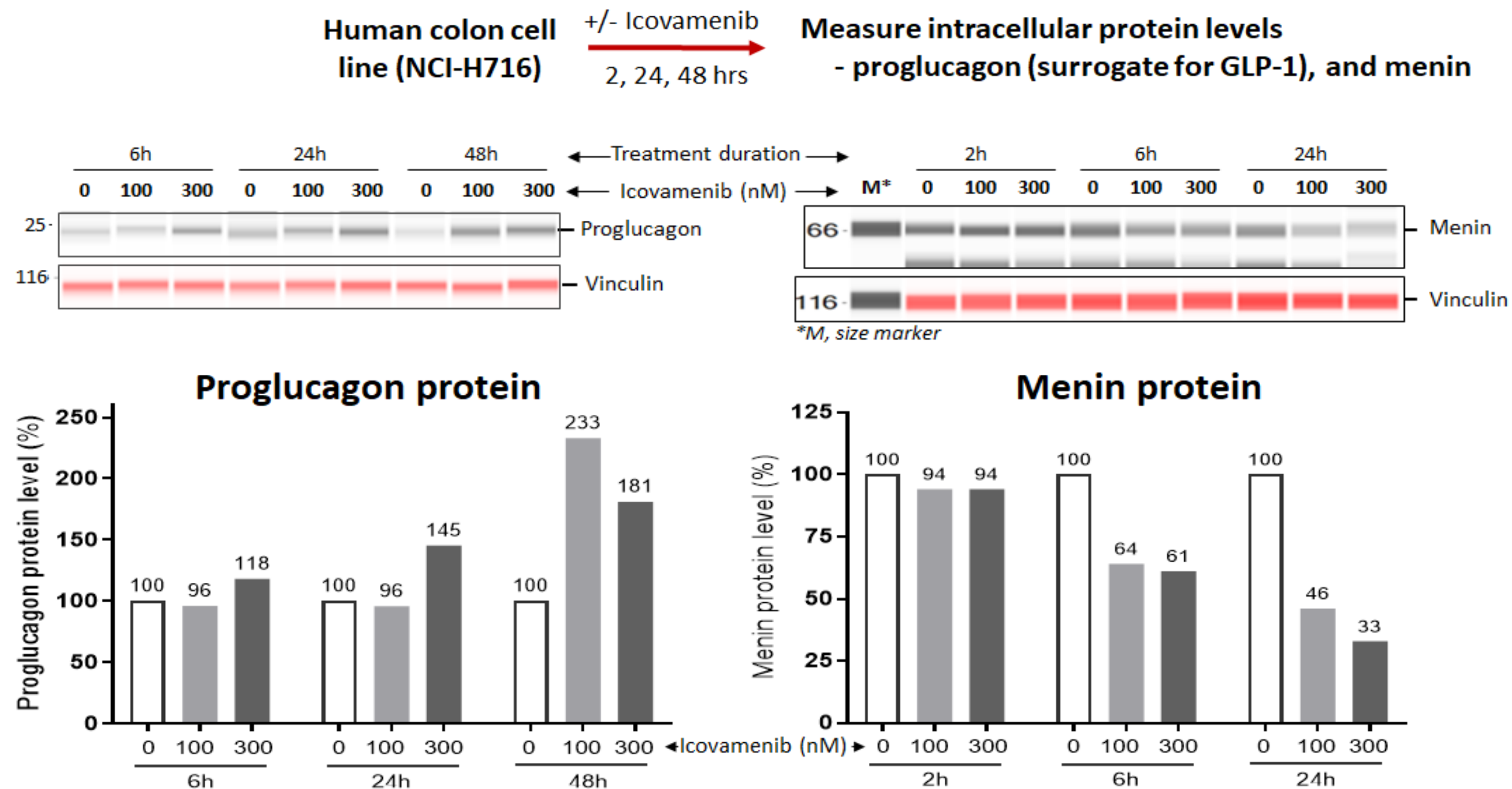
Somanath, et al. (ADA) Diabetes 2025;74 (Supplement_1):870-P

BODY WEIGHT REDUCTION



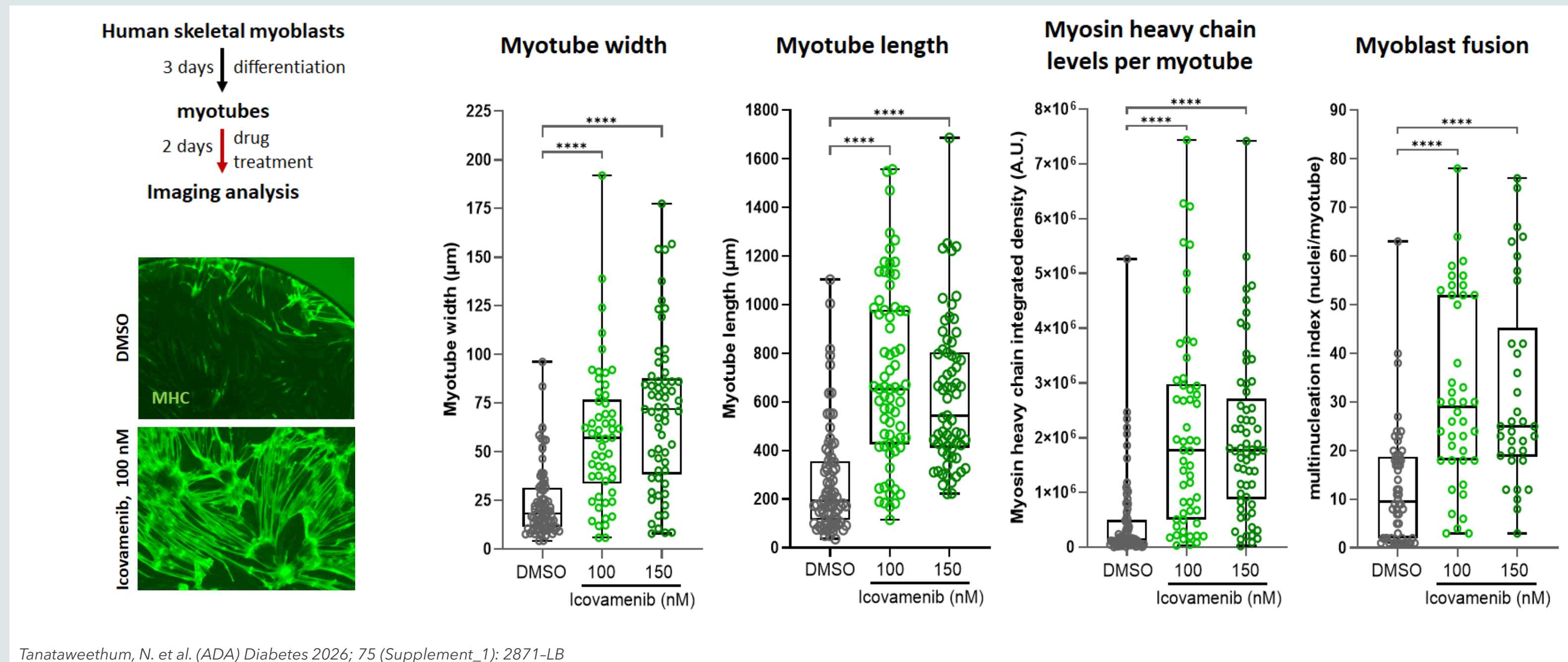
- ❑ SUPERIOR APPETITE SUPPRESSION WITH ABOUT 10% GREATER BODY WEIGHT REDUCTION THAN LOW-DOSE SEMAGLUTIDE ALONE
- ❑ THE OBSERVED BODY WEIGHT REDUCTION WAS PRIMARILY DUE TO FAT MASS LOSS WITH PRESERVATION OF LEAN MASS

Icovamenib enhanced intracellular proglucagon expression in a human colon L-cell model

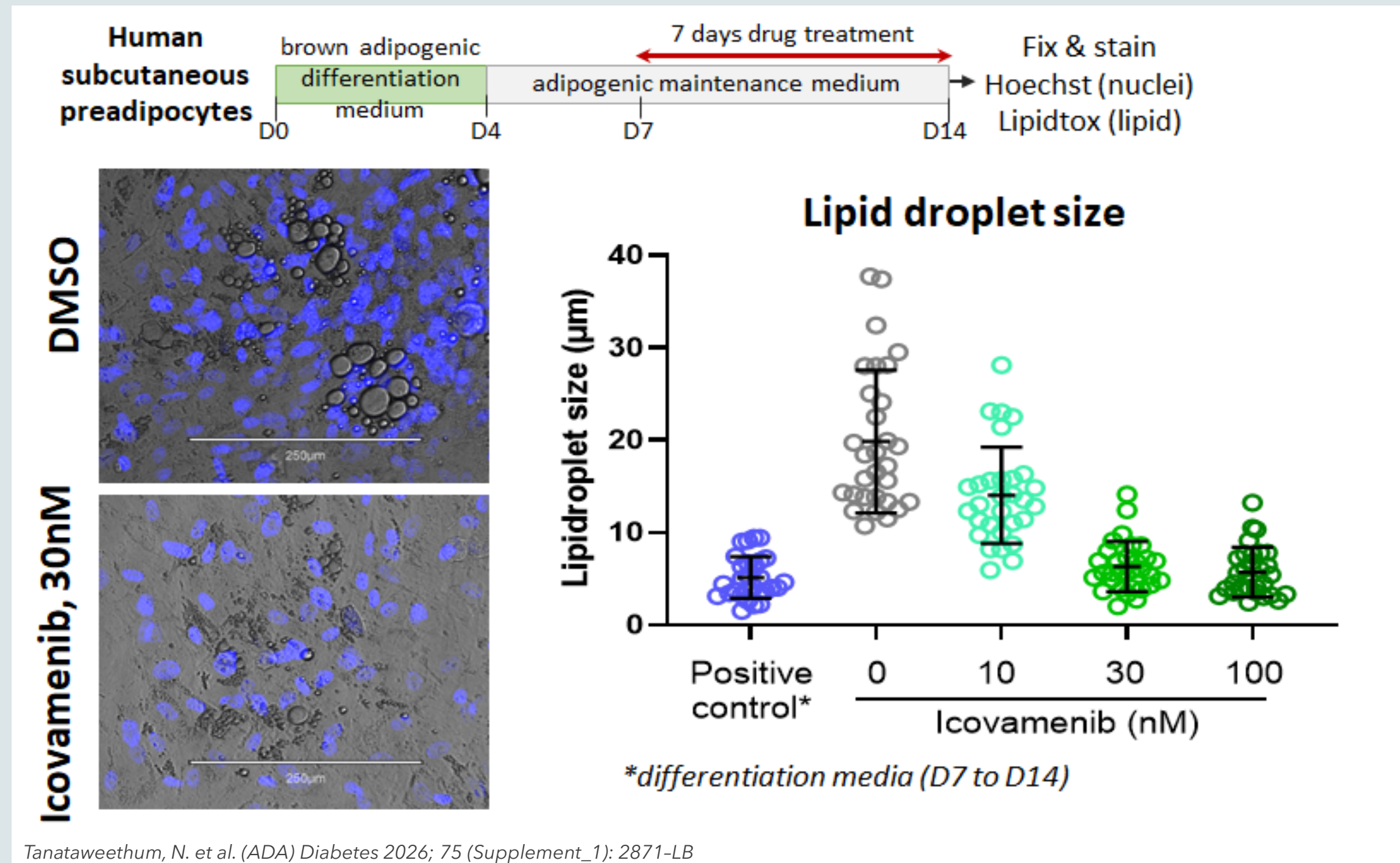


Tanataweethum, N. et al. (ADA) Diabetes 2026; 75 (Supplement_1): 2871-LB

Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes



Icovamenib promoted lipolysis in primary human adipocytes



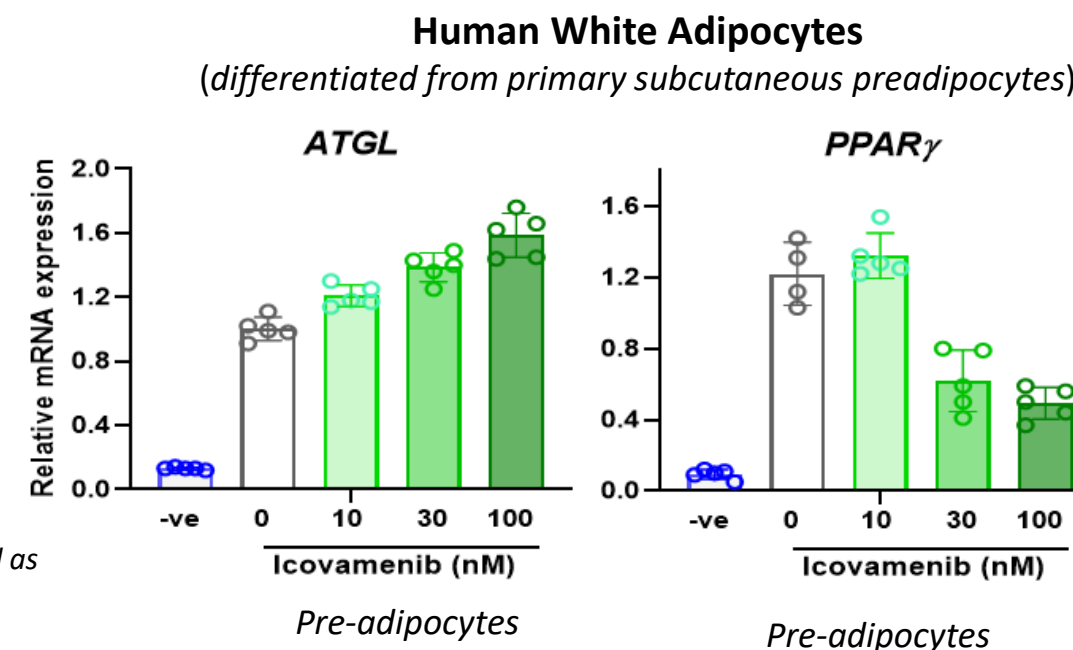
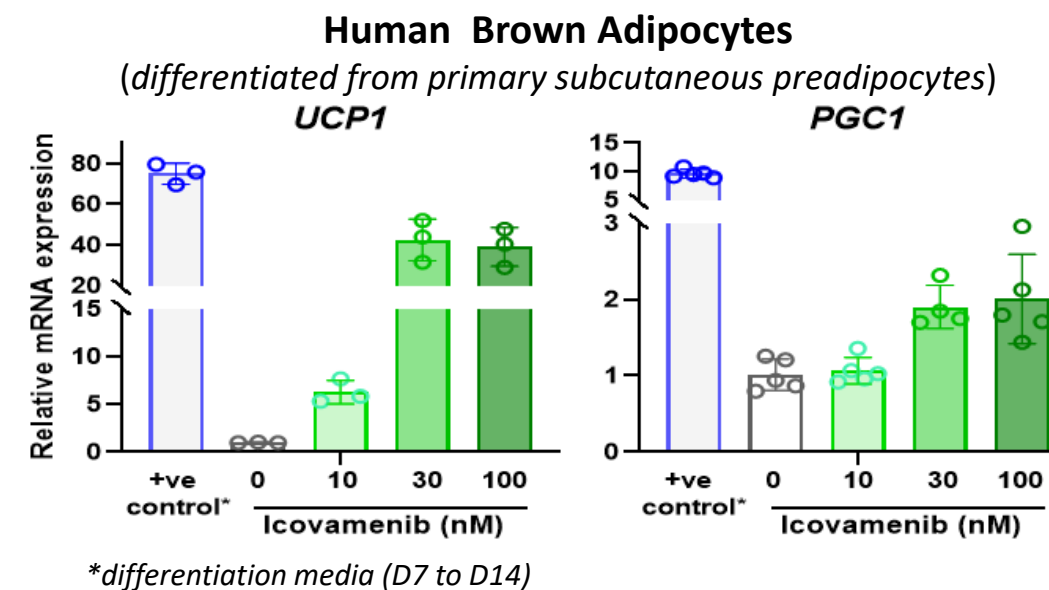
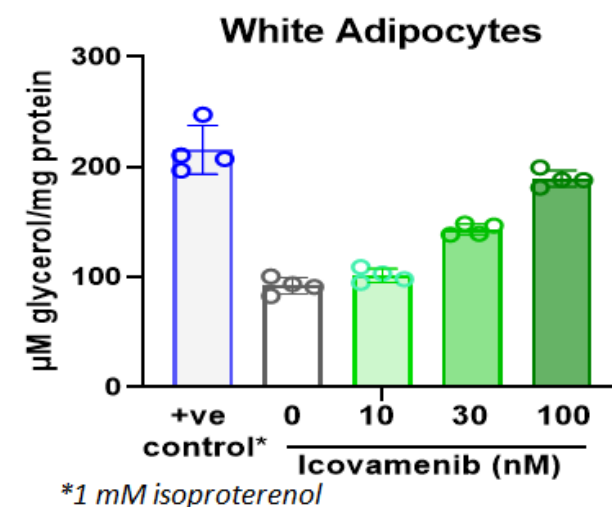
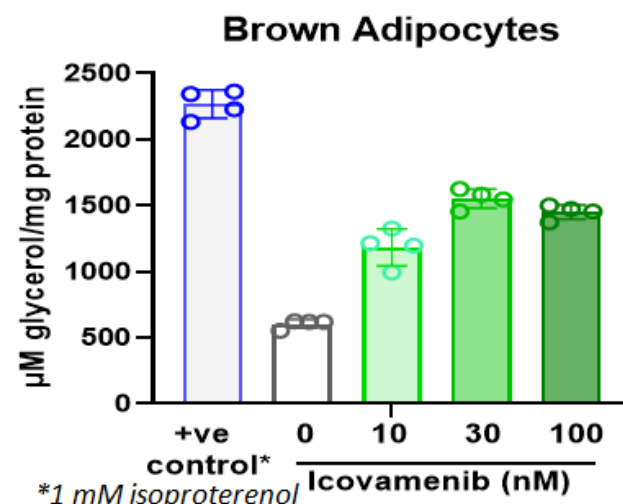
Tanataweethum, N. et al. (ADA) Diabetes 2026; 75 (Supplement_1): 2871-LB

Icovamenib promoted effects indicative of lipolysis and fat browning in primary human adipocytes

Enhanced Glycerol Release

Upregulation of thermogenic and lipolytic genes

Human subcutaneous preadipocytes differentiate to brown or white adipocytes 14 days → drug treatment 12 hrs → Measure glycerol in media & total protein (cells)



PPIA (Cyclophilin A) was used as housekeeping gene for normalization of data

A photograph of two scientists in a laboratory setting. One scientist, a man with dark hair and a beard, is wearing safety glasses and a white lab coat. He is looking down at a clipboard held by another scientist, whose back is to the camera. The background shows laboratory equipment and another person in the distance.

BMF-650

An investigational next-generation oral GLP-1 receptor agonist for obesity

- PRECLINICAL RESULTS and**
- CLINICAL OVERVIEW**

BMF-650: A potential best-in-class oral GLP-1 receptor agonist

THE CURRENT GLP-1 MARKET

Injectable GLP-1 RAs

-  Some patients averse to injections
-  Inconvenient
-  Injection site reactions

First Generation Oral GLP-1 RAs

-  High rates of GI side effects
-  Many do not reach maintenance dose
-  High discontinuation rates



Long, complex titration

Typically, 4-8+ steps, which can take 3-9 months depending on product



7 out of 10

Patients **discontinue** GLP-1 therapy due to side effects¹

BMF-650

Designed for sustainable weight loss management

Next Generation Oral GLP-1 RA



Oral administration

Convenience without injections



Designed for improved GI tolerability

Potential for better tolerability and adherence



Two-step titration

Faster path to maintenance dose



Built to improve persistence

Helping more patients stay on therapy



Chronic therapy in mind

Designed for sustainable weight loss management

THE PROJECTED IMPACT



Weight Loss Management

Better tolerability will lead to continuous weight management



Better Patient Experience

Simpler regimen and fewer GI side effects



Higher Persistence

More patients stay on therapy and reach therapeutic benefit



Long-term Health Benefits

Sustained weight management supports cardiometabolic health



BMF-650 is designed to be the oral GLP-1 RA patients can start, stay on, and have long term benefits from

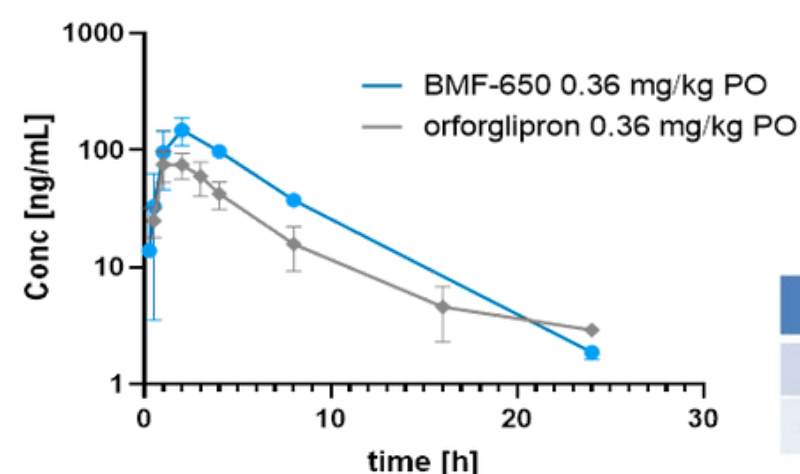
BMF-650 showed favorable in vitro on-target activity and off-target selectivity

Compound	GLP-1 human EC ₅₀		β -arrestin1 EC ₅₀	β -arrestin2 EC ₅₀
	25 °C	37 °C		
BMF-650	8.6 nM	2.6 nM	> 10 μ M	> 10 μ M
orforglipron	2.6 nM	0.1 nM	> 10 μ M	> 10 μ M

- Good potency on-target to achieve more efficient drug titration
- No off-target concerns from counter-screening assays

Pharmacokinetics of BMF-650 showed very good preclinical bioavailability with low inter-individual variability

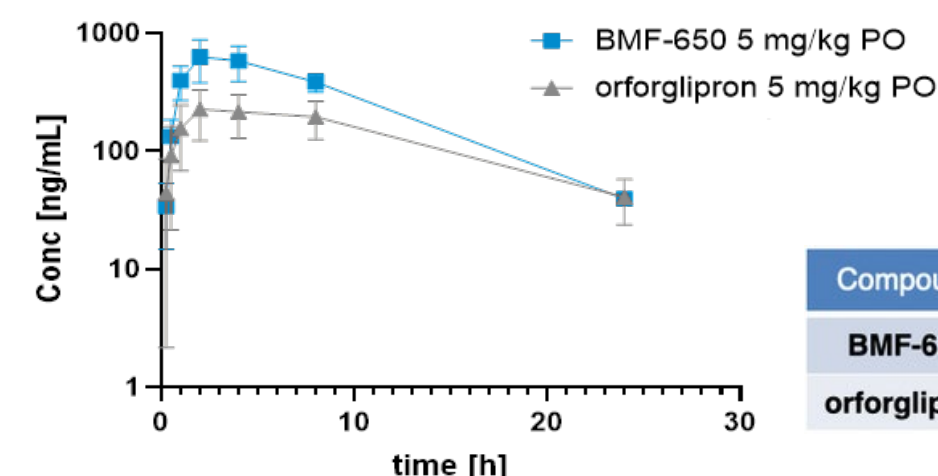
CYNOMOLGUS MONKEY PO PK



BMF-650 showed 2 - to 3-fold greater oral bioavailability in comparison to orforglipron

Compound	cyno PO	T _{1/2} (h)	%F
BMF-650	0.36 mg/kg	3.66	54.0
orforglipron	0.36 mg/kg	3.70	29.4

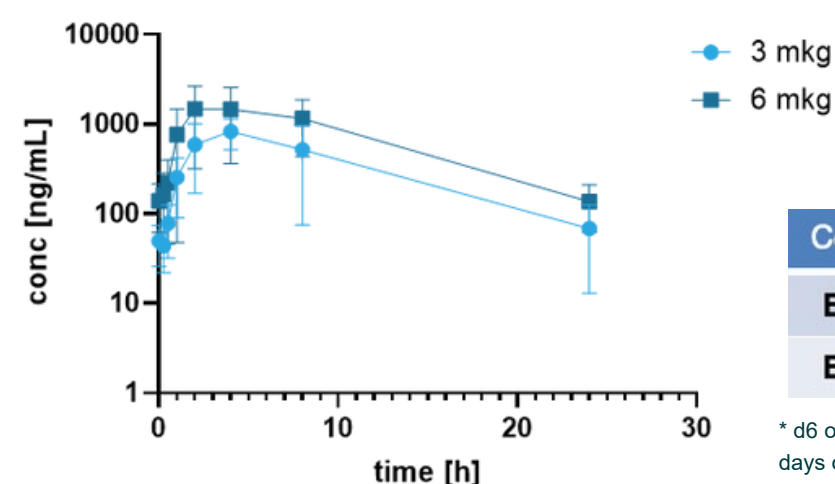
SPRAGUE-DAWLEY RAT PO PK



BMF-650 showed 2 - to 3-fold greater oral bioavailability in comparison to orforglipron

Compound	rat PO	T _{1/2} (h)	%F
BMF-650	5 mg/kg	5.14	32.6
orforglipron	5 mg/kg	7.44	11.2

CYNOMOLGUS MONKEY PK DAY 6 BMF -650



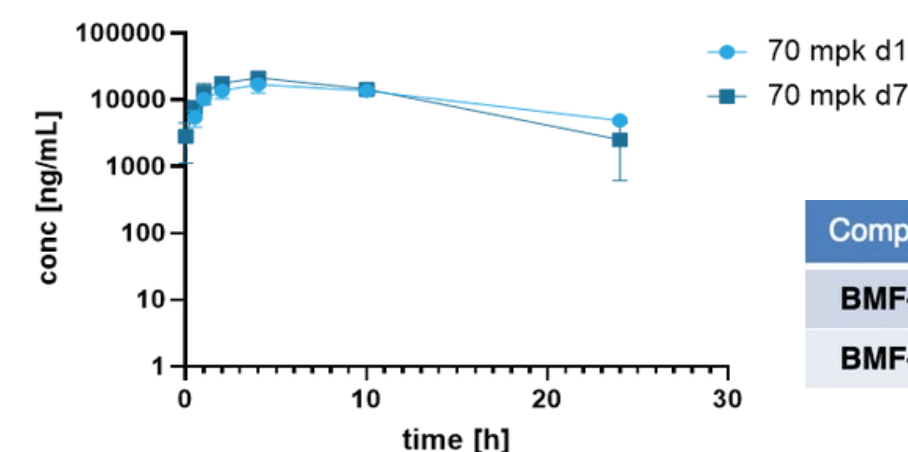
Dose Proportionate Exposure

Compound	cyno PO	Day	AUC**
BMF-650	3 mg/kg	6*	9,353
BMF-650	6 mg/kg	6#	19,918

* d6 of 6 days of daily PO dosing; d6# after 6 additional days of PO dosing at indicated dose level. ** hr*ng/mL

PO =per oral

SPRAGUE-DAWLEY RAT PK DAYS 1, 7 BMF -650



Continuous Exposure after multiple days

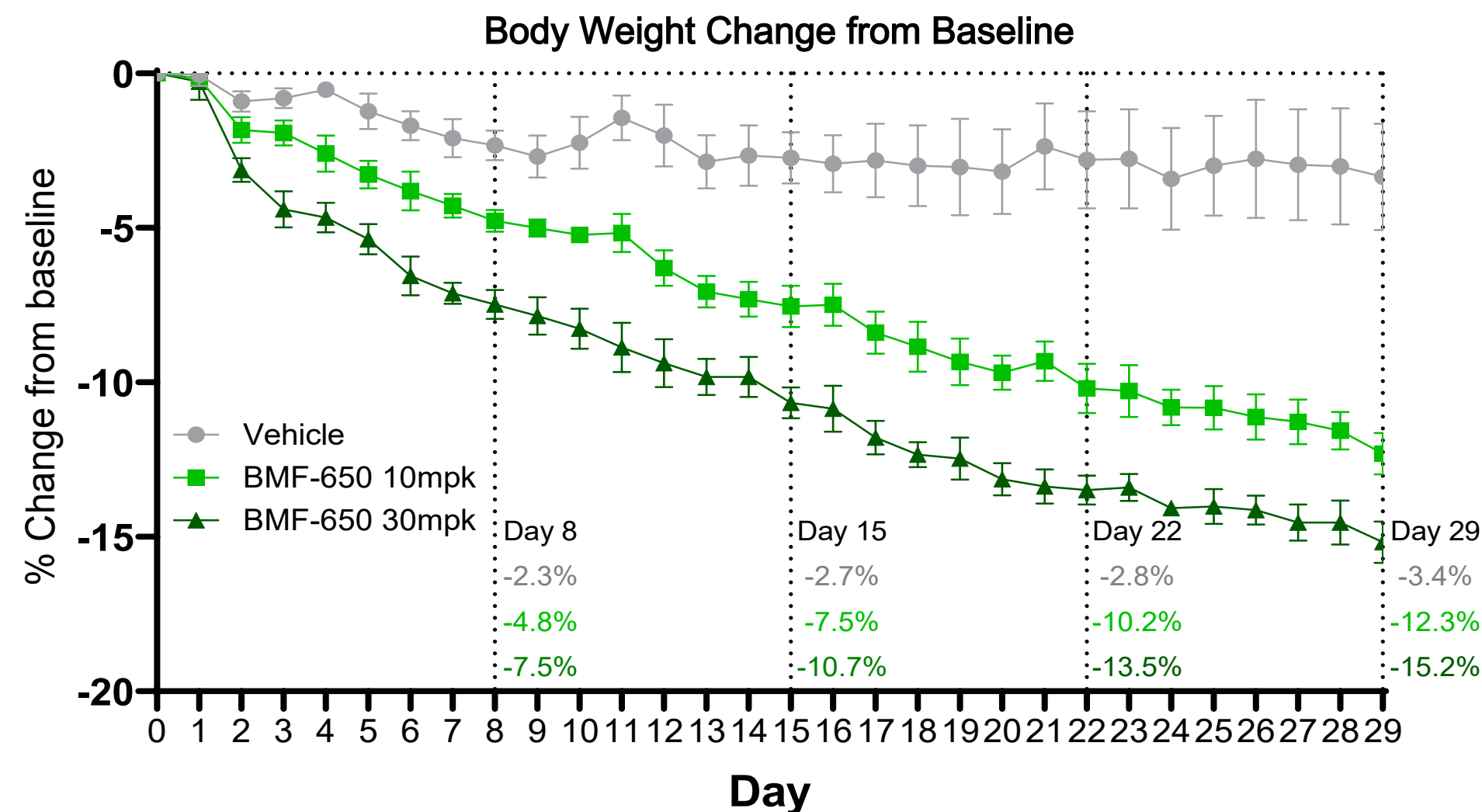
Compound	rat PO	day	AUC*
BMF-650	70 mg/kg	1	269,100
BMF-650	70 mg/kg	7	289,370



BMF-650 demonstrated robust, dose dependent weight loss in obese monkeys

Weight loss in cross-study comparison with CT-996 (Roche/Carmot), while not head-to-head appeared favorable

BMF-650 up to ~15% body weight reduction after 28-days



Wang, et al. Obesity 2025: 33 Sup 2 Poster #085

CT-996 body weight change

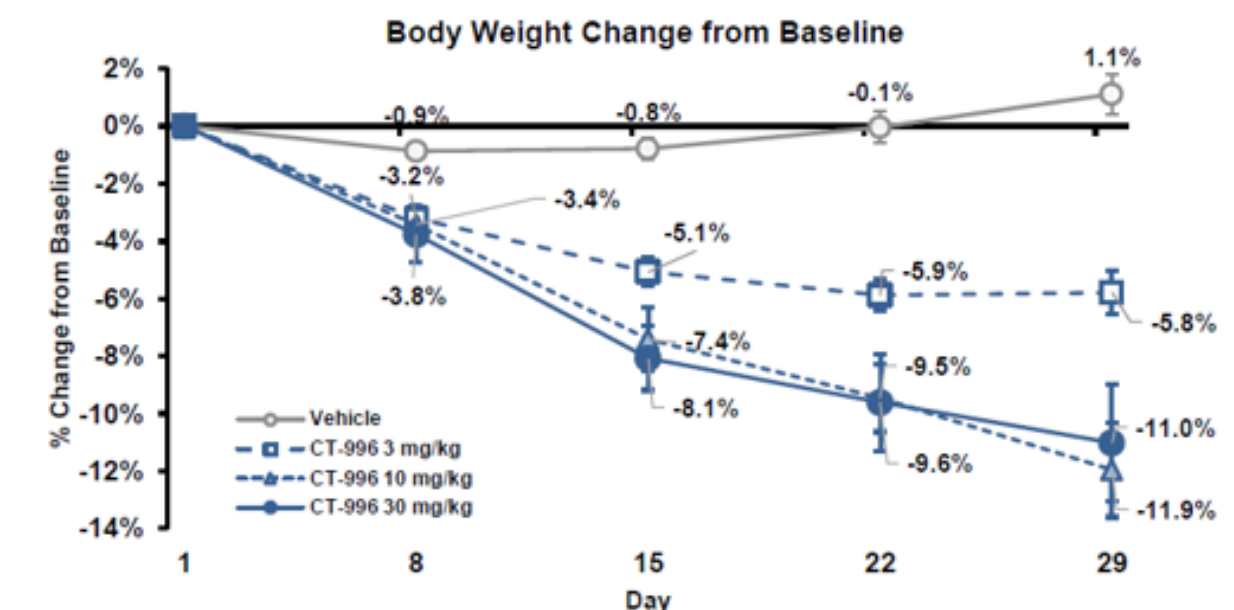


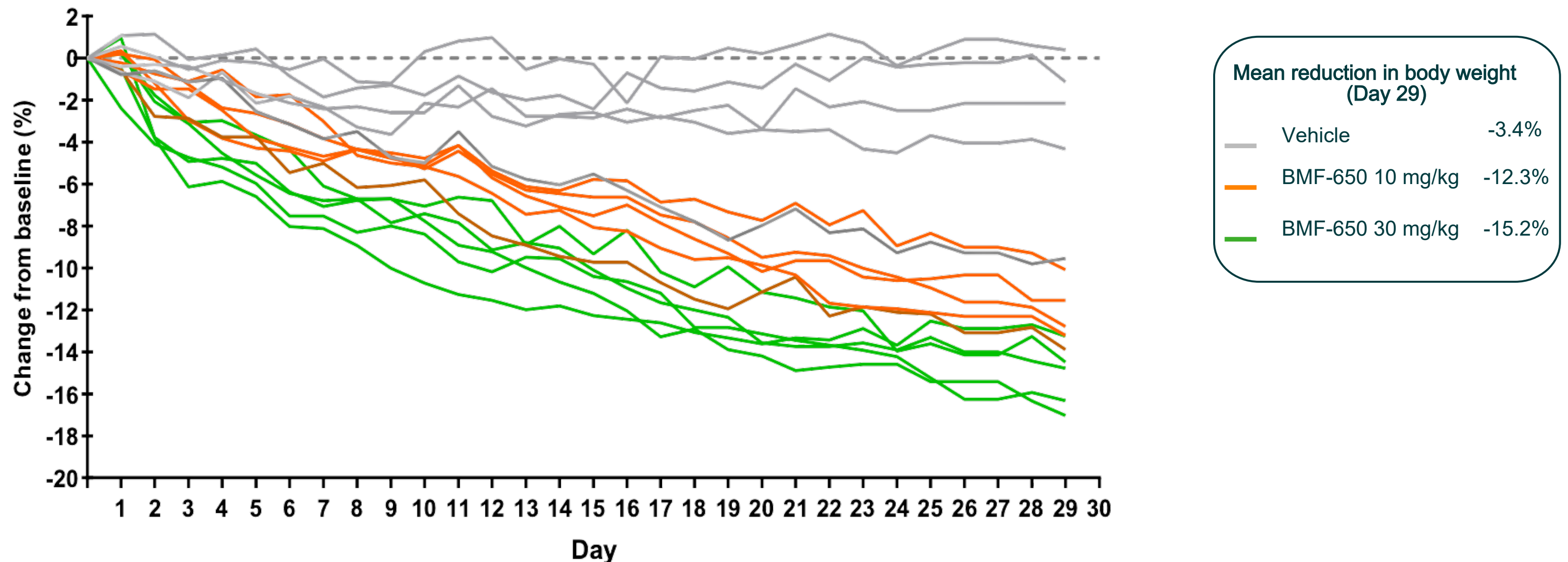
Figure 6. Effects of CT-996 on body weight in obese cynomolgus monkeys following once-daily oral administration. Weekly body weight percent change is represented as mean ($\pm$ SE) from baseline. N = 6/group.

Literature data; Carmot Therapeutics (now part of the Roche group), ADA 2024.



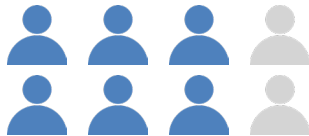
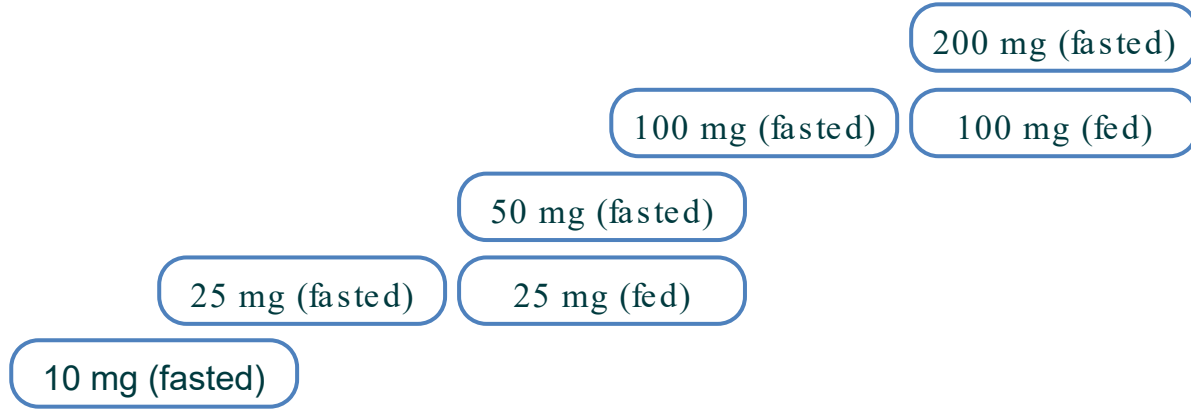
Oral BMF-650 demonstrates strong dose dependent body weight reduction in obese cynomolgus monkeys

BODY WEIGHT CHANGE (individual obese monkey)



A randomized, double-blind, placebo-controlled, Phase I study of an oral non-peptide GLP-1 receptor agonist

Part 1 is a single ascending dose (SAD) study and 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   Legend:  BMF-650 active drug  placebo		N=50 5 cohorts x  Week 1 → Week 2 → Week 3 → Week 4 <table><tr><th>COHORT</th><th></th></tr><tr><td>5</td><td>200 mg → 400 mg → 400 mg → 400 mg</td></tr><tr><td>4</td><td>75 mg → 200 mg → 400 mg → 400 mg</td></tr><tr><td>3</td><td>75 mg → 150 mg → 300 mg → 300 mg</td></tr><tr><td>2</td><td>50 mg → 100 mg → 200 mg → 200 mg</td></tr><tr><td>1</td><td>10 mg → 25 mg → 50 mg → 100 mg</td></tr></table>		COHORT		5	200 mg → 400 mg → 400 mg → 400 mg	4	75 mg → 200 mg → 400 mg → 400 mg	3	75 mg → 150 mg → 300 mg → 300 mg	2	50 mg → 100 mg → 200 mg → 200 mg	1	10 mg → 25 mg → 50 mg → 100 mg
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Oral BMF-650 generally well tolerated in 28-day preclinical animal study

Low rate of emesis events – mostly in one animal that decreased rapidly over time

WEEK	EMESIS (Events per 70 weekly dosing occurrences)
1	16%*
2	4.2%
3	4.2%
4	1.4%

*One monkey (#3) accounted for 8 of the 18 total events

SAFETY SUMMARY

- BMF-650 generally well tolerated with no elevations of AST or ALT
- With 420 dosing occurrences (280 active/140 placebo) there were only a total of 18 (6.4%) events of emesis in the active group
- Most events occurred early, with a marked decline after the first week
- Study was run without a titration scheme, once daily dosing over 28 days

Key milestones - overview



Icovamenib in Type 1 Diabetes

PLANNED T1D Investigator Sponsored Study | Phase 2 Study | n=40 | Enrollment anticipated to start 1Q 27

PLANNED T1D | Phase 2 Study | n=36 | Enrollment anticipated to start 1Q 27

T1D

FDA End of Phase 2 Meeting and Phase 3 Initiation



Icovamenib in Obesity

LEICESTER DIABETES CENTER in Obesity | Phase 2 Study | n=64 | Topline data anticipated: end of 27



Icovamenib in Type 2 Diabetes

- Insulin deficient
- GLP-1 uncontrolled

COVALENT-211 in insulin deficient T2D | Phase 2 Study | n=64 | Fully enrolled | Topline data anticipated: 1Q 27

COVALENT-212 in GLP-1 uncontrolled T2D | Phase 2 Study | n=60 | Start: 2Q 26 | Topline data anticipated: 2Q 27

T2D

FDA End of Phase 2 Meeting and Phase 3 Initiation

ICOVAMENIB

3Q 2026

4Q 2026

1Q 2027

2Q 2027

3Q 2027

4Q 2027

BMF-650



BMF-650

Obesity and weight management

GLP-131 in Obesity | Phase I | 28-day weight loss

Current Cash Position
Runway into 2Q 2027

BMF-650 Phase 2
Initiation depending on Phase I results

THANK YOU (NASDAQ: BMEA)

For questions or inquiries, please reach out to
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