

A photograph of two scientists in a laboratory. The scientist in the foreground is wearing a white lab coat with a 'biomea FUSION' logo on the chest and safety glasses. He is looking down at a piece of paper. The scientist in the background is also wearing a white lab coat and safety glasses, and is looking towards the first scientist. The background shows laboratory equipment and shelves.

Biomea Fusion Corporate Presentation

Q2 2026



Legal disclaimer & forward-looking statements



Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future business and financial performance of Biomea Fusion, Inc. (the "Company") and involve known and unknown risks, uncertainties, and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "potential" or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including any projections of financial information or profitability, including our expected cash runway, the initiation, timing and results of pending or future preclinical studies and clinical trials, the actual or potential actions of the U.S. Food and Drug Administration (FDA), the status and timing of ongoing research, development and corporate partnering activities, any statements about historical results that may suggest trends for the Company's business; any statements of the plans, strategies, and objectives of management for future operations and any statements of expectation or belief regarding future events, potential markets or market size, or technology developments. The Company has based these forward-looking statements on its current expectations, assumptions, estimates, and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company's control. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K filed with the Securities and Exchange Commission (the SEC), as well as discussions of potential risks, uncertainties, and other important factors in our other subsequent filings with the SEC. The forward-looking statements in this presentation are made only as of the date hereof. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company's expectations. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Transforming diabetes and obesity with novel oral medicines

Biomea funded through key clinical readouts for icovamenib and BMF-650 into 1Q of 2027

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

Clinical-stage company advancing two differentiated metabolic investigative programs

ICOVAMENIB

Potential first-in-class oral small molecule targeting menin - the control switch to beta cell restoration

Restores functional beta-cell mass and improve endogenous insulin production in both type 1 and type 2 diabetes



Critical unmet need: In **type 1 diabetes**, there are no approved therapies that directly restore or preserve beta-cell function, and patients rely on lifelong insulin therapy.¹ In **type 2 diabetes**, approximately 1/3 of all diabetes patients fail standard of care and progress to insulin dependence driving complications such as kidney disease, nerve damage, vision loss, and cardiovascular issues.²⁻⁴ In **obesity** and overweight individuals, current therapies have substantially improved weight loss, but may also result in loss of lean muscle mass, raising concerns about preservation of physical function and quality of life.⁵

BMF-650

Next-generation oral GLP-1 receptor agonist

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

Critical unmet need: Real world evidence indicates that up to 70% of patients on currently available GLP-1 based therapies drop out within the first year due to gastrointestinal adverse events and other tolerability considerations.⁴

Biomea pipeline

Biomea Fusion retains full worldwide rights across all programs and is currently funded through major catalysts into 1Q 2027

PROGRAM	INDICATION	PHASE I	PHASE II	PHASE III	UPCOMING MILESTONES
ICOVAMENIB Potential first-in-class oral menin inhibitor	Type 2 diabetes Patients with insulin deficiency (~7M U.S. Patients) ¹		COVALENT-211 (study enrolling)		Phase II 26-week data (primary endpoint) anticipated 4Q 2026
	Type 2 diabetes Patients not controlled on GLP-1 based therapies (15-45% U.S. Patients on GLP-1RA) ^{2,3}		COVALENT-212 (study enrolling)		Phase II 26-week data (primary endpoint) anticipated 4Q 2026
ICOVAMENIB with low dose Semaglutide	Obesity/Overweight (>190M U.S. Patients) ⁵ Sponsored by Leicester Diabetes Center		OPAL Study		Phase II initiation anticipated in 2H 2026
BMF-650 Potential best-in-class oral GLP-1 RA	Obesity (>100M U.S. Patients) ⁵		GLP-131 (study enrolling)		Phase I 28-day weight reduction data anticipated in 3Q 2026

1. International Diabetes Federation. IDF Diabetes Atlas www.diabetesatlas.org (Based on company calculations)

2. NHANES analyses of glycemic control among U.S. adults with diabetes (JAMA; Diabetes Care);

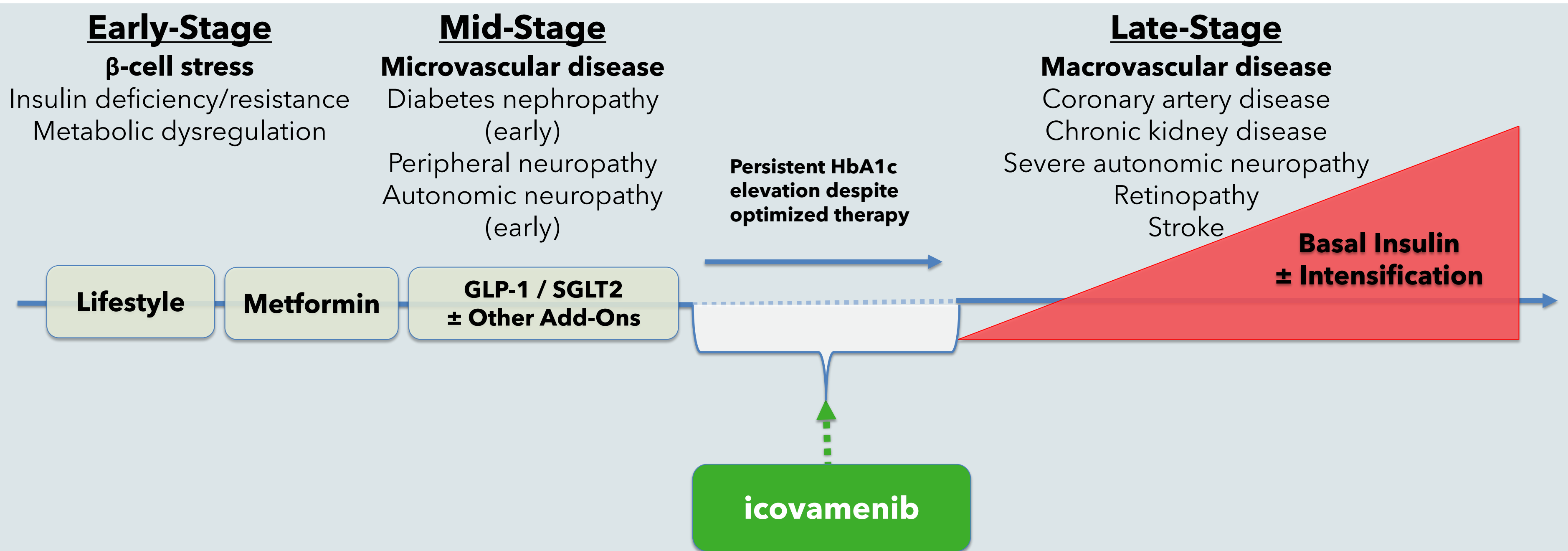
3. SUSTAIN, AWARD, and SURPASS clinical trial programs for GLP-1 receptor agonists

4. Mayer-Davis et al., NEJM / CDC updates

5. National Center for Health Statistics August 2023. [Accessed June 10, 2026](#)

Icovamenib aims to delay need for insulin therapy

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*

1.NHANES analyses of glycemic control among U.S. adults with diabetes (JAMA; Diabetes Care); 2.SUSTAIN, AWARD, and SURPASS clinical trial programs for GLP-1 receptor agonists

Diabetes patients are poorly controlled with 1:3 U.S. diabetes patients estimated to require insulin

Icovamenib targets menin to allow for beta-cell restoration which may delay or prevent onset of end-stage diabetes



80%

of people with diabetes will die from the disease¹

The end-stage in the evolution of diabetes is insulin-dependence, which drives complications such as kidney disease, nerve damage, vision loss, and cardiovascular issues.

12-14 years

of life lost from diabetes²

Diabetes today remains poorly controlled in 50% of patients treated with standard of care agents³ The burden to the healthcare system is immense.

60+

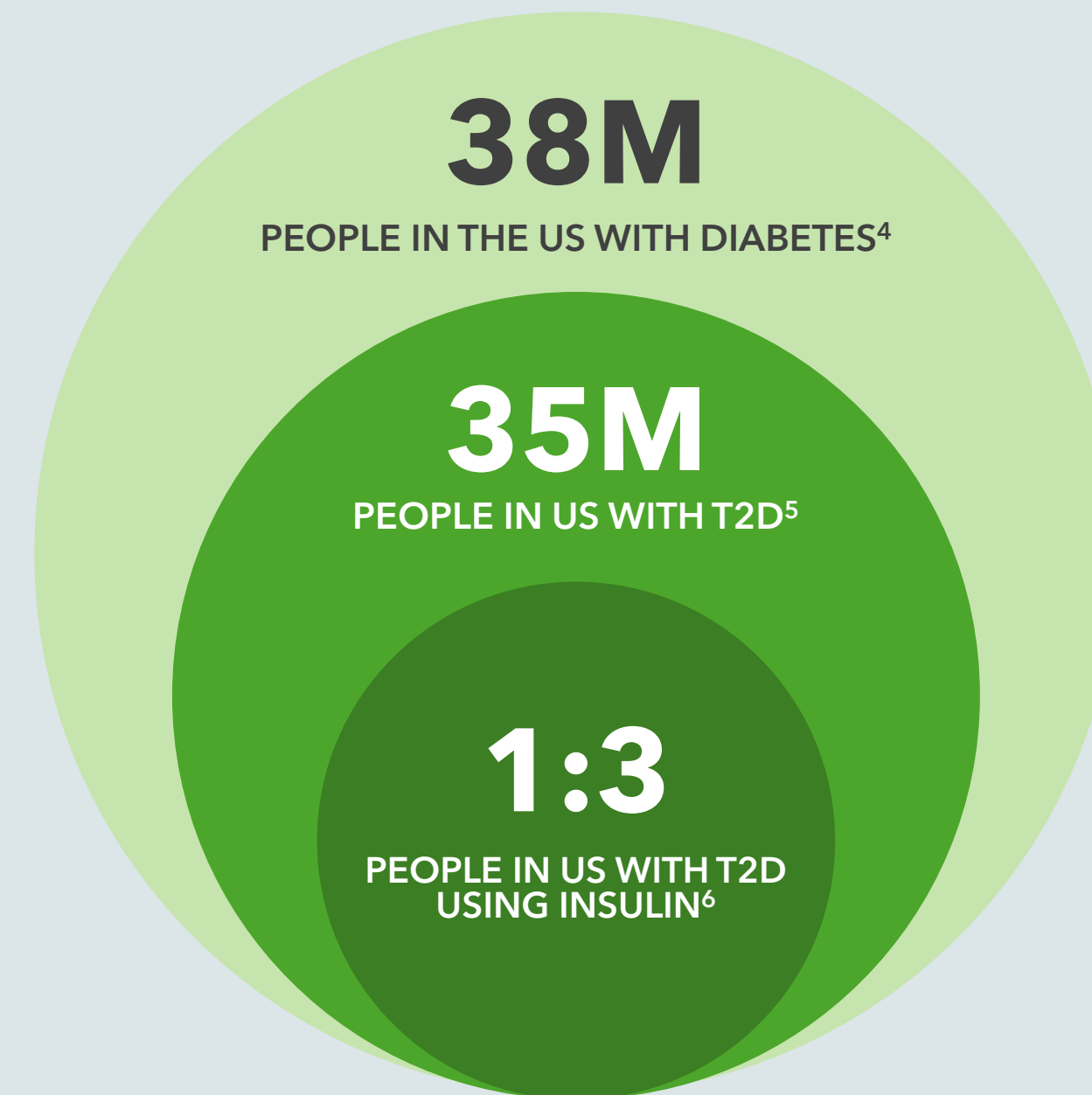
Approved therapies are not adequately resolving the growing problem of type 2 diabetes.

No current therapy restores beta-cell function

1. Tabish Int J Health Sci. 2007 Jul;1(2):V-VIII

2. National library of Medicine 1(2); 2007 Jul PMC3068646

3. Zohu Lancet 2024; 404:2077-93



4. CDC, Natl. Diabetes Stat. Rep., 2022

5. ADA, Standards of Care in Diabetes, Diabetes Care, 2024

6. Li J Diabetes Complications 2012;26(1):17-22

Type 1 diabetes at-a-glance

T1D is caused by autoimmune destruction of insulin-producing pancreatic islet beta cells



~50%

Annual loss of beta cell capacity¹

Patients with symptomatic T1D (Stage 3) typically lose yearly ~50% of their beta cell capacity over the first 7 years



~9.5M

People live with T1D globally in 2025²

~1.8M in the U.S.³



~513K

New diagnoses T1D per year globally in 2025²

~64K new diagnoses/year in the U.S.⁴

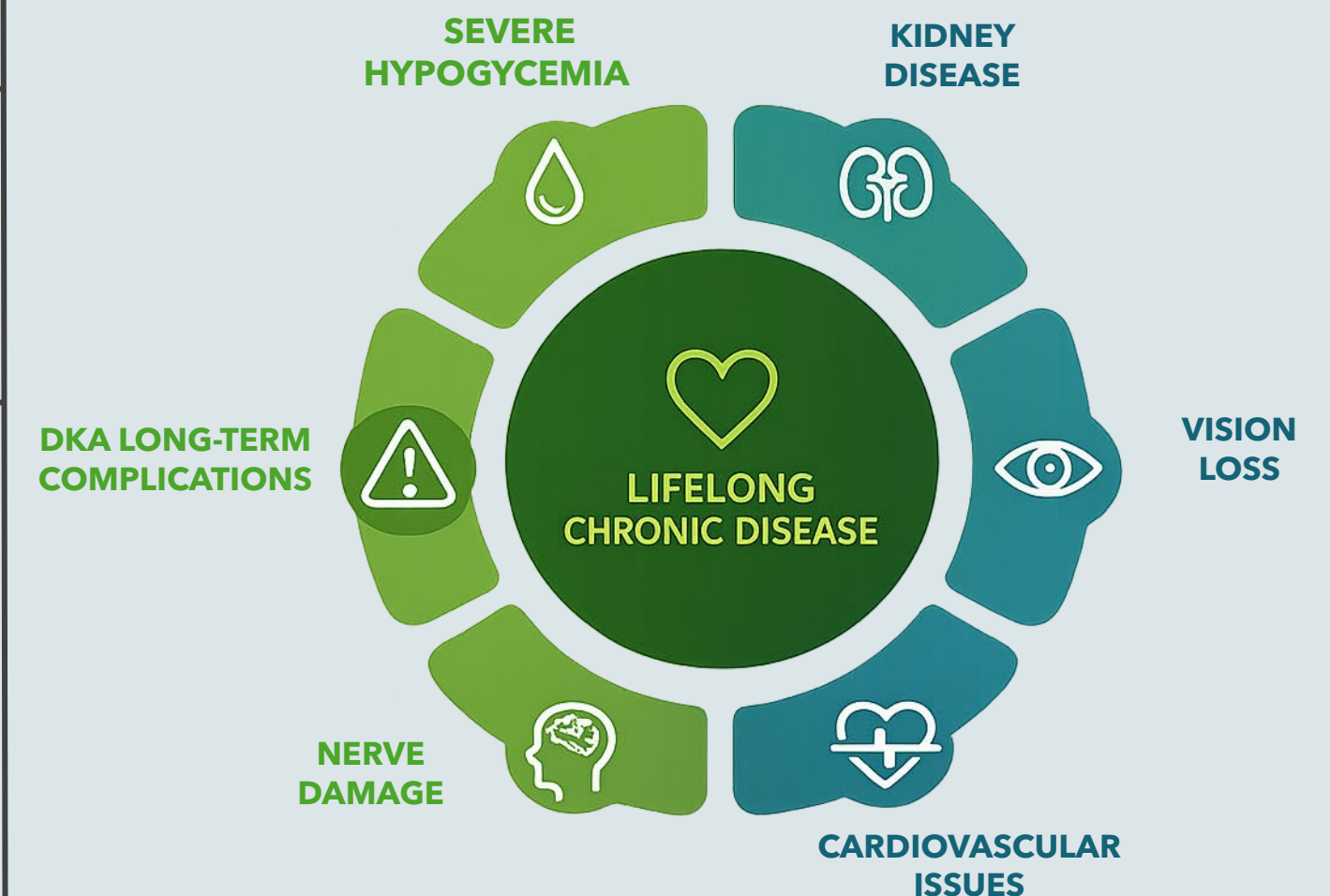


0

Approved therapies for Stage 3⁵

There are no approved therapies other than exogenous insulin that address the dysglycemia associated with the progressive decline of C-peptide in Stage 3

T1D is considered a lifelong chronic disease and carries substantial acute risk



1. Diabetes Care. 2018 Jun 7;41(7):1486-1492

2. Ogle, et al. Diabetes Research and Clinical Practice 2025, 225, 112277

3. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2023

4. Mayer-Davis et al., NEJM / CDC updates

5. Front. Endocrinol., 05 November 2024

6. American Diabetes Association. Standards of Care in Diabetes-2025

Obesity remains inadequately controlled despite GLP-1 therapies, with millions discontinuing or failing treatment



Obesity is a chronic, progressive disease associated with cardiometabolic complications and increased mortality

42%

Of U.S. adults have obesity¹

Obesity is a chronic disease characterized by excess adiposity and metabolic dysfunction. It is strongly associated with type 2 diabetes, cardiovascular disease, fatty liver disease, and certain cancers.

50-70%

Of patients discontinue GLP-1 therapy within 12 months²

Real-world data show high discontinuation rates due to GI side effects, cost, access barriers, and tolerability challenges. Weight regain is common after discontinuation.

>60%

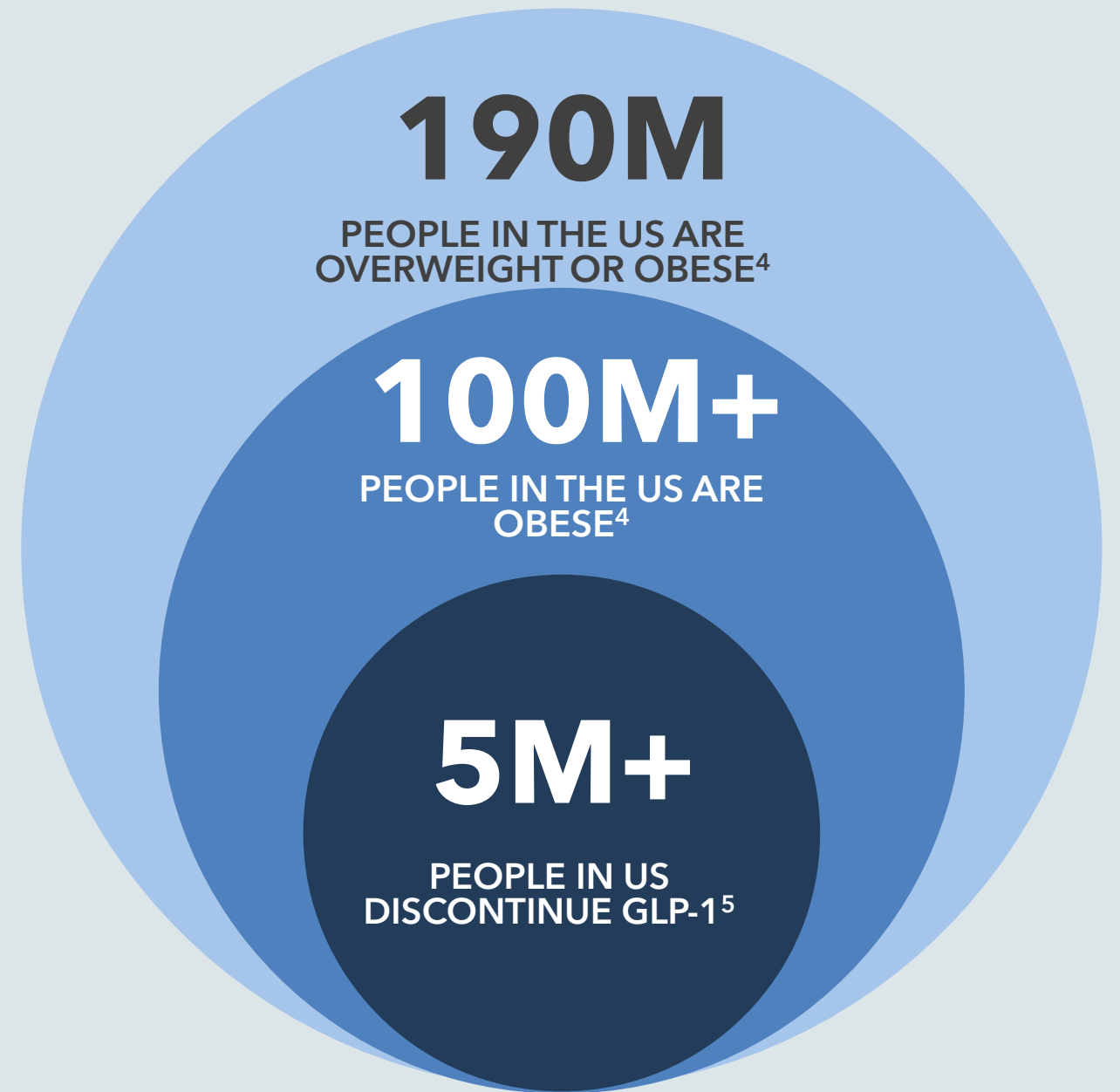
of adults with obesity have at least one obesity-related comorbidity³

Despite lifestyle interventions and approved pharmacotherapies, many patients discontinue treatment or fail to achieve sustained weight loss. Long-term disease modification remains an unmet need.

1. CDC Adult Obesity Facts, 2023

2. Real-world GLP-1 discontinuation analyses (claims database studies 2023-2024)

3. STEP and SURMOUNT program responder analyses



4. CDC National Health and Nutrition Examination Survey

5. IQVIA prescription data

ICOVAMENIB

Potential first-in-class menin inhibitor for 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}"

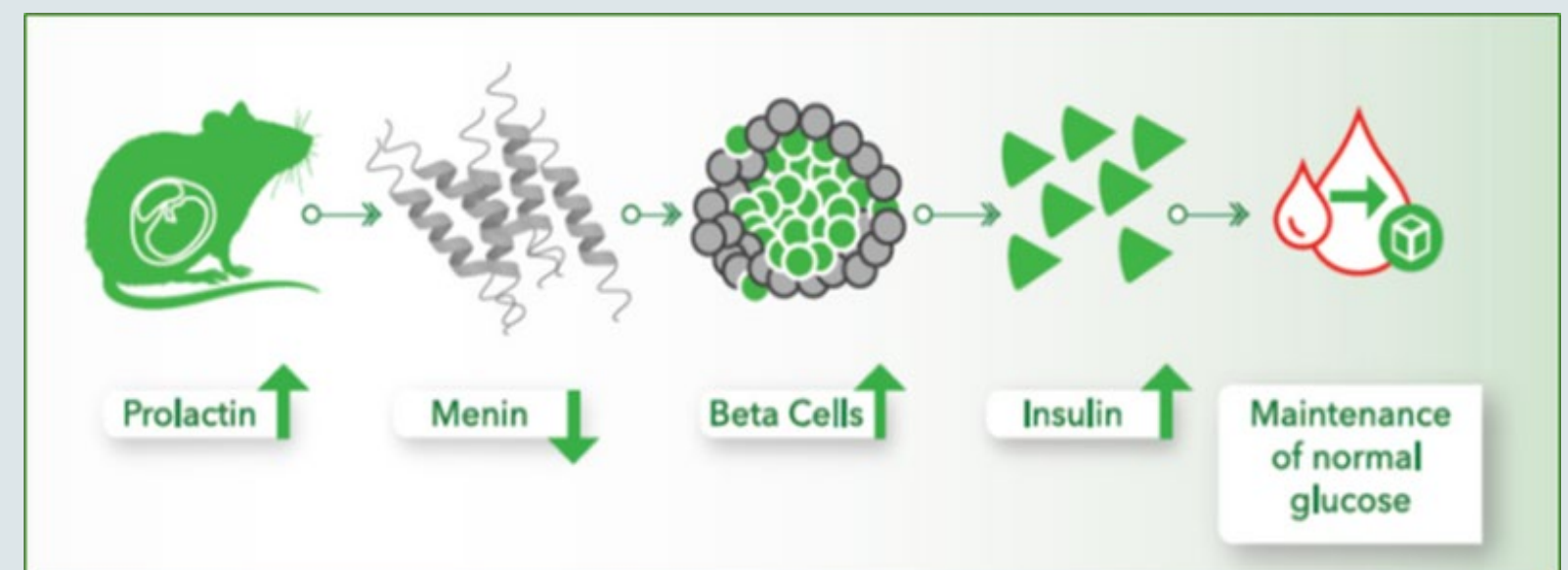
- Icovamenib has been shown to directly inhibit menin, aiming to pharmacologically replicate a naturally occurring, validated biologic process



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†}

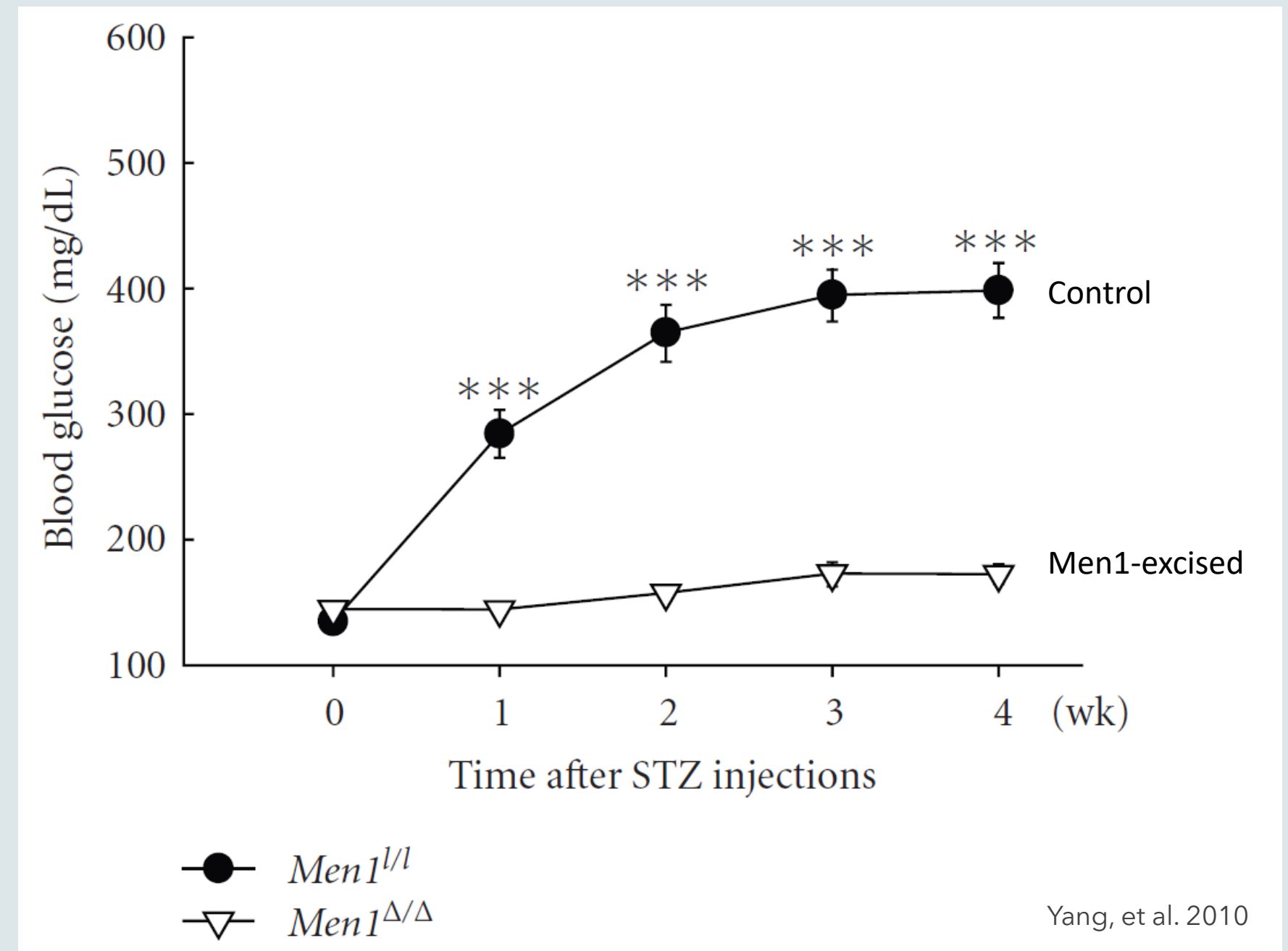
Karnik SK, et al. Science. 2007;318:806-809



Potential for Menin Inhibition Demonstrated by Beta Cell Ablation Diabetes Model in MEN1-Excised Mice

MEN1 Excision Prevents Development of STZ-induced Hyperglycemia

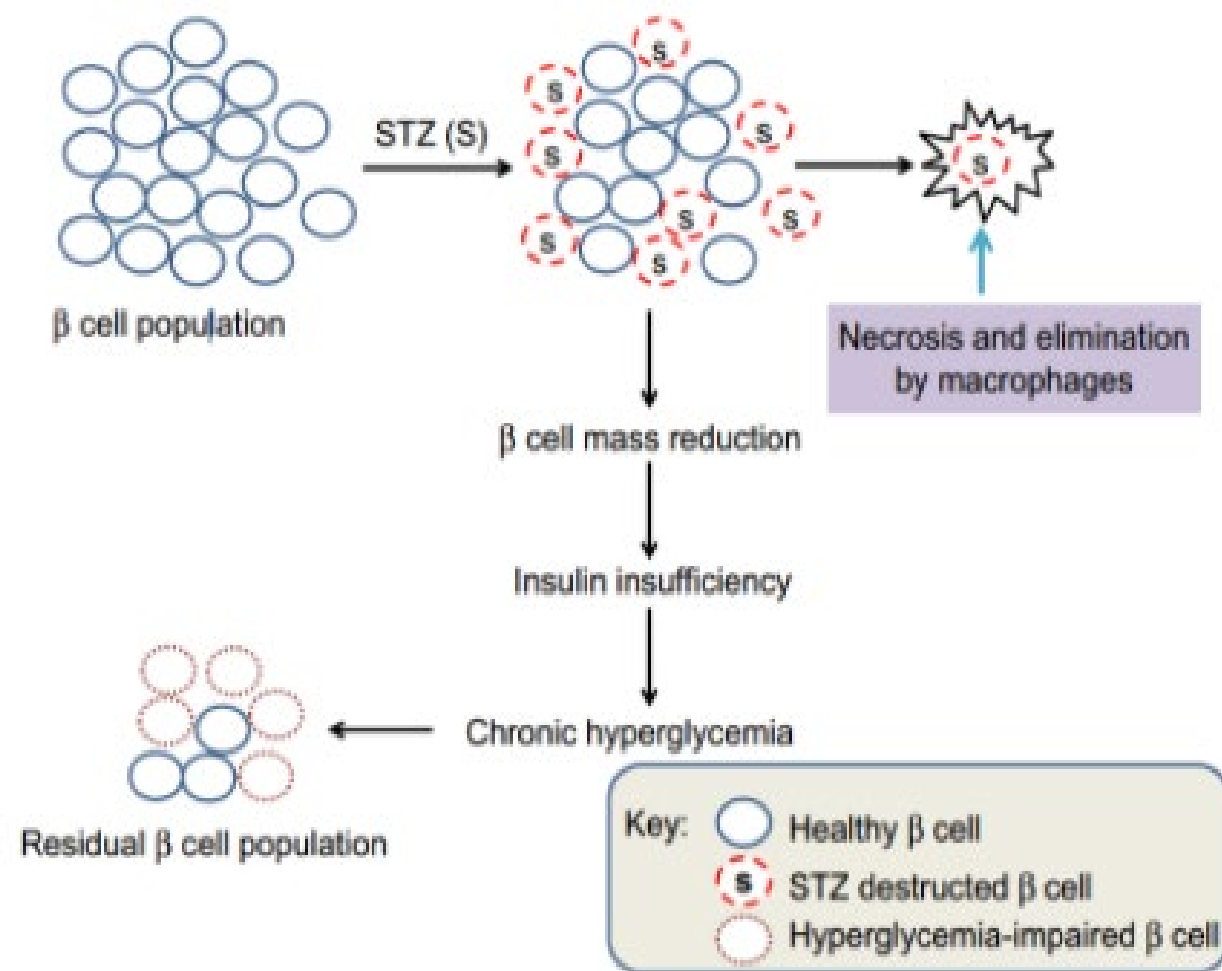
- Menin is a scaffold protein, encoded by the gene MEN1, that has been recognized for its role in Type 2 Diabetes Mellitus (T2DM) as a key regulator of beta-cell proliferation.
- Men1 knockout mice demonstrate increased beta-cell mass generation (Yang et al., 2010) and menin inhibition has previously 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

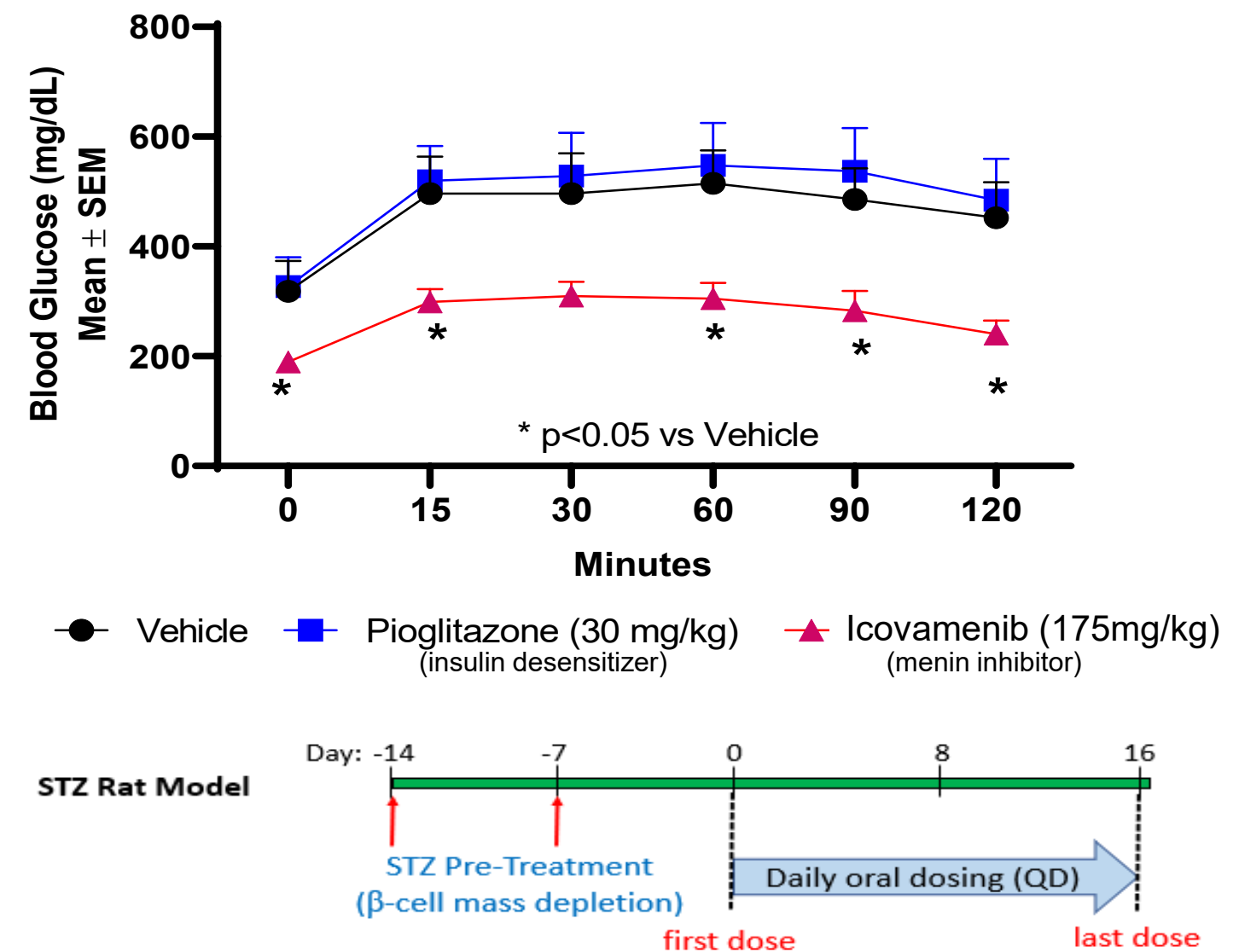
Icovamenib significantly reduced blood glucose in STZ rats (a model in which only insulin decreases blood glucose levels)

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

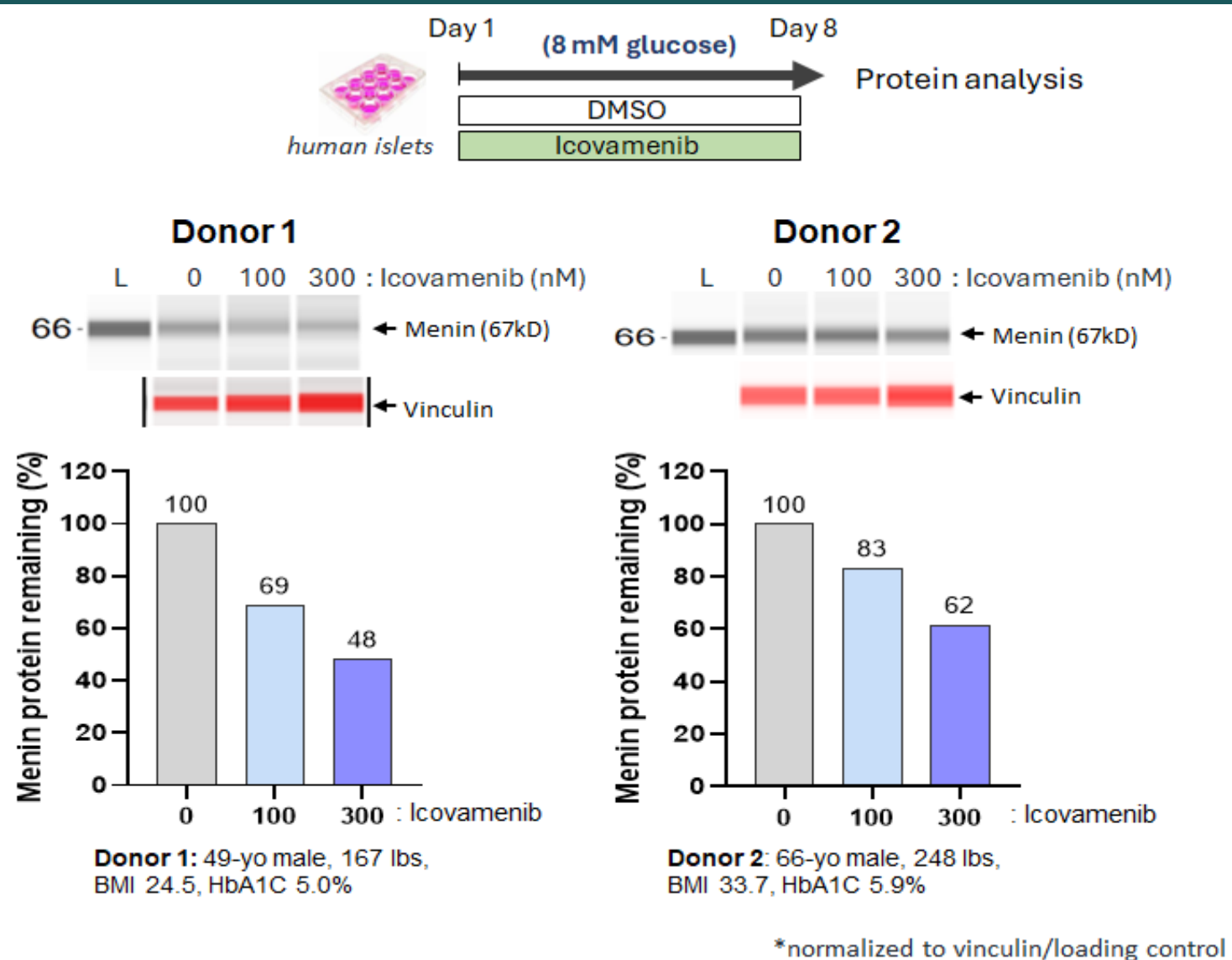
ORAL GLUCOSE TOLERANCE TEST (DAY 17)



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

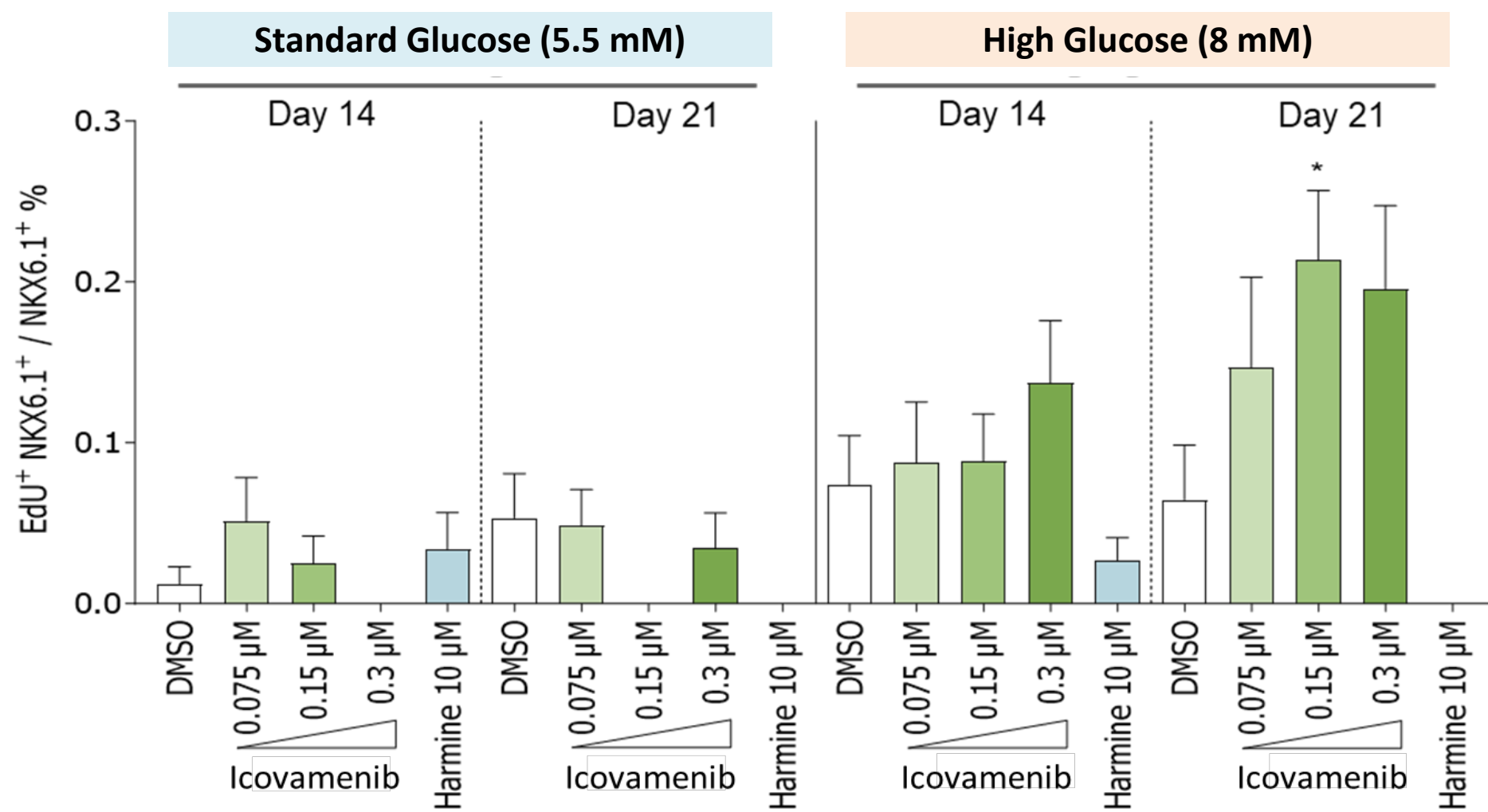
Icovamenib downregulated menin protein levels & promoted beta cell proliferation in ex vivo human islet cultures

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

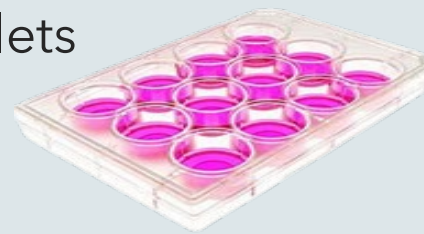


Frias, et al. (WCIRDC) Metabolism, Vol153, Supplement, 2023, #88

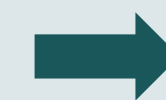
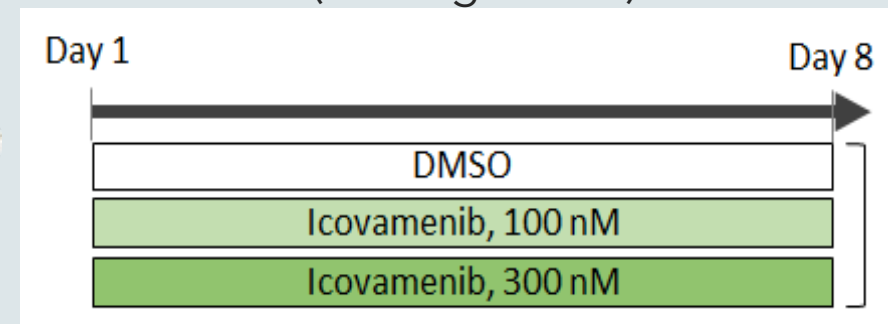
Icovamenib enhanced GLP-1 receptor & insulin expression in human islets



Cadaver derived human islets

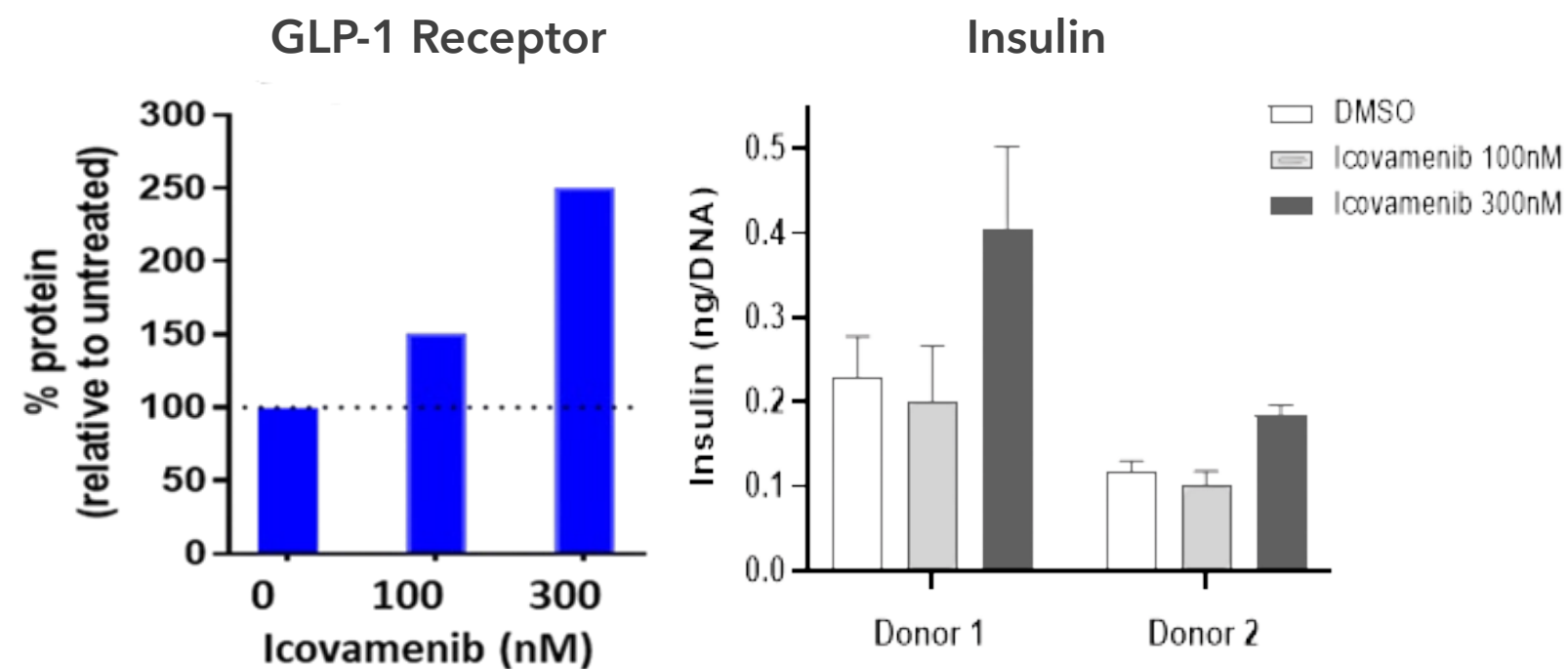


Culture 7 days under glucotox conditions (8mM glucose)

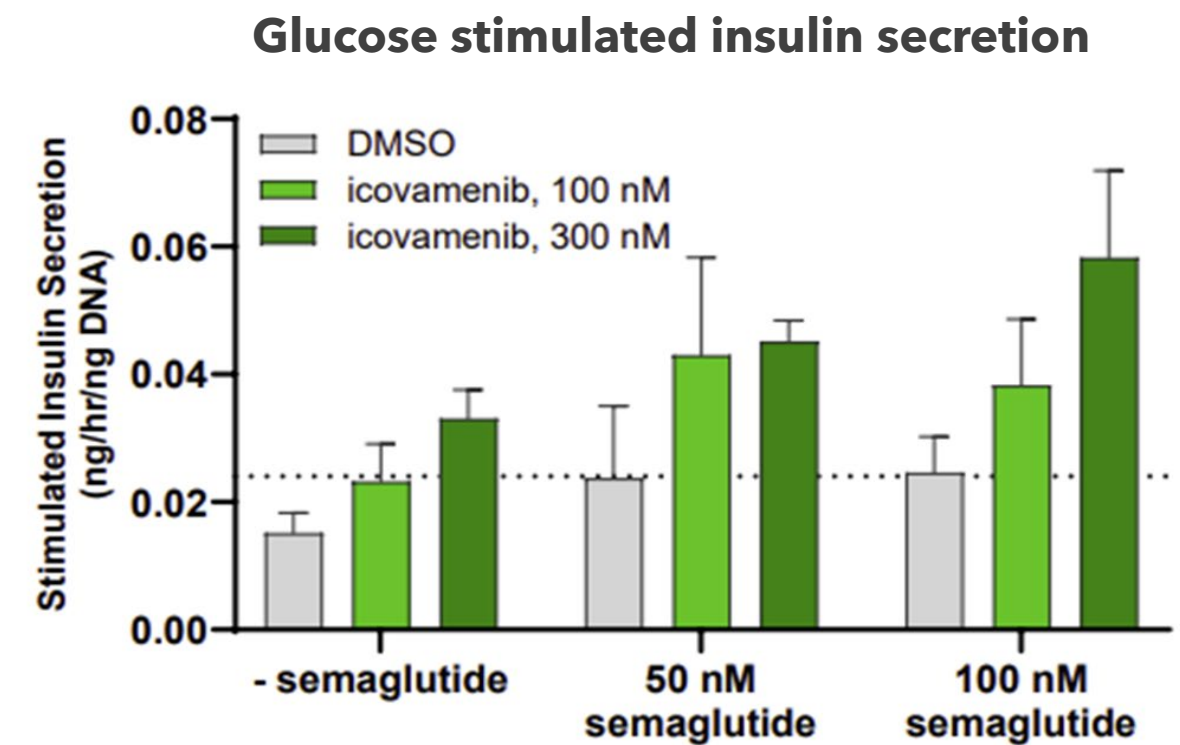


- Gene expression & Protein analysis
- Glucose Stimulated Insulin Secretion +/- Semaglutide

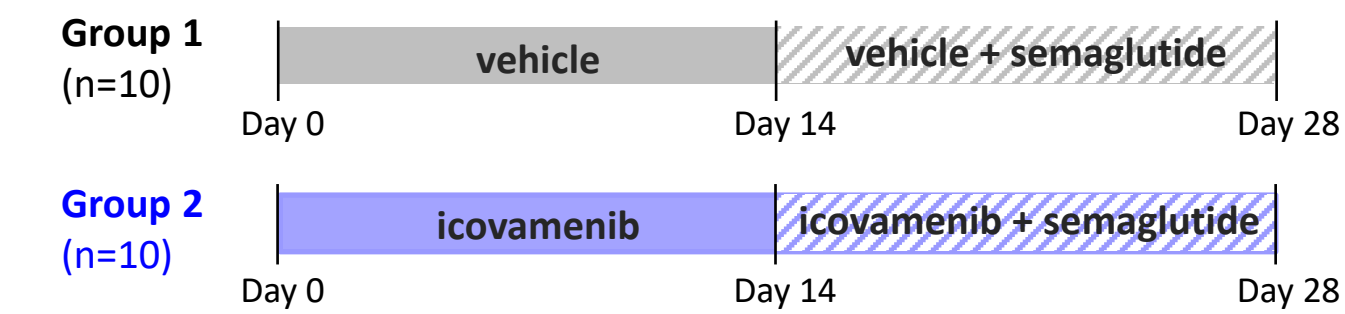
ICOVAMENIB INCREASED GLP-1 RECEPTOR AND INSULIN PROTEIN LEVELS



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

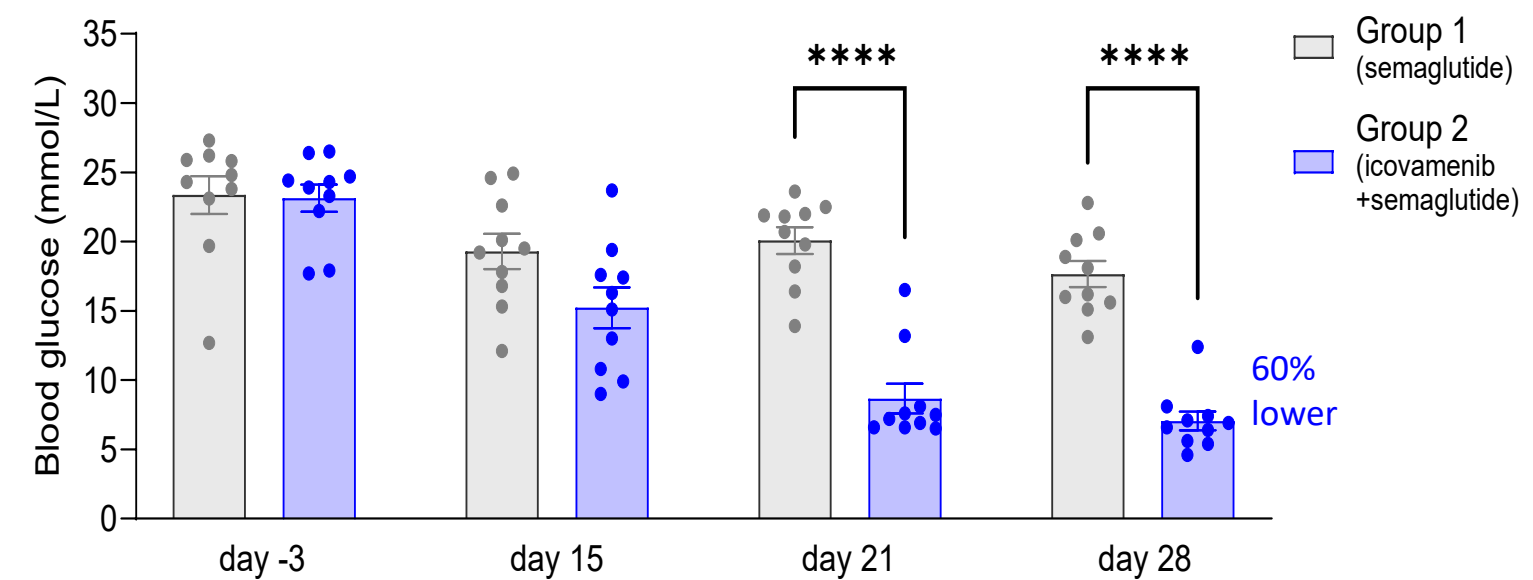


Combination treatment of icovamenib & low-dose semaglutide improved glycemic control in ZDF rats

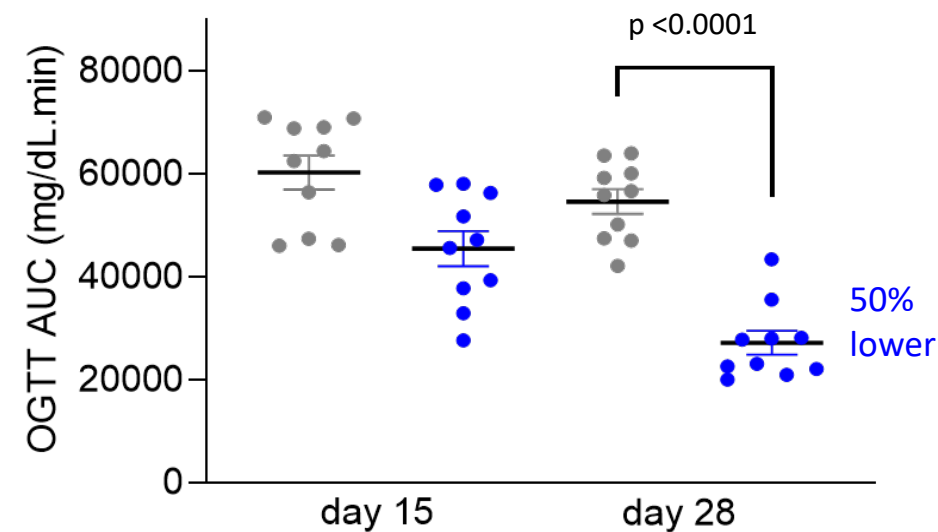


semaglutide low dose, 5 nmol/kg, s.c. QD
icovamenib, 200 mg/kg, p.o. QD

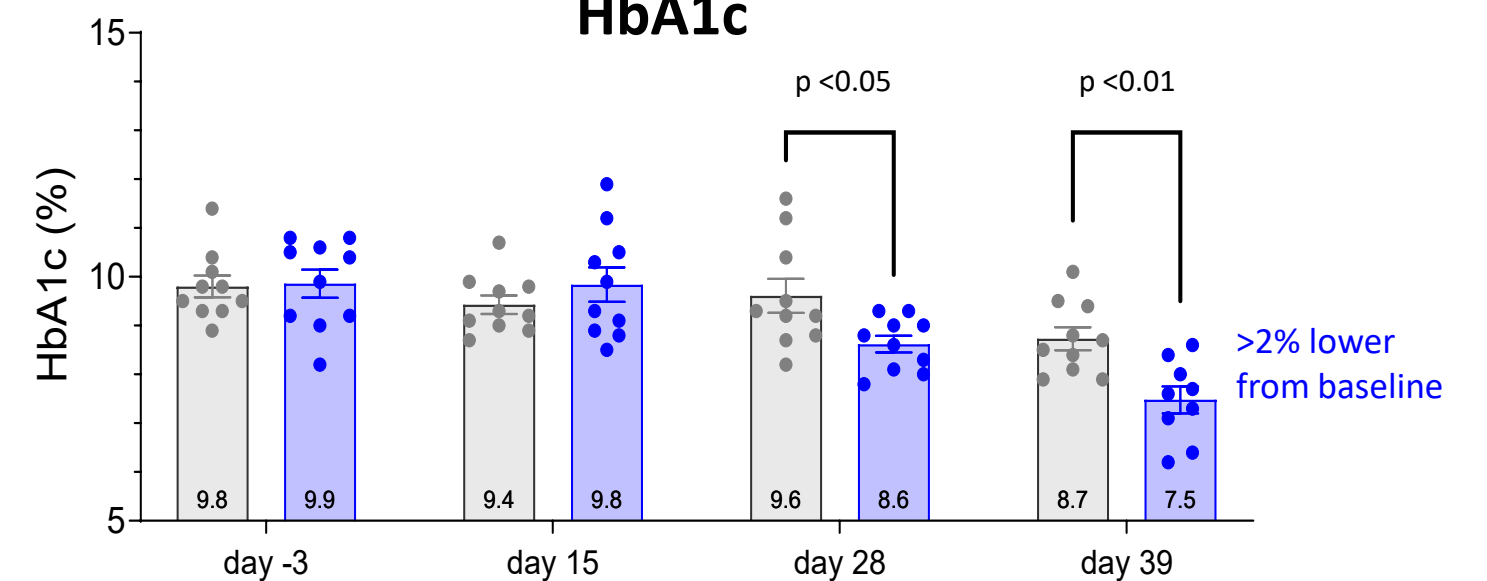
Fasting Blood Glucose[†]



Glucose AUC during Oral Glucose Tolerance Test



HbA1c

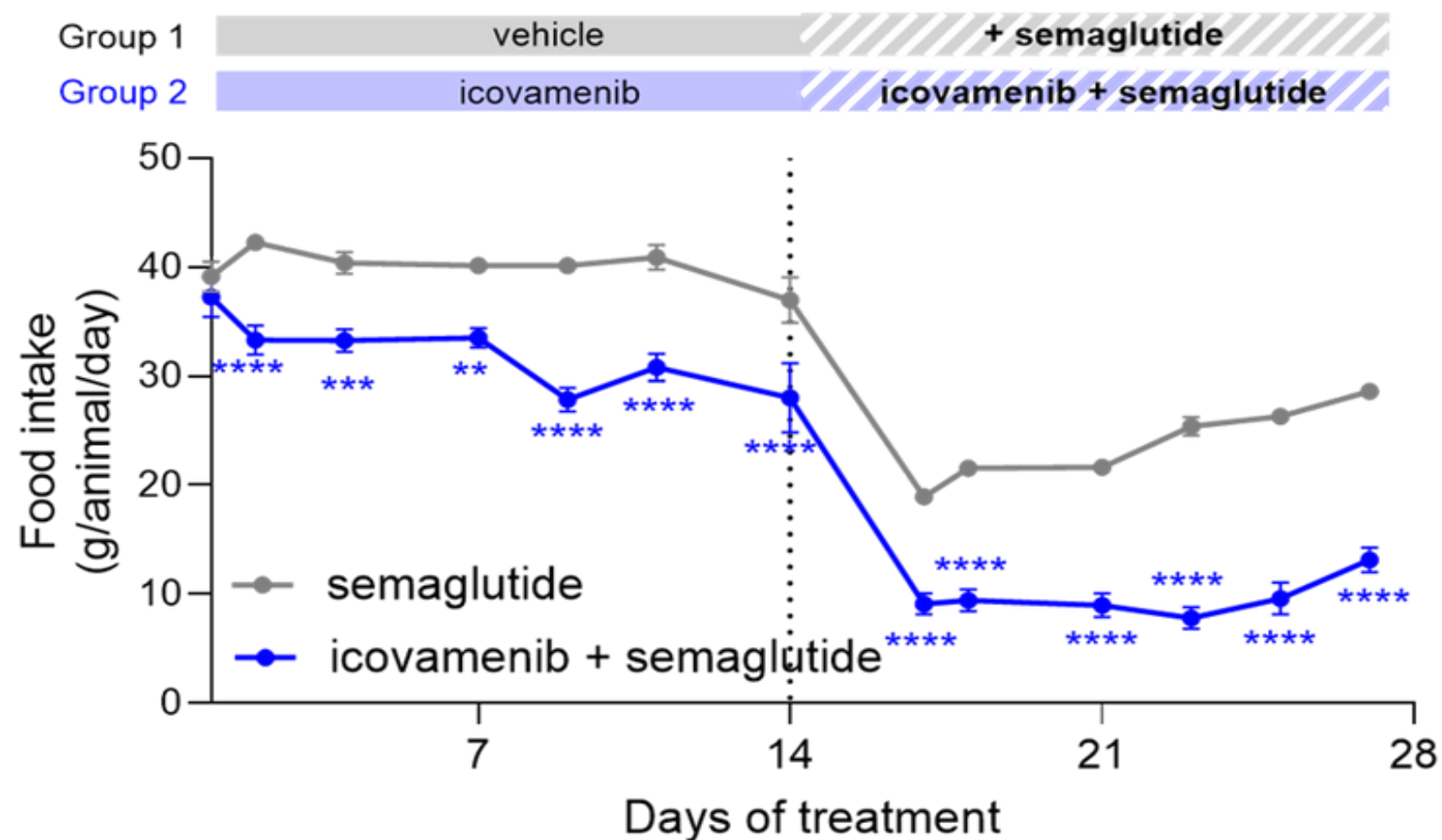


Plots represent mean ± SEM
Dots represent data for individual animal
† 6hr fasting on days -3 and 21, overnight fasting on days 15 and 28.

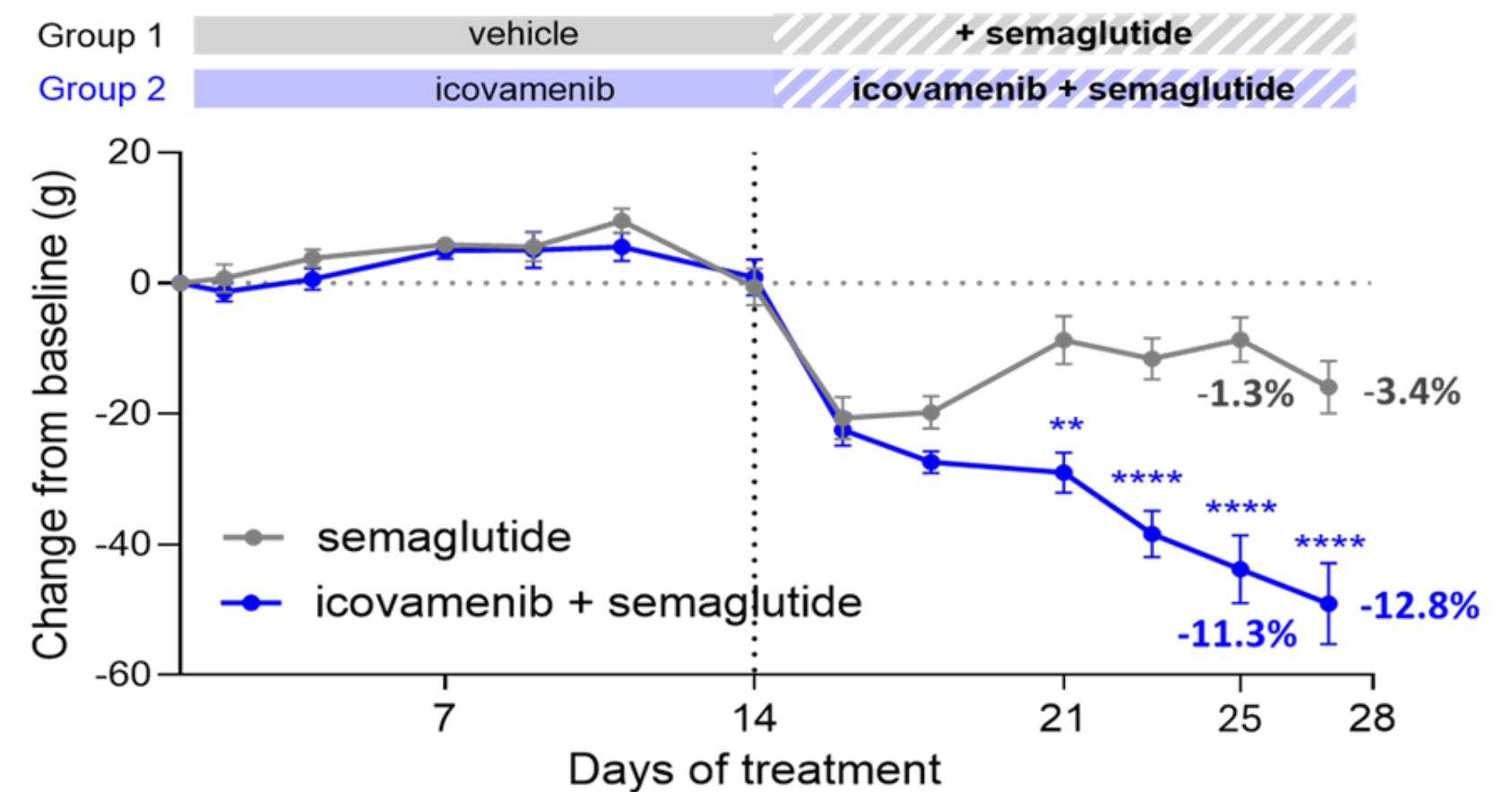
Combination Treatment of Icovamenib & Low-dose Semaglutide Reduces Food Intake & Body Weight



APPETITE SUPPRESSION

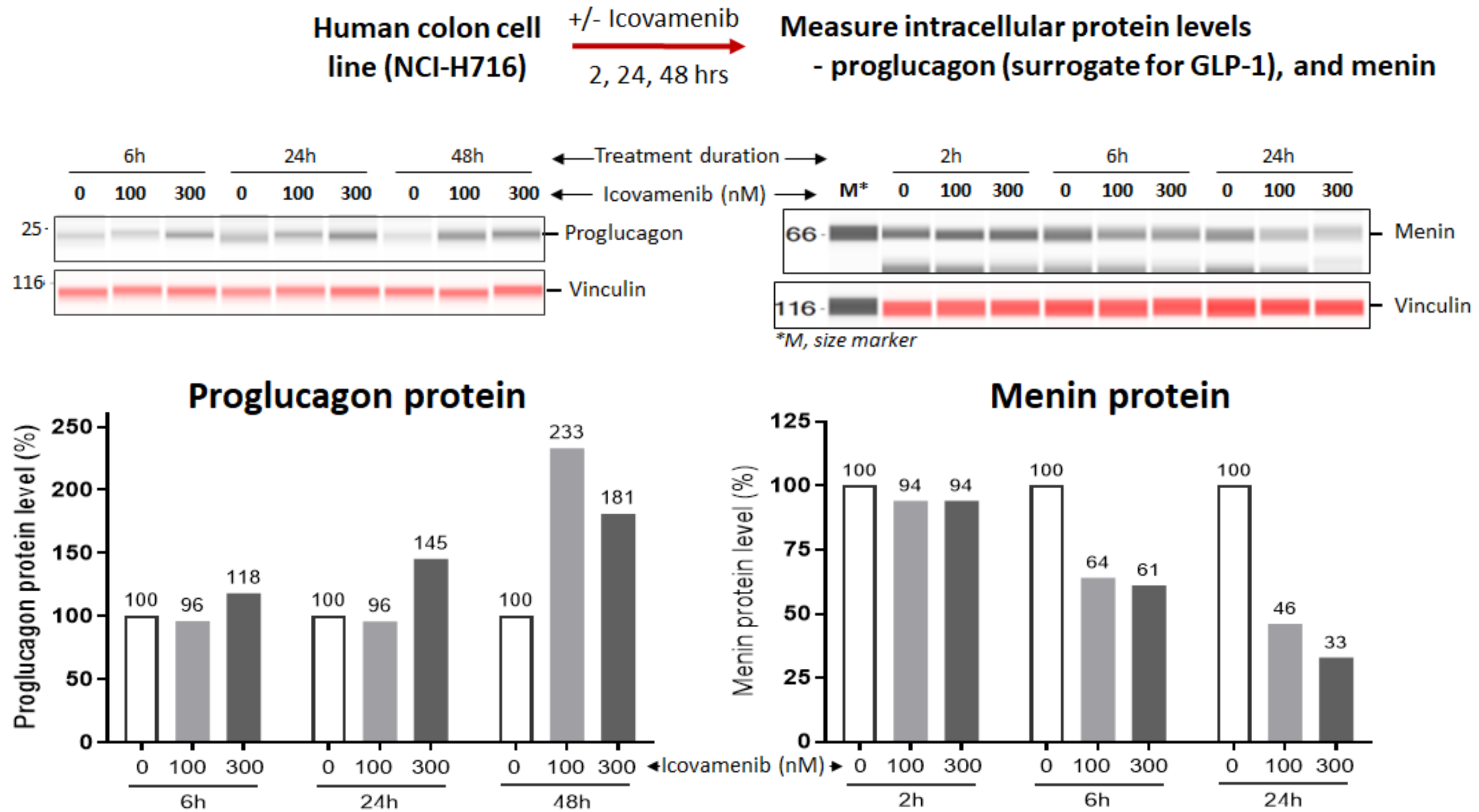


BODY WEIGHT REDUCTION



- ❑ 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



Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes

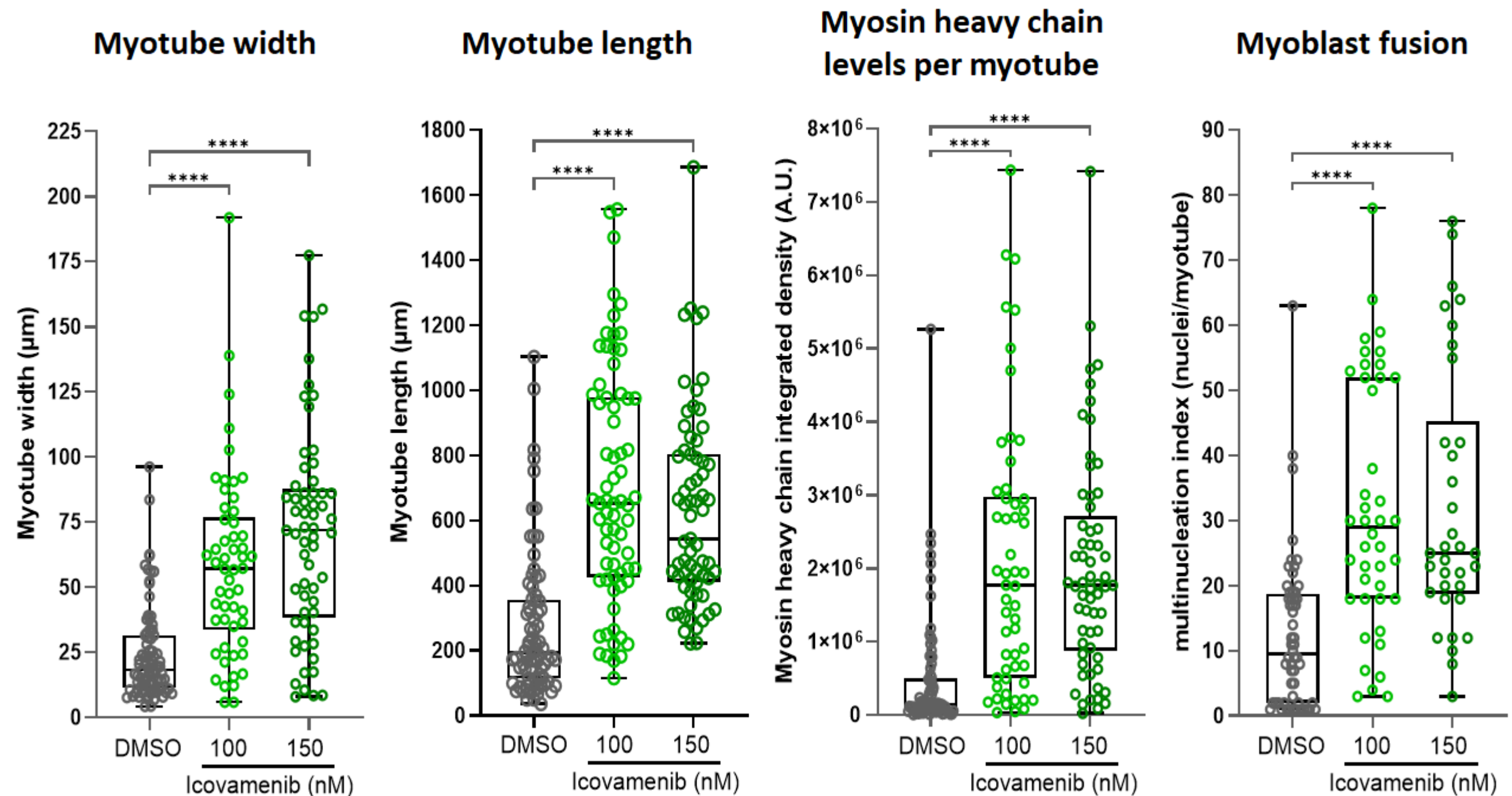
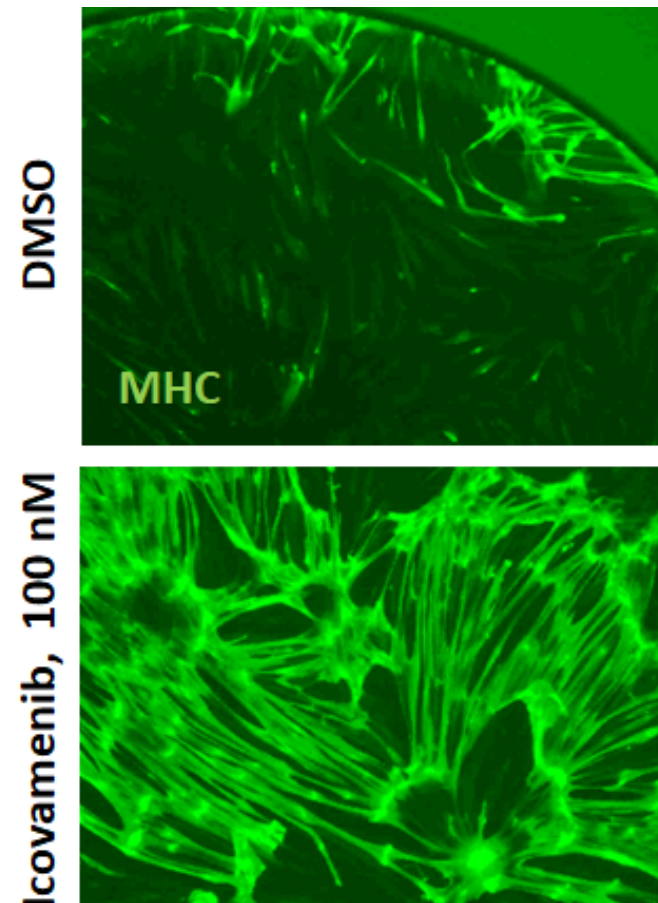
Human skeletal myoblasts

3 days ↓ differentiation

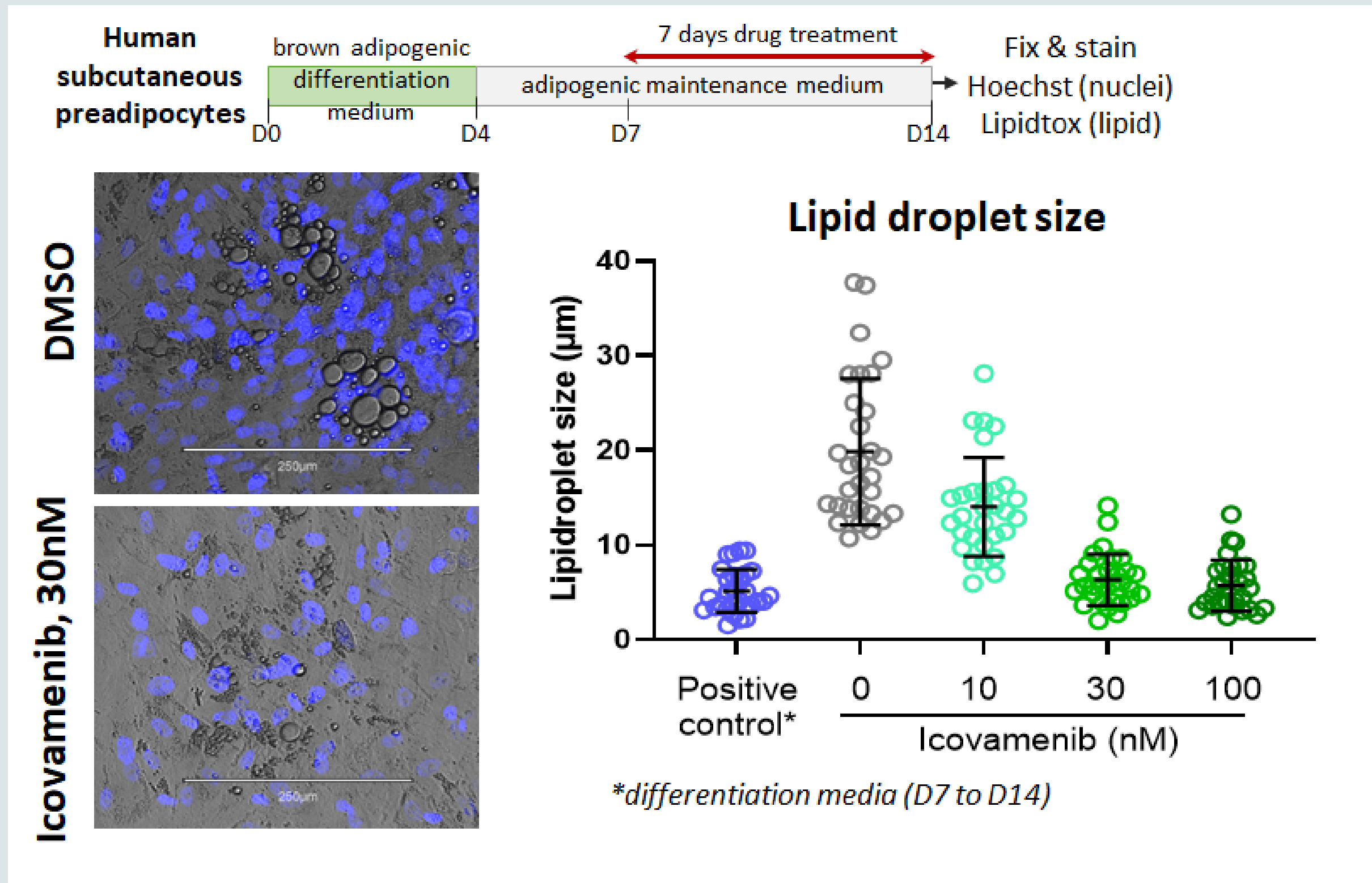
myotubes

2 days ↓ drug treatment

Imaging analysis

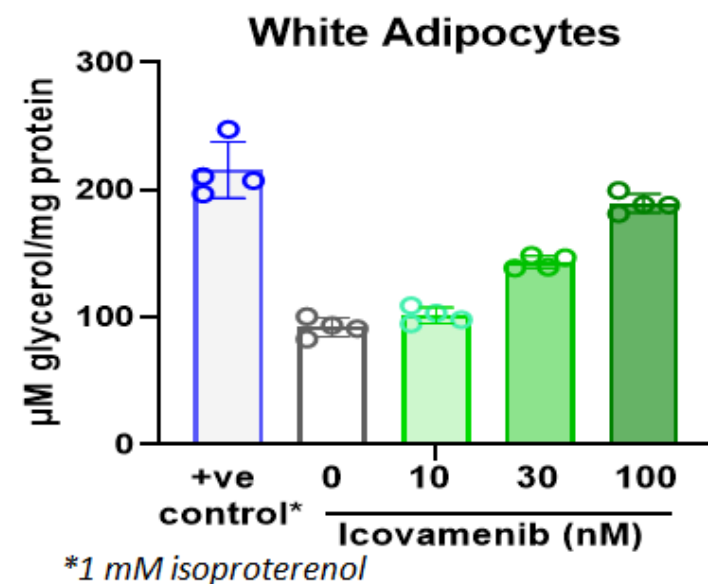
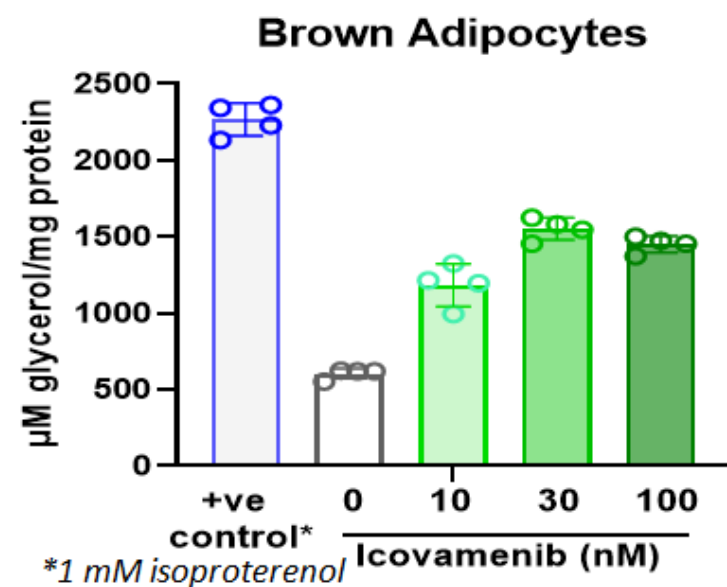
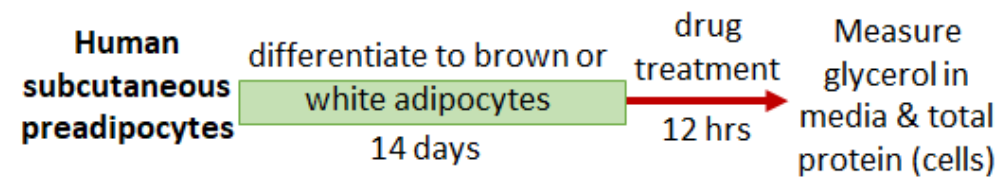


Icovamenib Promoted Lipolysis in Primary Human Adipocytes



Icovamenib Promoted Effects Indicative of Lipolysis and Fat Browning in Primary Human Adipocytes

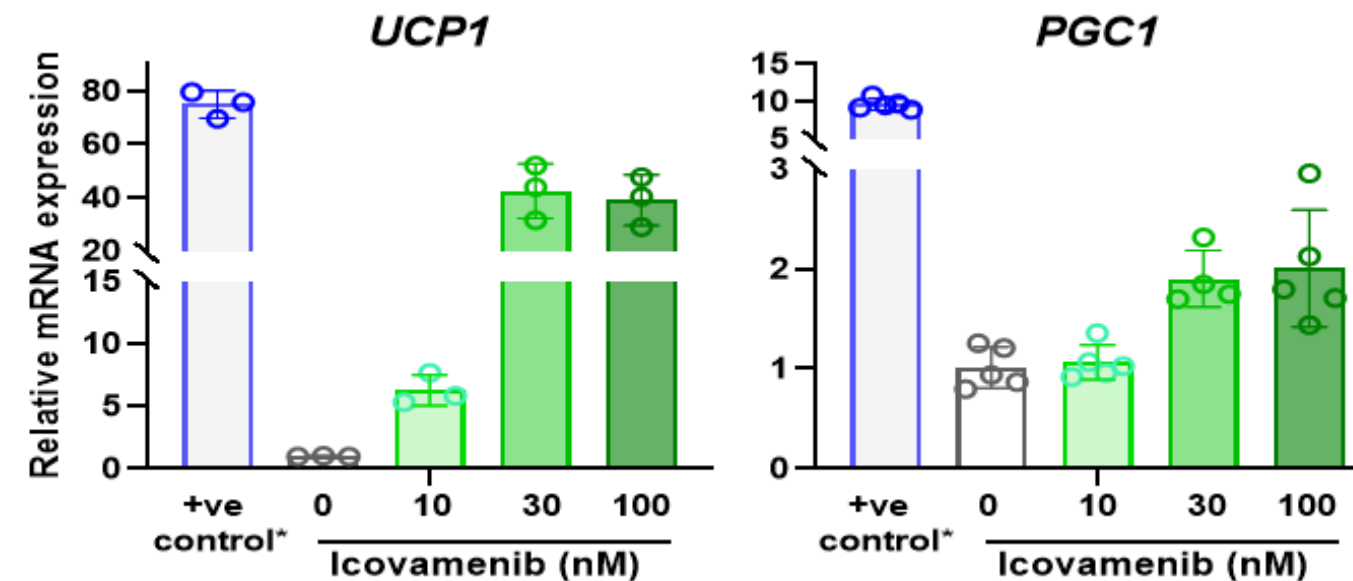
Enhanced Glycerol Release



Upregulation of thermogenic and lipolytic genes

Human Brown Adipocytes

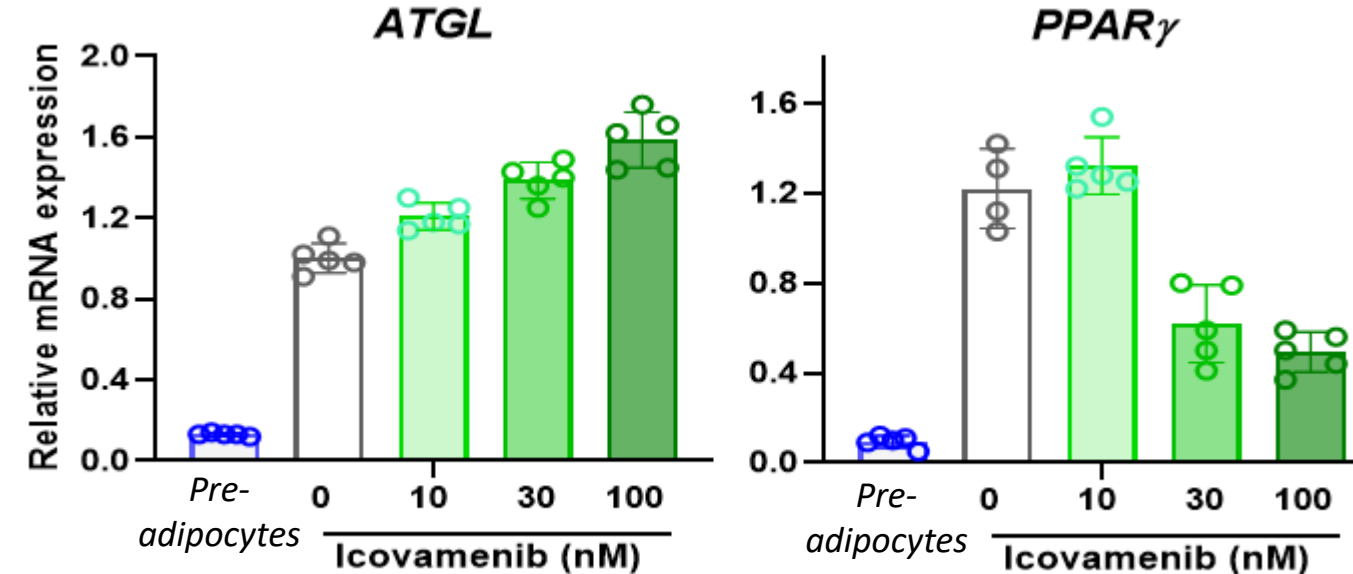
(differentiated from primary subcutaneous preadipocytes)



*differentiation media (D7 to D14)

Human White Adipocytes

(differentiated from primary subcutaneous preadipocytes)



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

ICOVAMENIB | COVALENT-112

Potential first-in-class menin inhibitor for diabetes

Clinical results in Type 1 Diabetes

Treatment Landscape:

Limitations of current approaches in stage 3 T1D

- Most investigational therapies in T1D focus on immune modulation to slow autoimmune destruction or on preserving residual beta cell function¹
- C-peptide area under the curve (AUC) has become the accepted endpoint, driving enrollment early after diagnosis (<90 days, new-onset T1D) to preserve residual beta-cell function²
- To date, most investigational therapies have not demonstrated durable restoration of beta cell function or sustained increases in C-peptide, outside of cell-based transplantation approaches³

The Next Frontier:

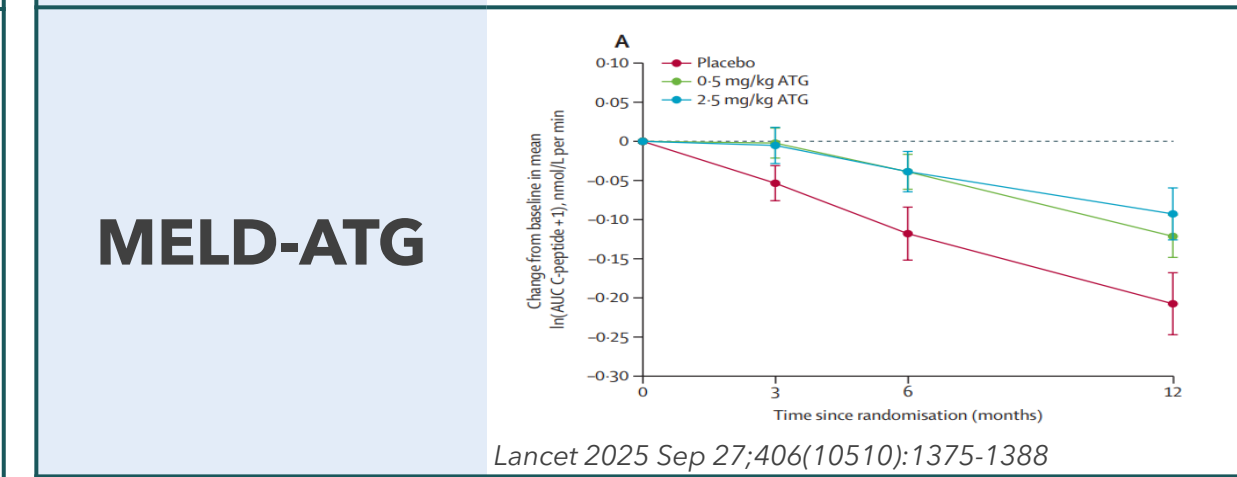
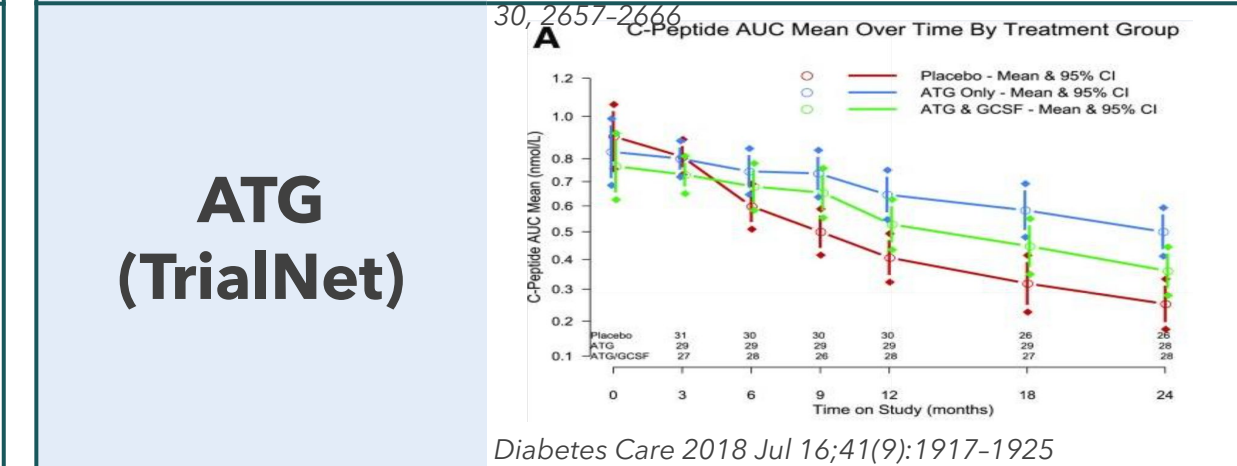
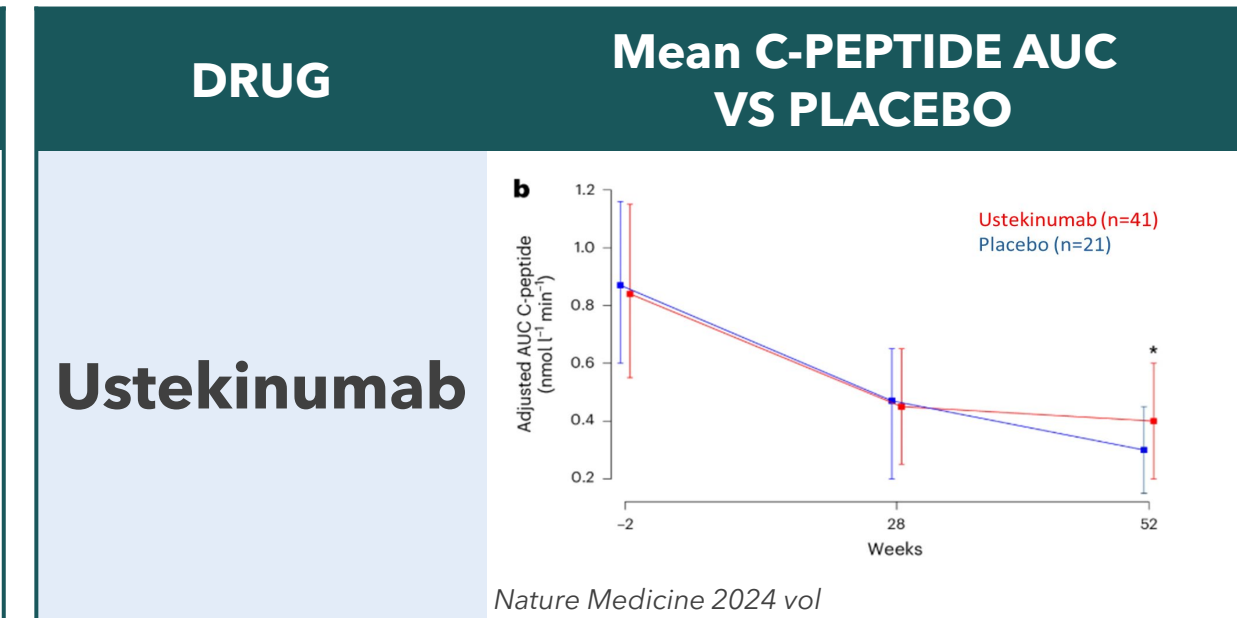
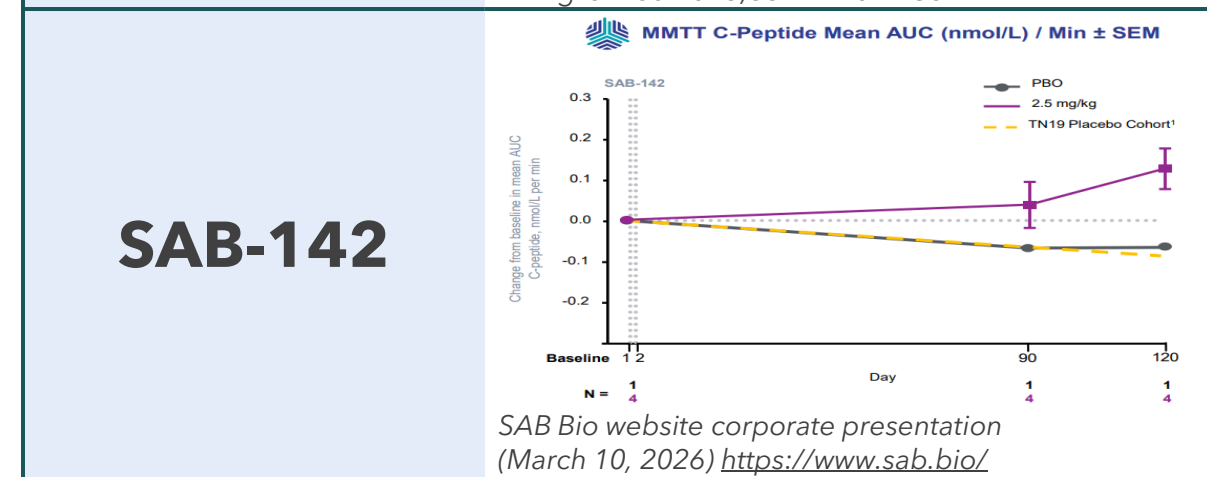
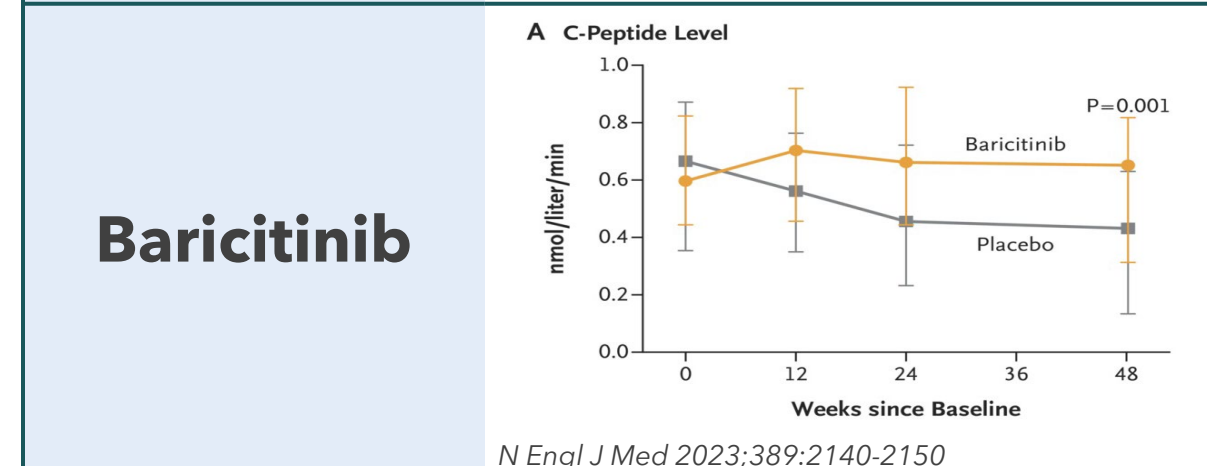
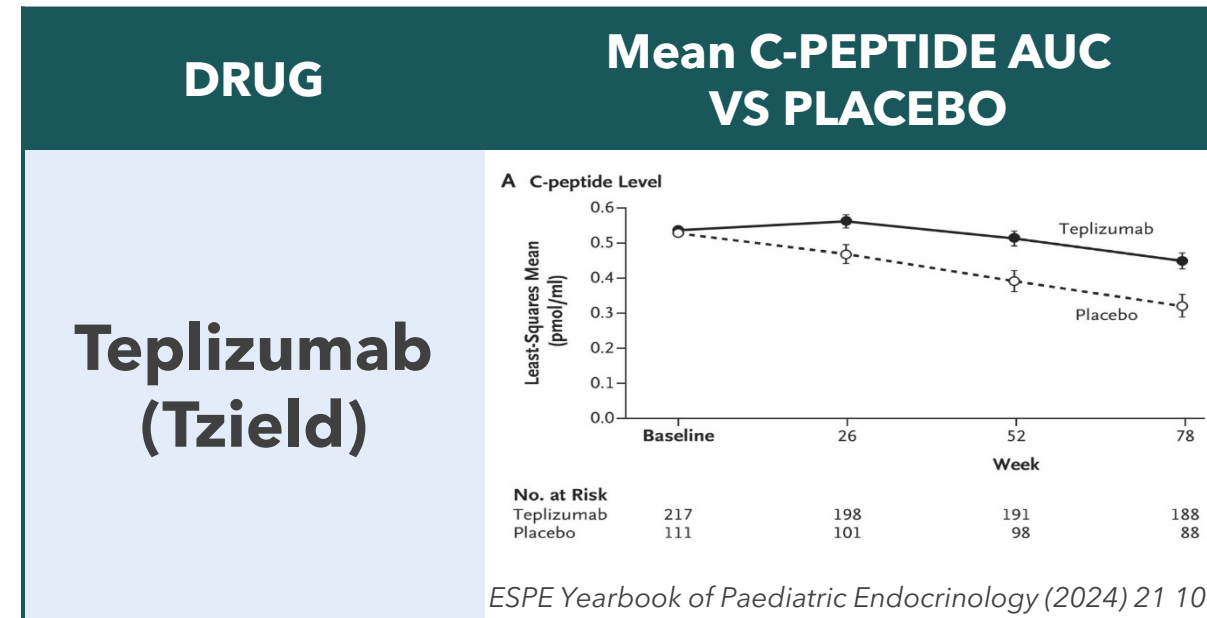
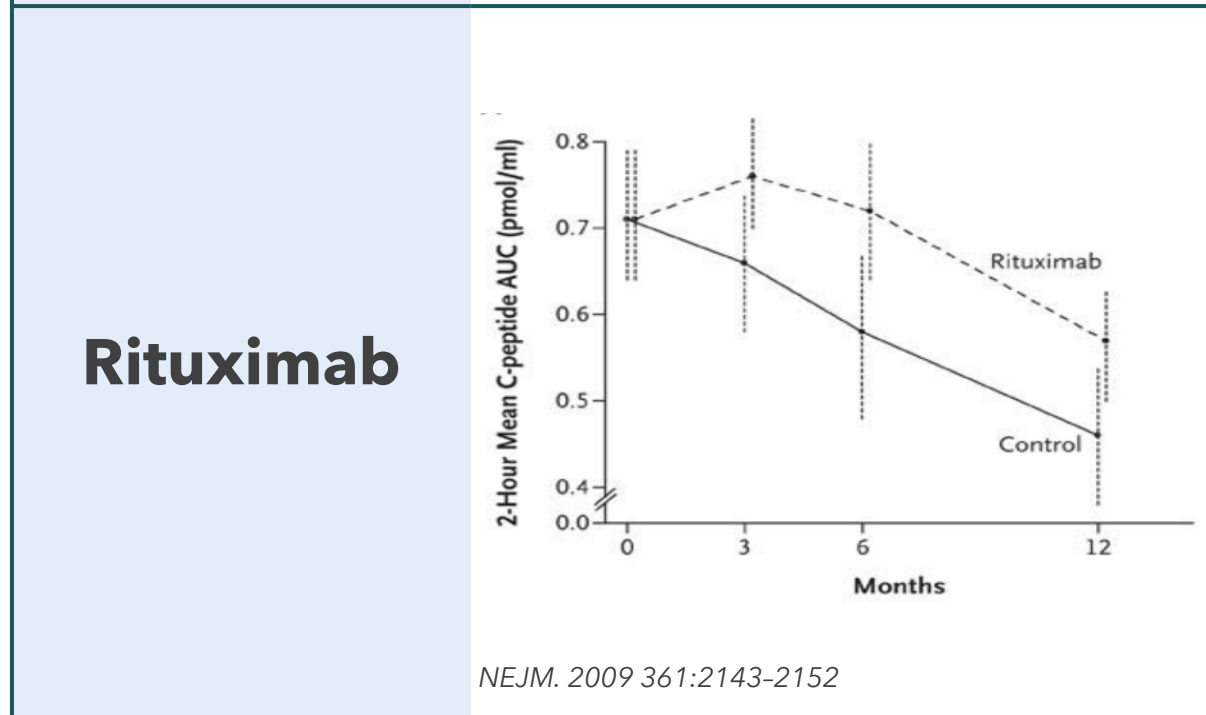
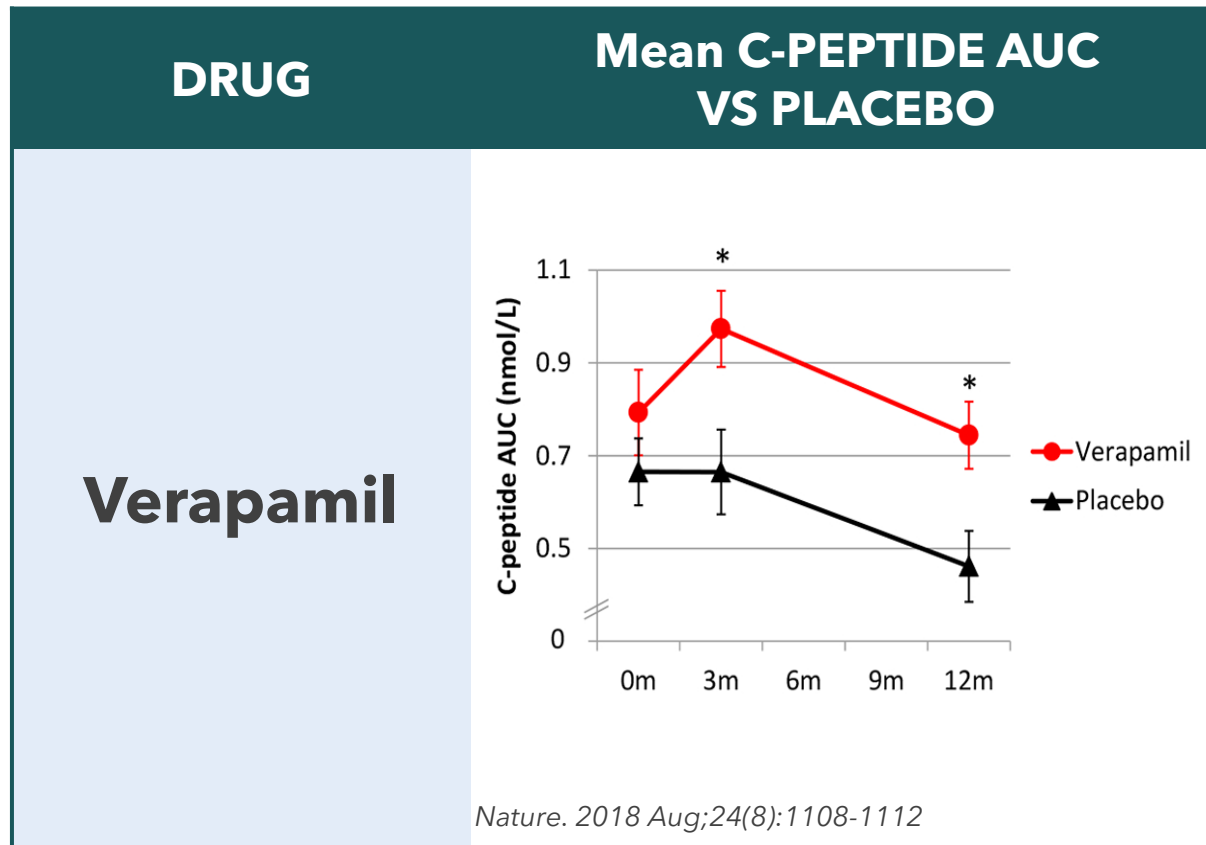
- Restoring beta cell function and mass, beyond only slowing the decline of C-peptide
- Expanding the treatment window beyond early, new onset T1D populations
- Enabling persistence of newly generated beta cells despite autoimmune pressure

1. Zarei M et al. *Diabetes Epidemiology and Management* 2025;17

2. *Diabetes Care* 2025

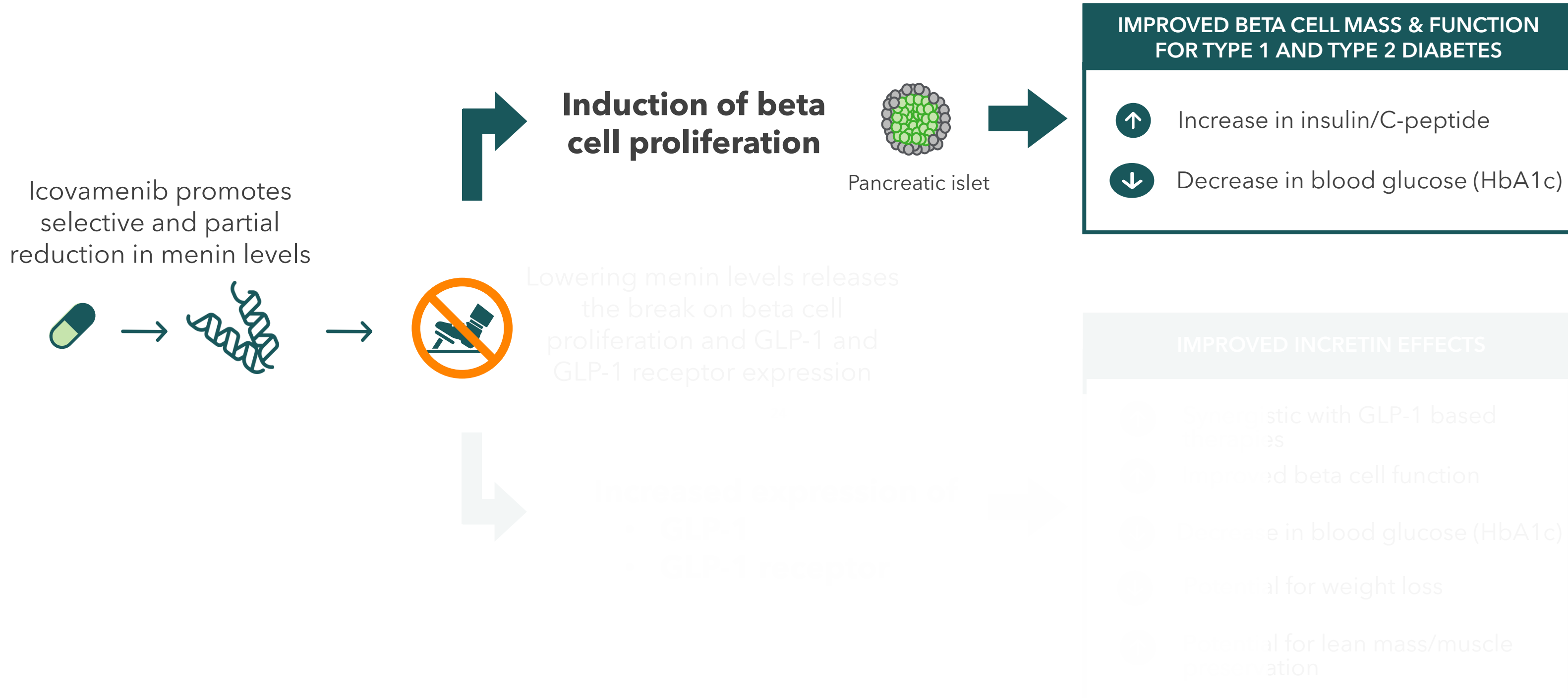
3. NIDDK. *Diabetes in America*, 2024

Most therapies in development for stage 3 T1D show limited and non-durable C-peptide impact



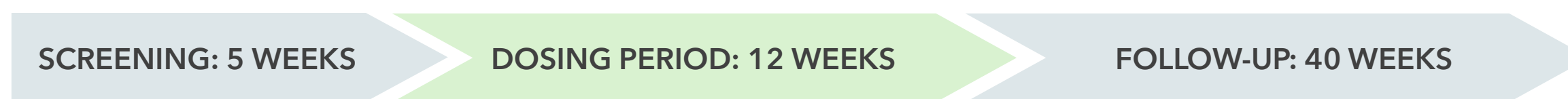
*Ladarixin and Diamyd, both Immune modulating, not mentioned here as they demonstrated no meaningful difference compared to placebo

Icovamenib's mechanism of action



Study Design

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.



Cohort 1

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

ARM A
N = 10

Icovamenib 100 mg QD

ARM B
N = 10

Icovamenib 200 mg QD

Cohort 2

T1D diagnosed between 3-15 years with a C-peptide ≥ 0.08 nmol/L

ARM A
N = 10

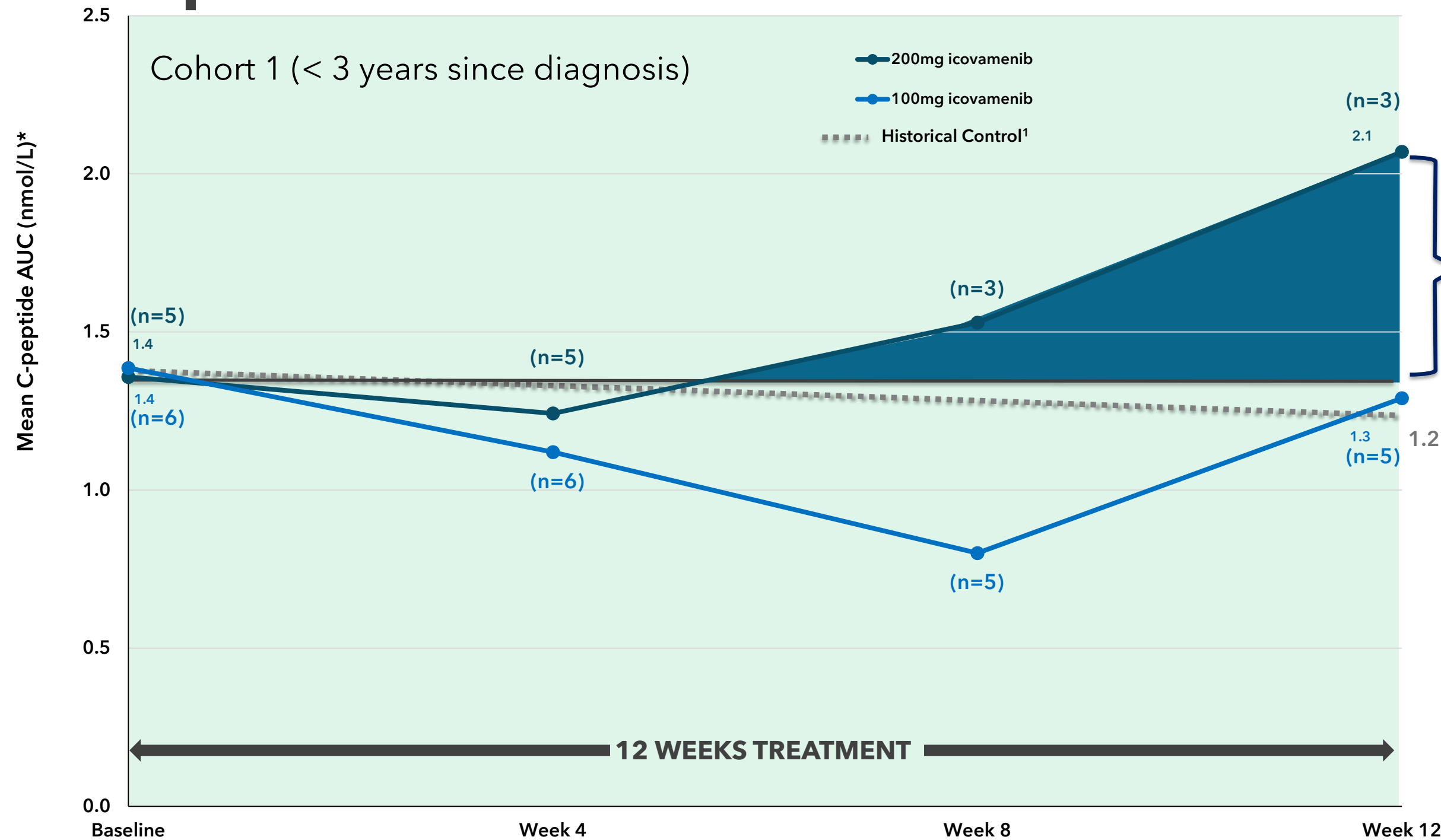
Icovamenib 100 mg QD

ARM B
N = 10

Icovamenib 200 mg QD

Study enrollment and dosing were interrupted in May 2024 due to an FDA clinical hold, which was subsequently resolved, but reduced the number of patients enrolled and followed through to the 52-week readout.

52% mean increase in C-peptide during the 12 weeks treatment period of icovamenib



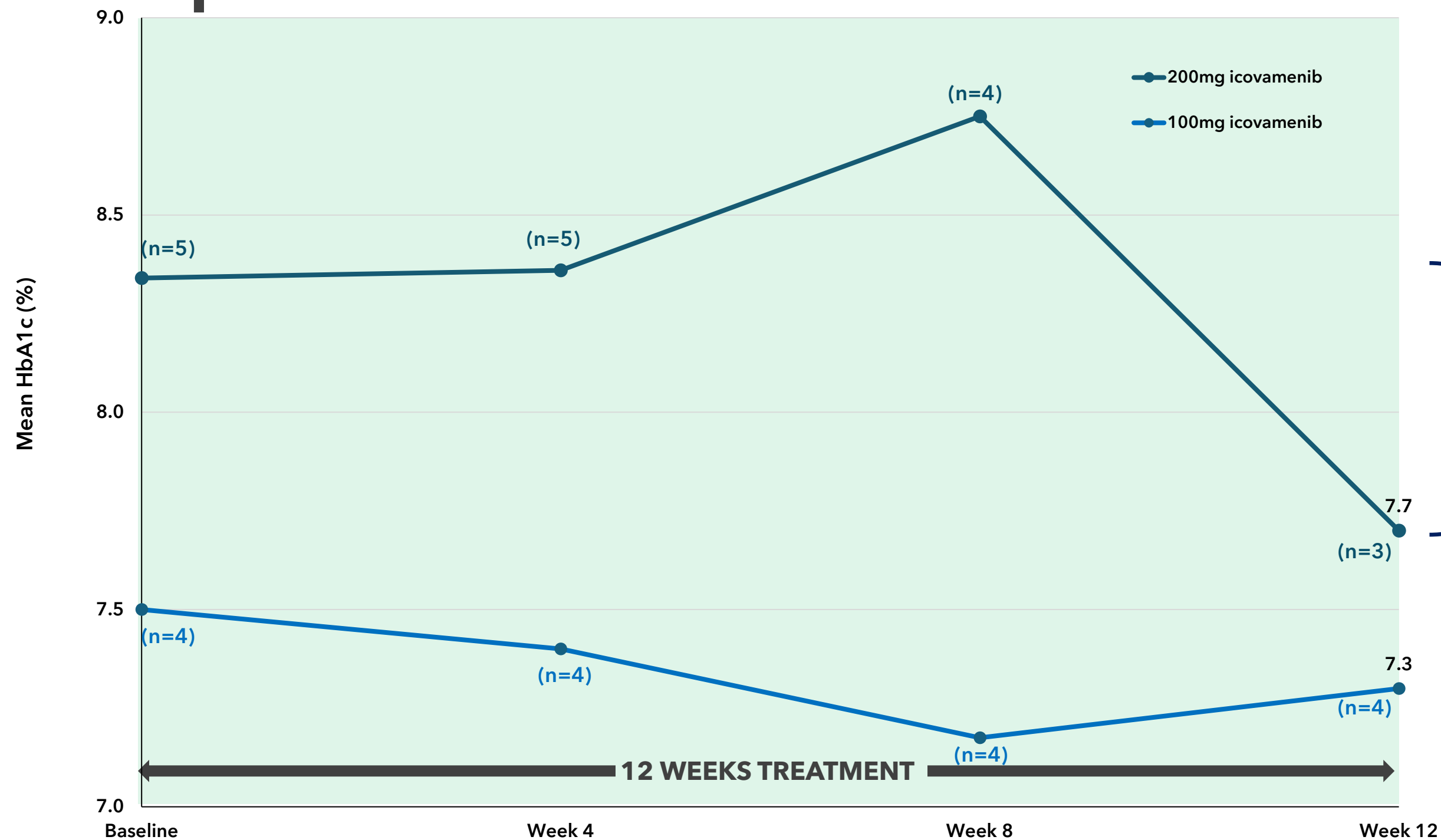
52% mean increase from baseline
+0.7
P<0.001

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

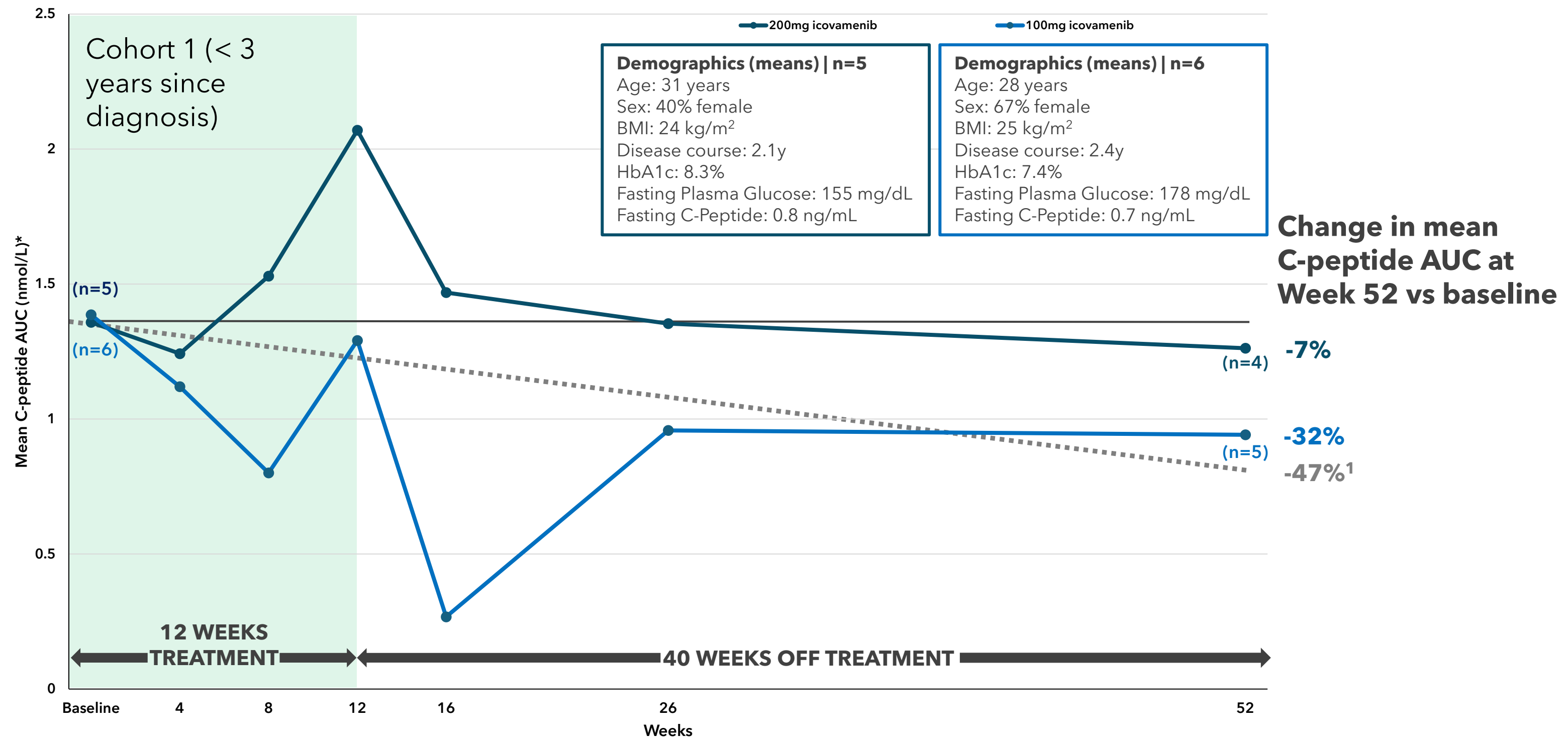
* 4-hour Mixed Meal Tolerance Test (MMTT)

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



0.6% reduction in mean HbA1c from baseline

Baseline C-peptide levels sustained through week 52 with minimal decline (only -7.1%) observed post 12 weeks of 200mg daily icovamenib



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)

Cytokine Profiling of Cohort 1 (<3 year 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). Cytokine profiling showed no evidence of systemic immune activation in Cohort 1 participants receiving 200 mg icovamenib
- All cytokines remained classified as Non-Inflammatory through Week 52
- Small Week 12 increases in IL-1 β , 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
- **These findings suggest that increased 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**

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

Optimal dose pool and target population identified for T1D phase 2 program

T1D insights:

- ✓ Dose response: 200 mg demonstrated stronger clinical activity vs 100 mg
- ✓ Potential early intervention advantage: T1D patients dosed ≤ 3 years showed greater response vs those 3-15 years from diagnosis
- ✓ 12-week treatment showed continuous and improved responses, supporting potential for greater benefit with extended dosing
- ✓ Cytokine profiling showed no evidence of systemic immune activation, with inflammatory markers remaining stable or reduced through Week 52
- ✓ Preclinical chronic toxicology studies support longer term dosing
- ✓ Generally well-tolerated, with a favorable safety profile maintained through the 52-week observation period

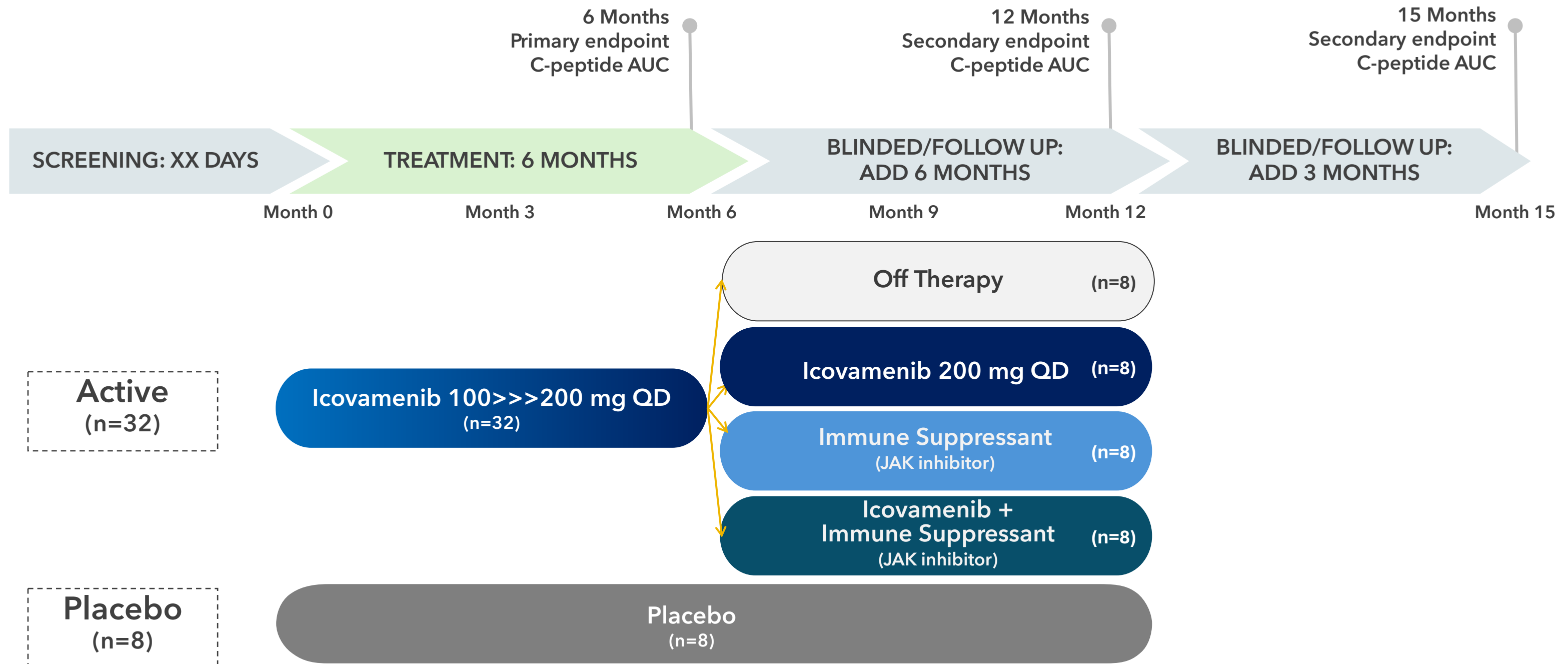
T1D development focus:

- Potential to further increase C-peptide AUC in T1D with extended or continuous dosing
- Opportunity to potentially enhance outcomes through combination with immunomodulation therapies

Proposed phase 2 trial design*

Inclusion Criteria

- Adult participants with T1D diagnosed within 3 years with a C-peptide ≥ 0.2 nmol/L
- Background therapy maintained unless rescue required



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

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.



Barbara Davis Center
for Diabetes

Sub-Investigators

Jason Gaglia, MD, MMSc

Ass. Professor | Joslin Diabetes Center, Harvard Medical School

Worlds 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

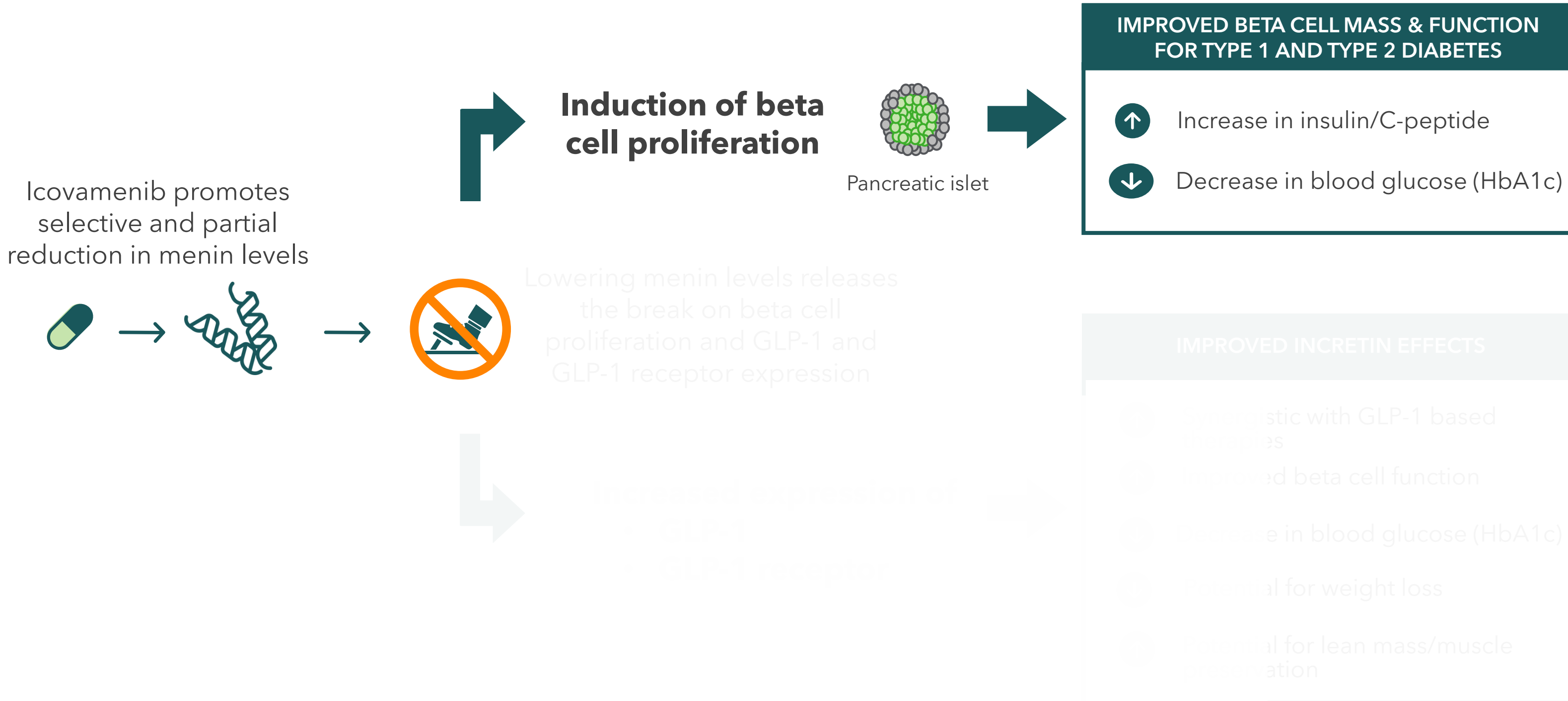
ENDOCRINOLOGIST, PROFESSOR OF MEDICINE UTHSCSA

ICOVAMENIB | COVALENT-111

Potential first-in-class menin inhibitor for diabetes

Clinical results in Type 2 Diabetes

Icovamenib's mechanism of action



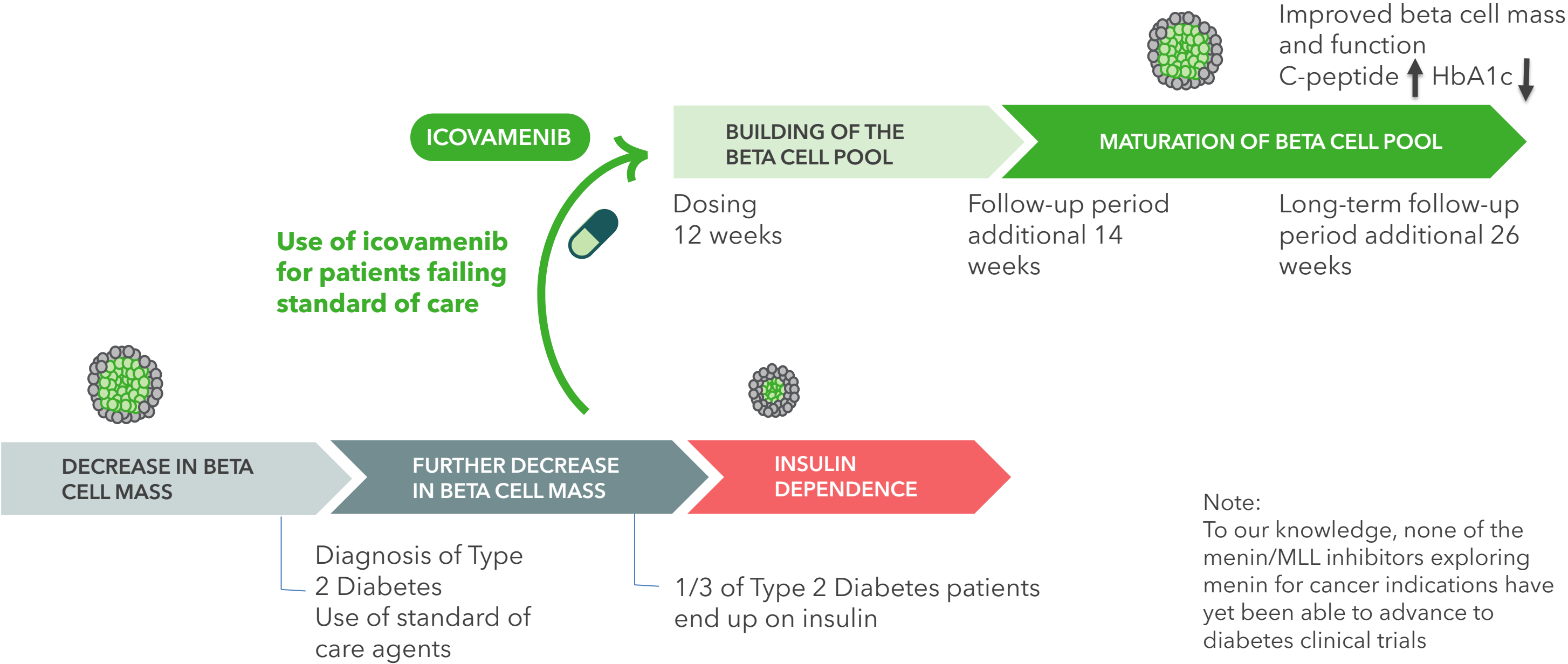
Baseline demographics & characteristics

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)

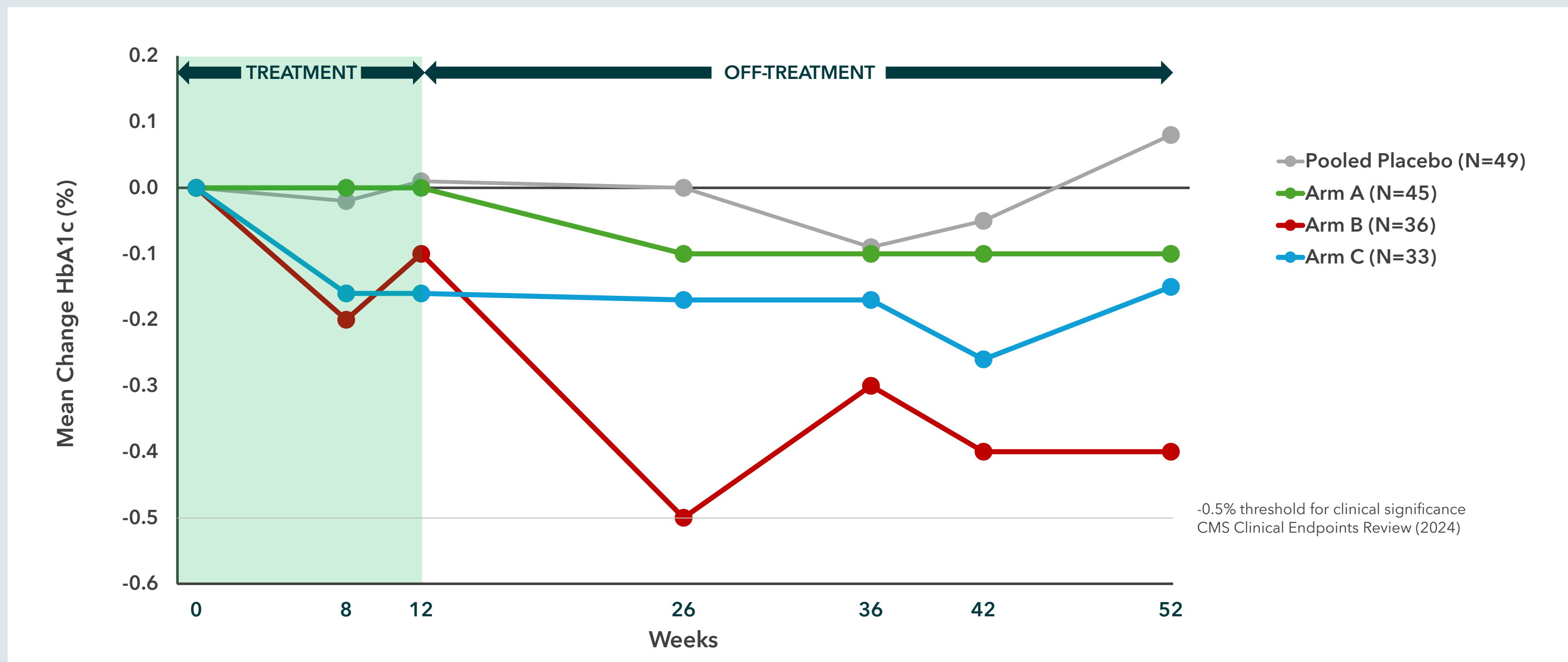
*Per the COVALENT-111 Protocol the population analyzed includes only subjects who received ≥80% of their planned dosing. A clinical hold interrupted the dosing. Patients were also excluded if they had significant protocol deviation.

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

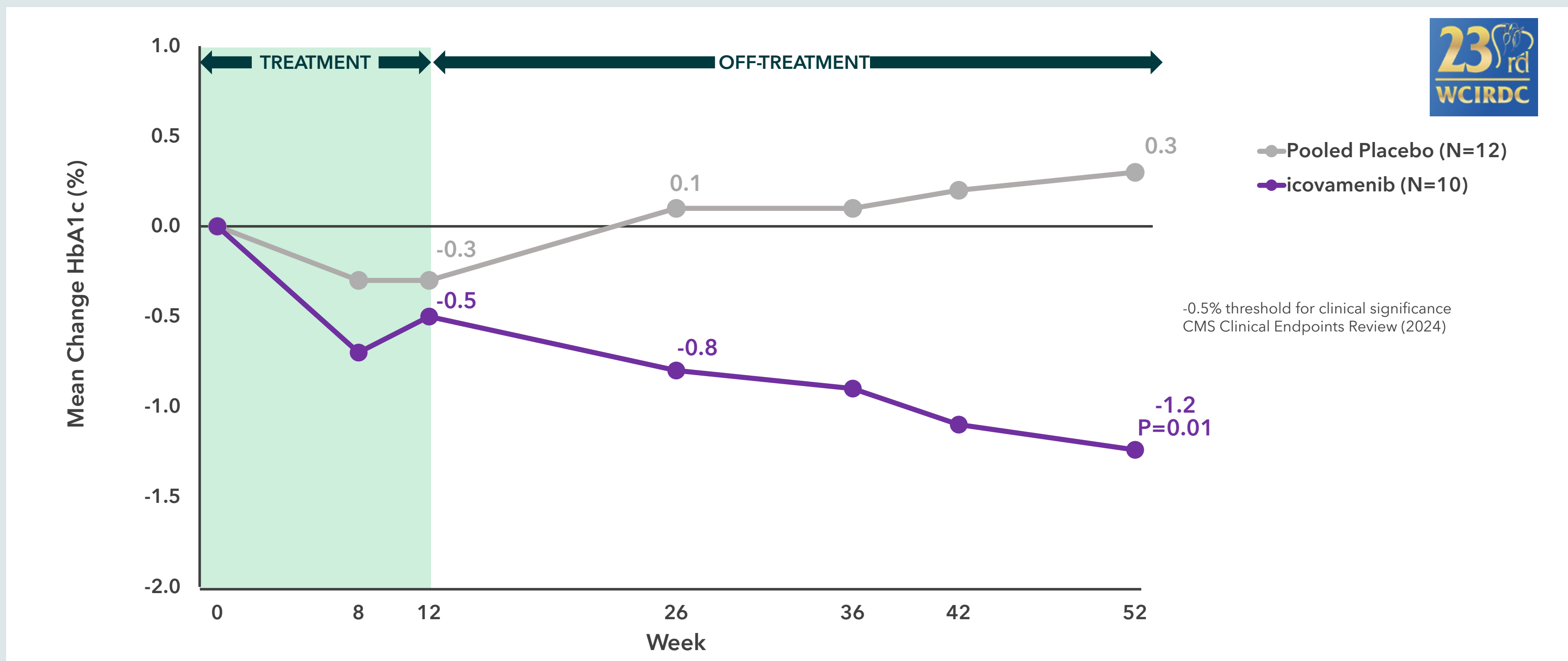


Change in HbA1c from baseline through week 52 - all subtypes

Across treatment durations (Arm A = 8 weeks 100 mg, Arm B = 12 weeks 100 mg, Arm C = 8 weeks 100 mg 4 weeks at 200 mg) per protocol participants taking one or more antihyperglycemic medications at baseline

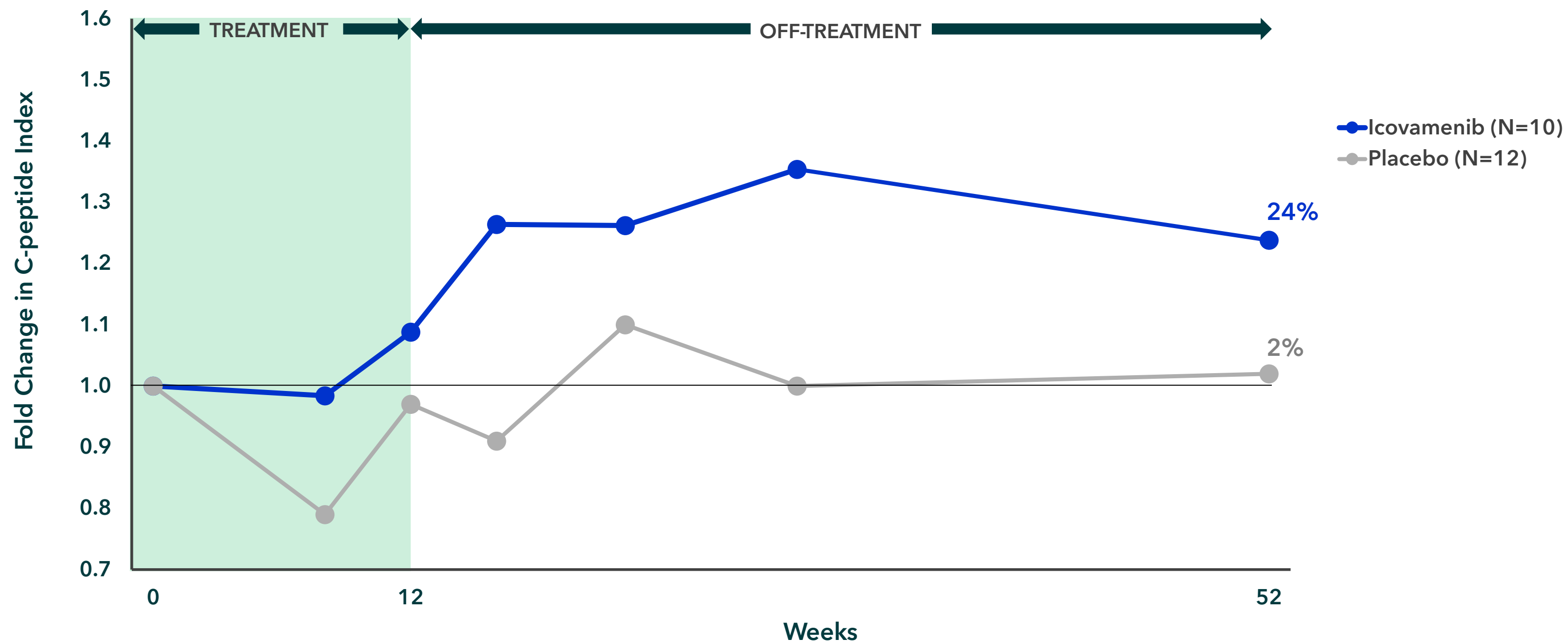


12 weeks of dosing (arms B&C) delivered lasting benefit through 52 weeks for severe insulin-deficient diabetes patients



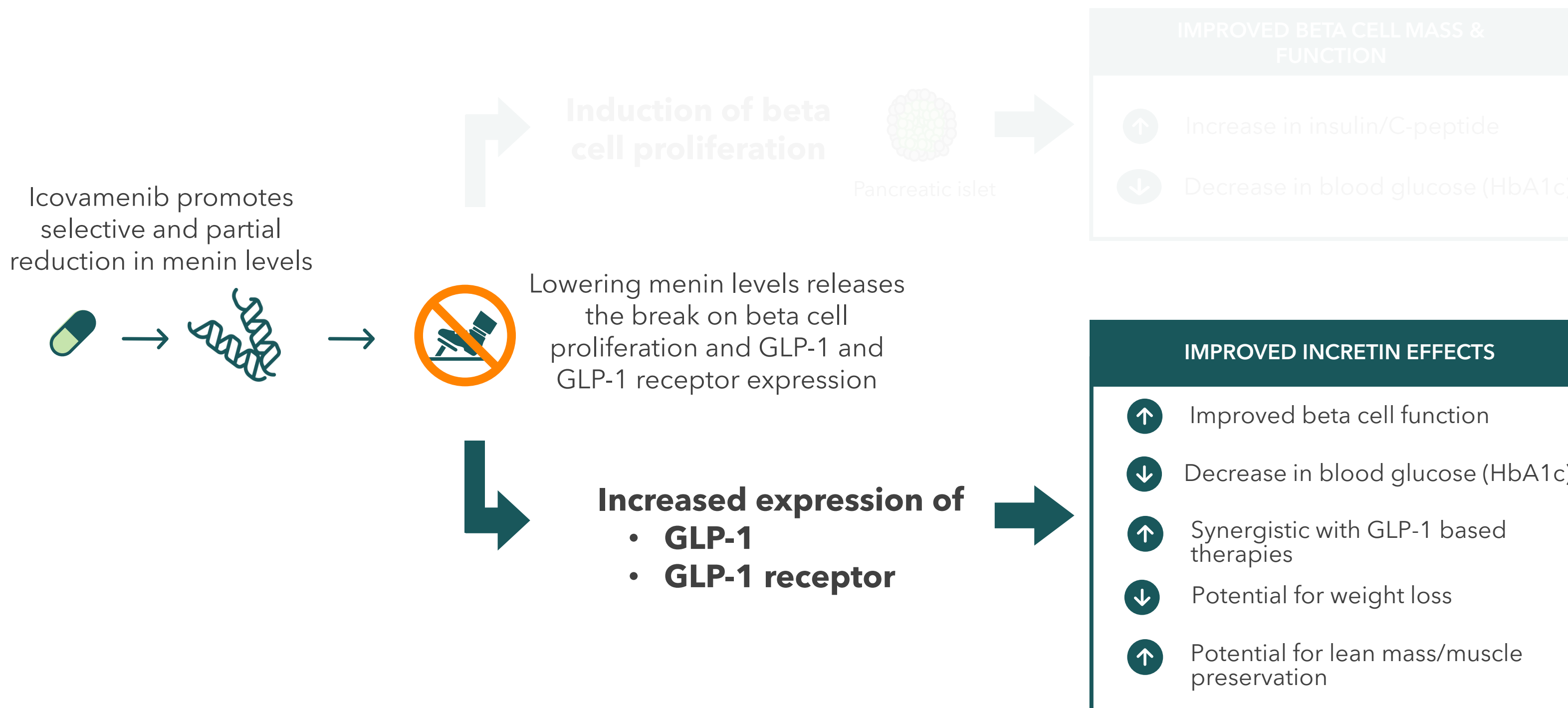
Arm A was excluded from this analysis because it included only 8 weeks of dosing which the company is not planning to pursue.

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

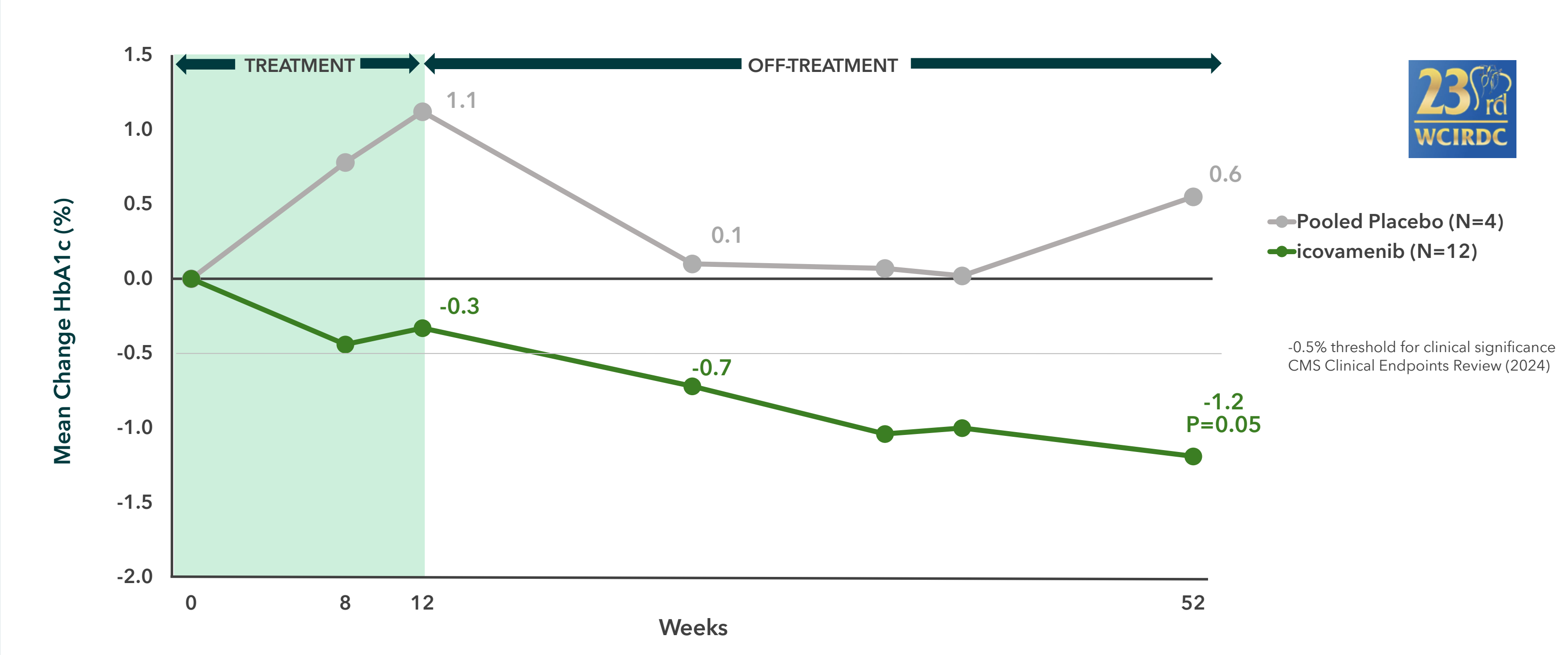


Data censored at onset of rescue medication, defined as any modification in antihyperglycemic therapy

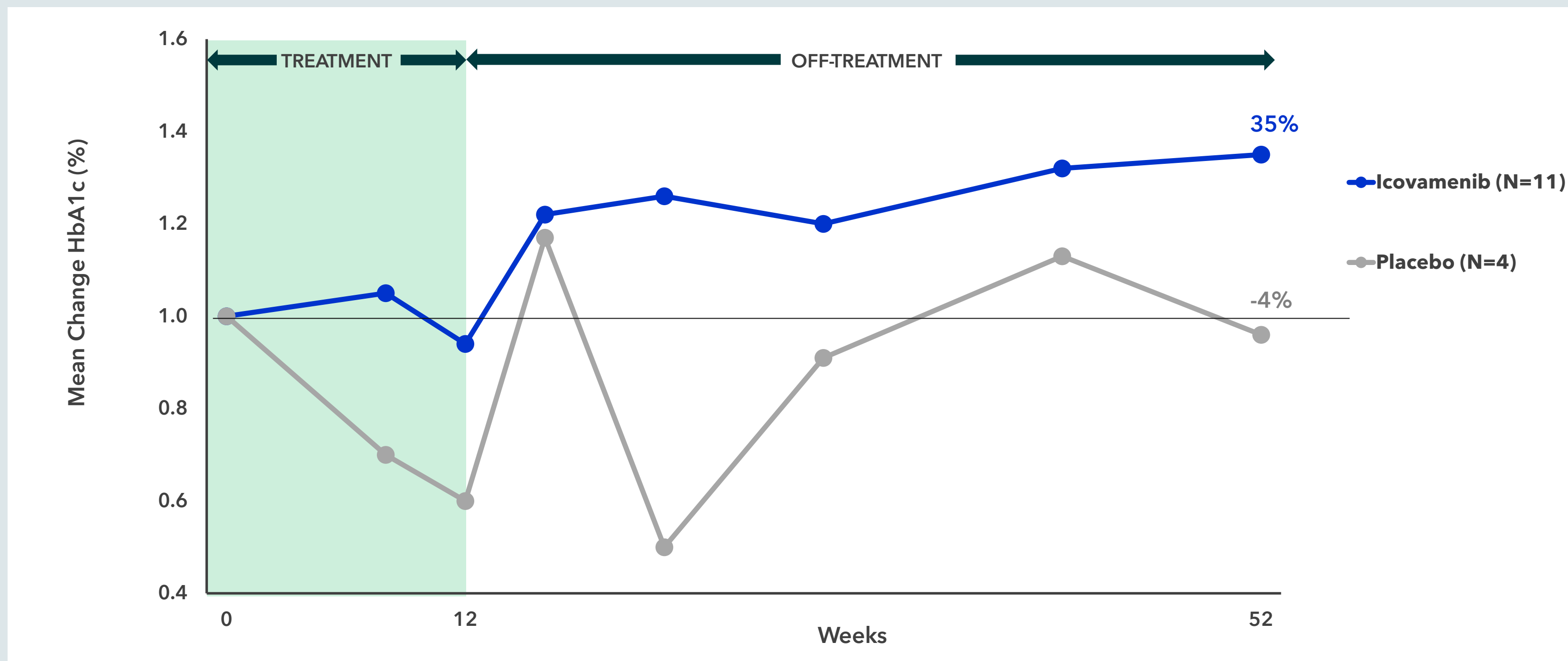
Icovamenib's mechanism of action



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)

Data are n (%) TEAE = Treatment Emergent Adverse event. SAE = Serious Adverse Event. Data are n (%) of TEAE with ≥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

ICOVAMENIB

Potential first-in-class oral menin inhibitor for diabetes

Ongoing Phase II Studies

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

ICOVAMENIB

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

Direct application in Phase II Studies

COVALENT-211

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

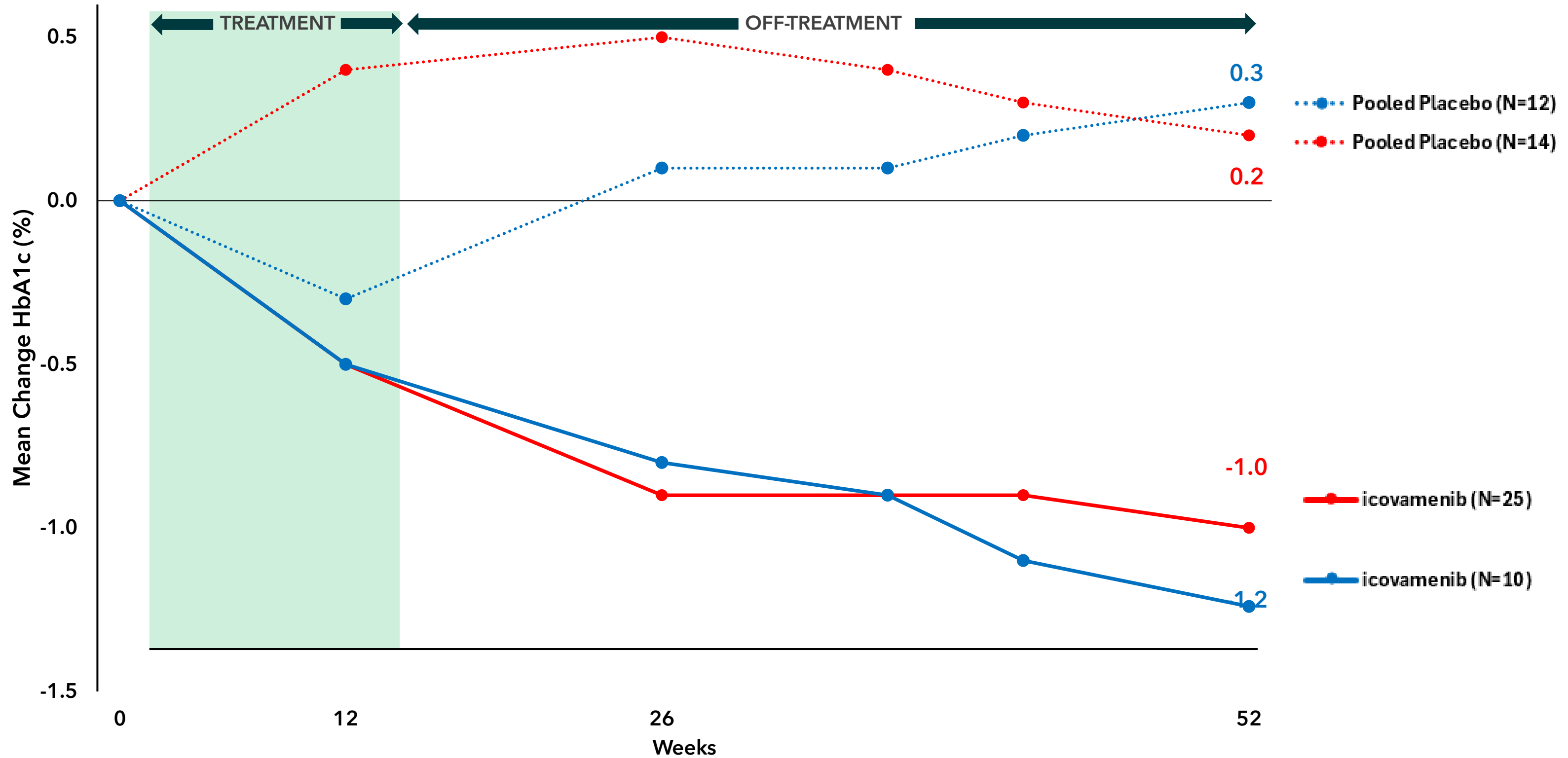
- Adult participants with T2D who were treated with 1-3 antidiabetic medications
- HbA1c 7.5%-10.5% and BMI ≤ 32 kg/m²
- Background therapy maintained unless rescue required

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 $\geq 7.5\%$ and $\leq 9.5\%$ and BMI 25 to 40 kg/m²
- Background therapy maintained unless rescue required

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



BMF-650

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

Preclinical results and clinical overview

Developed to deliver strong efficacy with improved oral tolerability

An Investigational Next-Generation Oral GLP-1 Receptor Agonist

Proposed differentiated properties of BMF-650



Improved PK Profile

Greater oral exposure with lower variability observed in preclinical studies



Generally Favorable Safety Profile

Better tolerability associated with higher plasma protein binding in preclinical models



Patient Friendly Design

Oral delivery with the potential for simplified dose escalation

Greater therapeutic window matters

- Only 3 of 10 patients remain on GLP-1 therapy at one year due to tolerability, GI effects and complexity of use.¹
- An oral agent with improved tolerability could potentially expand the long-term use.

Intellectual Property

- U.S. patent allowance received December 2025 covering BMF-650 composition.
- U.S. and PCT applications published and proceeding through examination.

1. Khan, et al. JAMA 2024 doi:10.1001/jama.2024.22284.

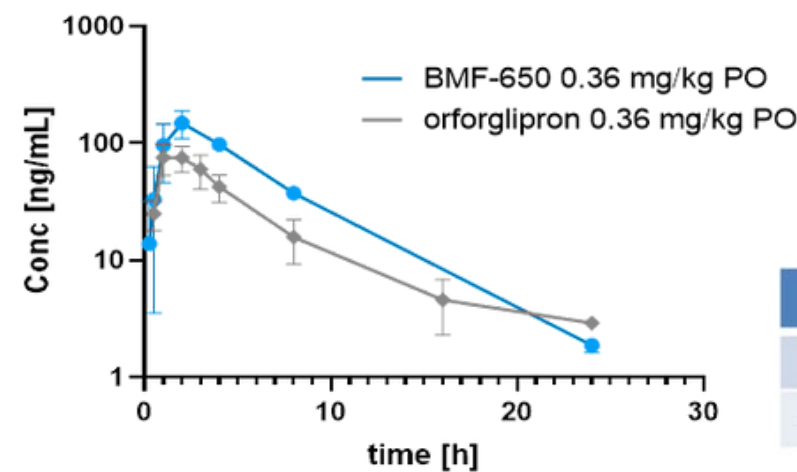
BMF-650 showed favorable in vitro on-target activity and off-target selectivity

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 μM	> 10 μM
orforglipron	2.6 nM	0.1 nM	> 10 μM	> 10 μM

- 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

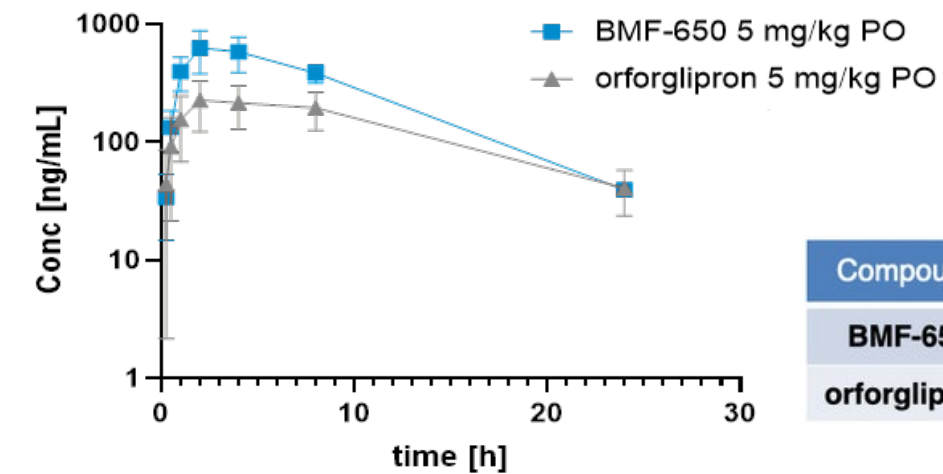
CYNOMOLGUS MONKEY PO PK



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

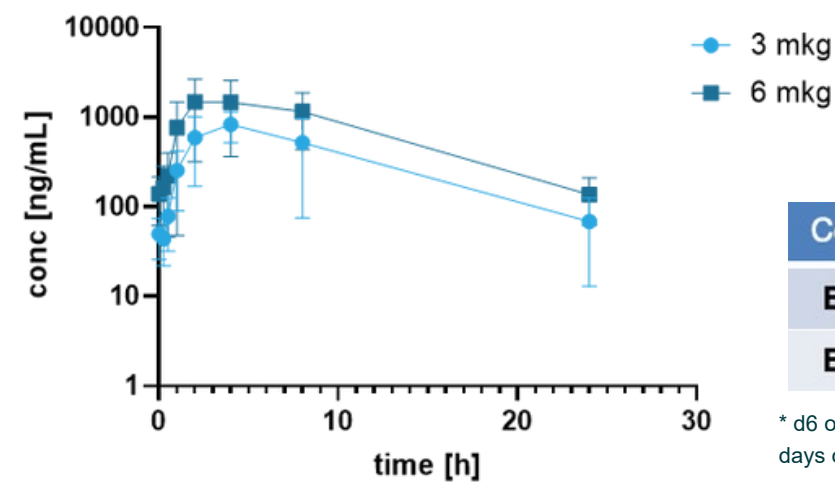
SPRAGUEDAWLEY RAT PO PK



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



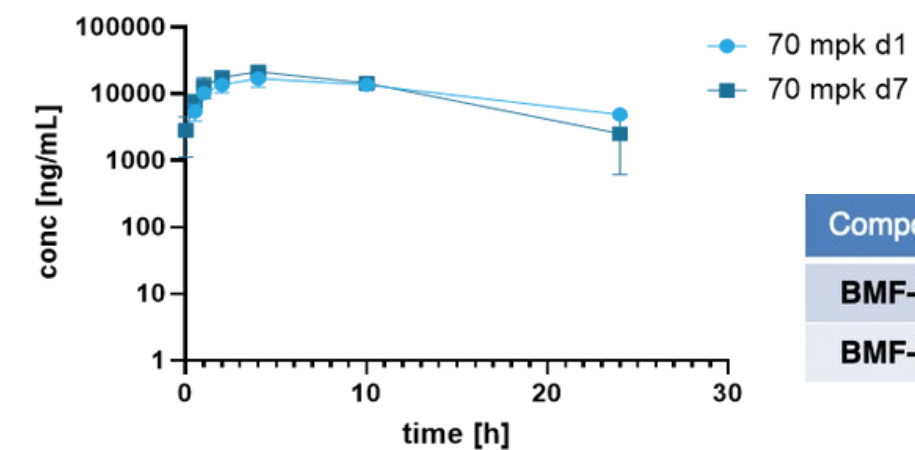
Dose Proportionate Exposure

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

SPRAGUEDAWLEY RAT PK DAYS 1, 7 BMF -650



Continuous Exposure after multiple days

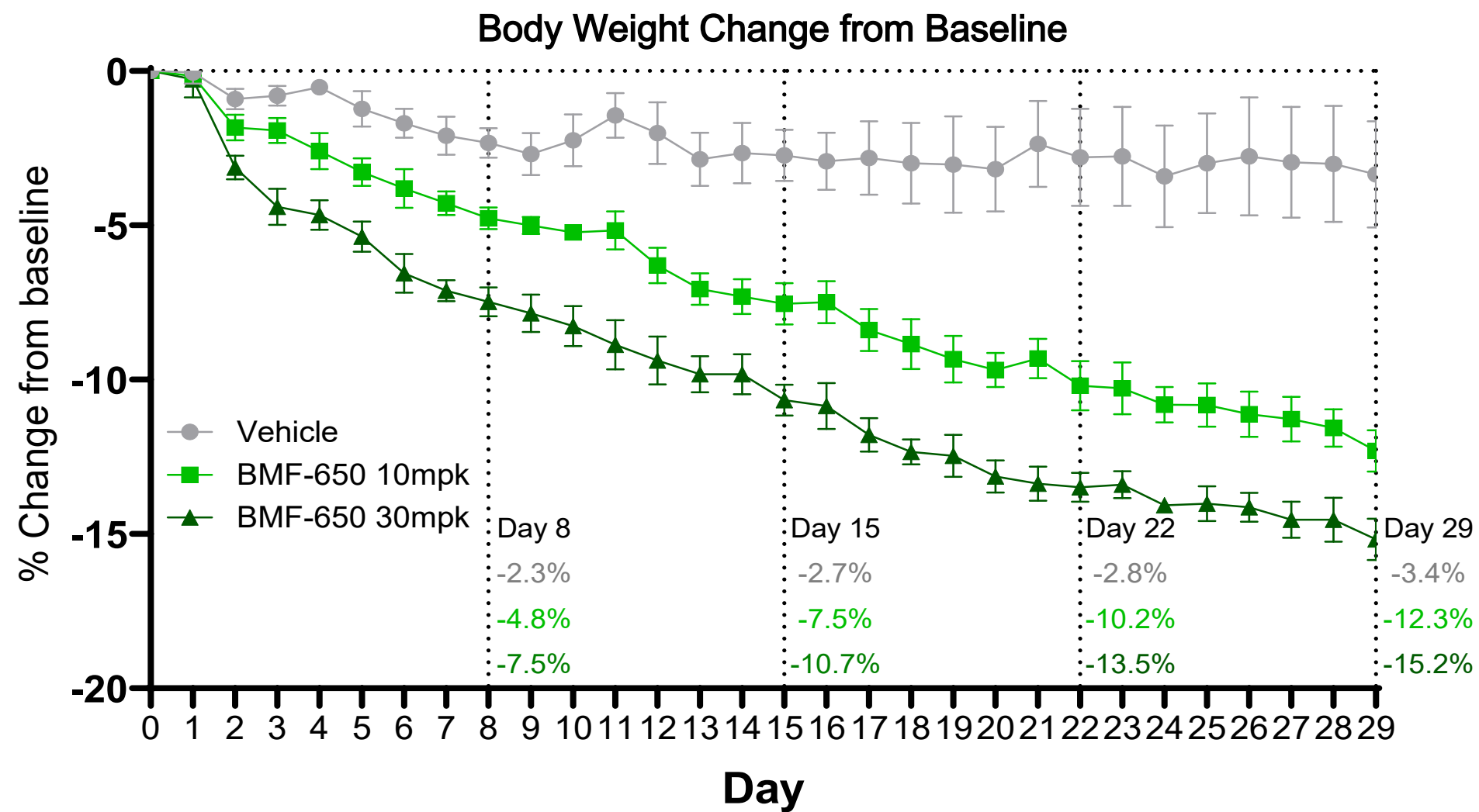
Compound	rat PO	day	AUC*
BMF-650	70 mg/kg	1	269,100
BMF-650	70 mg/kg	7	289,370



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



CT-996 body weight change

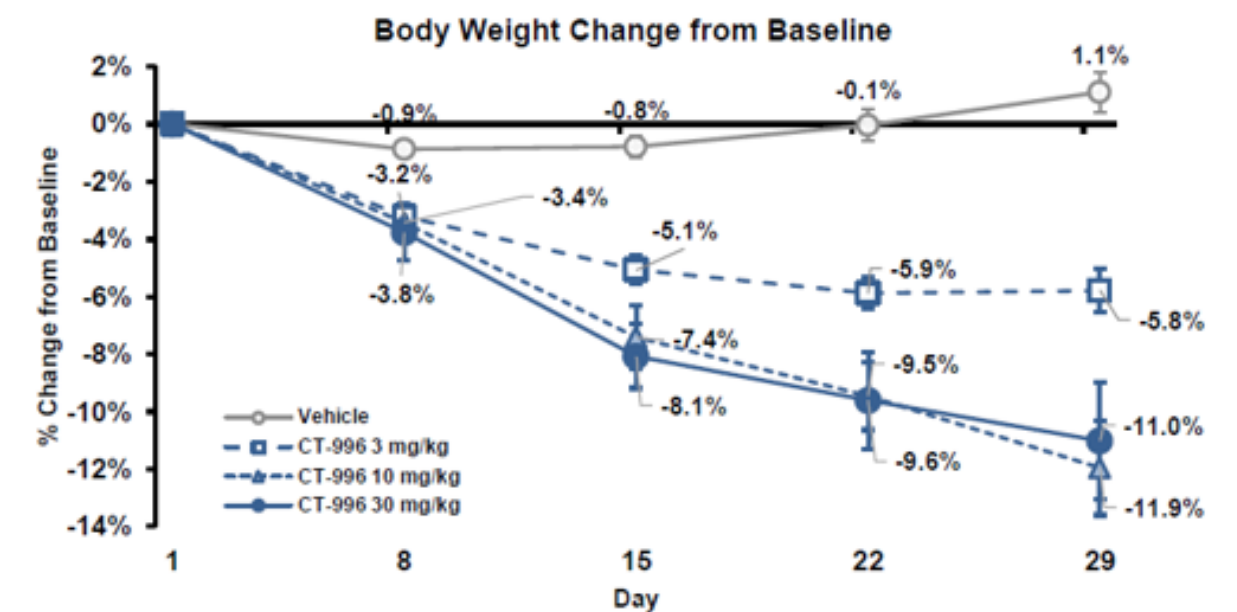


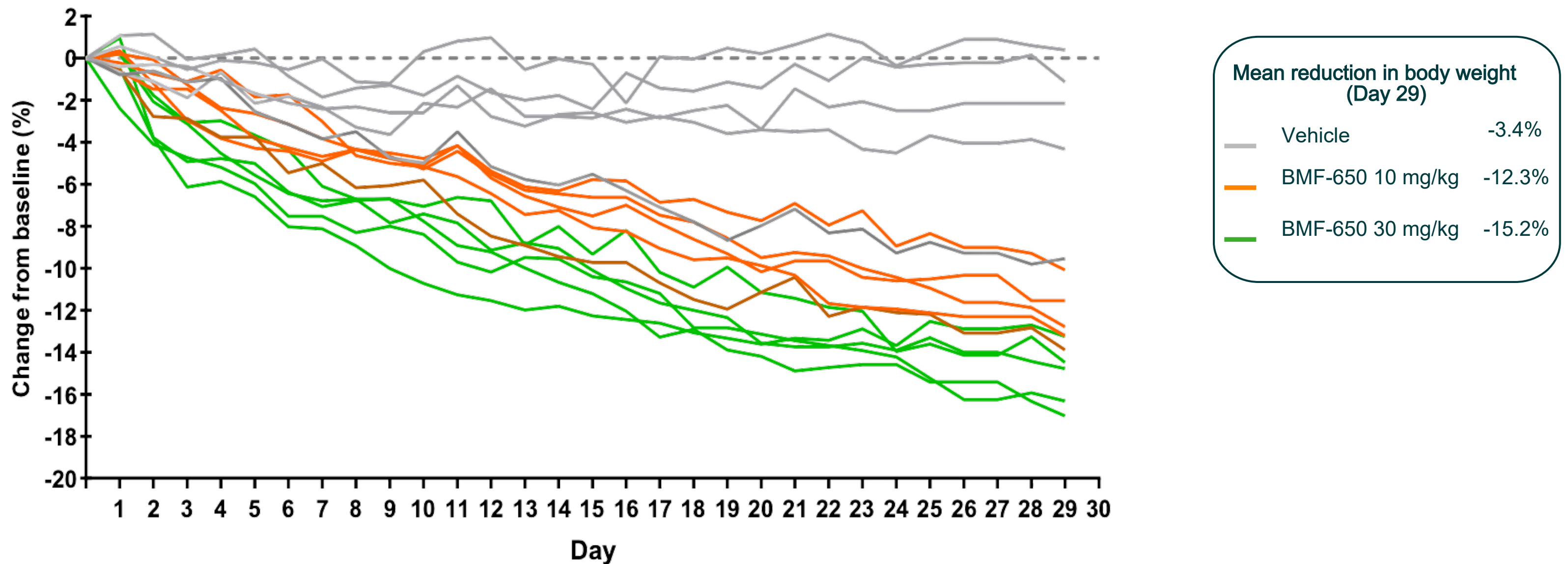
Figure 6. Effects of CT-996 on body weight in obese cynomolgus monkeys following once-daily oral administration. Weekly body weight percent change is represented as mean (± SE) from baseline. N = 6/group.

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, FIH 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/m ²)	Healthy overweight or obese patients (BMI 30.0–45.0 kg/m ²)
Design	<p>N=40 5 cohorts x </p>	<p>N=40 4 cohorts x </p> <p>COHORT</p> <p>7 DAYS → 7 DAYS → 7 DAYS → 21 DAYS</p> <p>4: 75 mg → 200 mg → 400 mg → 400 mg</p> <p>3: 75 mg → 150 mg → 300 mg → 300 mg</p> <p>2: 50 mg → 100 mg → 200 mg → 200 mg</p> <p>1: 10 mg → 25 mg → 50 mg → 100 mg</p> <p>Body weight at Baseline versus Day 28 and Day 42 on treatment</p>

BMF-650 active drug
 placebo

A randomized, double-blind, placebo-controlled, FIH 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/m ²)	Healthy overweight or obese patients (BMI 30.0–45.0 kg/m ²)
Design	<p>N=40 5 cohorts x </p>	<p>N=40 5 cohorts x </p> <p>COHORT 7 DAYS → 7 DAYS → 7 DAYS → 21 DAYS</p> <p>5 200 mg → 400 mg</p> <p>4 75 mg → 200 mg → 400 mg → 400 mg</p> <p>3 75 mg → 150 mg → 300 mg → 300 mg</p> <p>2 50 mg → 100 mg → 200 mg → 200 mg</p> <p>1 10 mg → 25 mg → 50 mg → 100 mg</p>

Body weight at Day 29 and Day 43 versus Baseline

BMF-650 active drug
 placebo

Biomea pipeline

Biomea Fusion retains full worldwide rights across all programs and is currently funded through major catalysts into 1Q 2027

PROGRAM	INDICATION	PHASE I	PHASE II	PHASE III	UPCOMING MILESTONES
ICOVAMENIB Potential first-in-class oral menin inhibitor	Type 2 diabetes Patients with insulin deficiency (~7M U.S. Patients) ¹		COVALENT-211 (study enrolling)		Phase II 26-week data (primary endpoint) anticipated 4Q 2026
	Type 2 diabetes Patients not controlled on GLP-1 based therapies (15-45% U.S. Patients on GLP-1RA) ^{2,3}		COVALENT-212 (study enrolling)		Phase II 26-week data (primary endpoint) anticipated 4Q 2026
ICOVAMENIB with low dose Semaglutide	Obesity/Overweight (>190M U.S. Patients) ⁵ Sponsored by Leicester Diabetes Center		OPAL Study		Phase II initiation anticipated in 2H 2026
BMF-650 Potential best-in-class oral GLP-1 RA	Obesity (>100M U.S. Patients) ⁵		GLP-131 (study enrolling)		Phase I 28-day weight reduction data anticipated in 3Q 2026

1. International Diabetes Federation. IDF Diabetes Atlas www.diabetesatlas.org (Based on company calculations)

2. NHANES analyses of glycemic control among U.S. adults with diabetes (JAMA; Diabetes Care);

3. SUSTAIN, AWARD, and SURPASS clinical trial programs for GLP-1 receptor agonists

4. Mayer-Davis et al., NEJM / CDC updates

5. National Center for Health Statistics August 2023. [Accessed June 10, 2026](#)

THANK YOU (NASDAQ: BMEA)

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

www.biomeafusion.com



KEY OPINION LEADERS HIGHLIGHT ICOVAMENIB'S POTENTIAL TO TRANSFORM DIABETES TREATMENT



“Icovamenib's recent data has shown an impressive restoration of beta cell function as demonstrated by significant elevations in C-peptide even after the treatment period ended.

This data validates the mechanism of action of this menin inhibitor as a disease modifying agent and helps address the poor adherence and persistence commonly seen in type 2 diabetes.”



Steve Edelman, M.D.

ENDOCRINOLOGIST, PROFESSOR OF MEDICINE UCSD / VA SAN DIEGO

“The icovamenib data looks exciting. The data presented today help to confirm icovamenib’s mechanism of action. We have not previously seen data like this with any antihyperglycemic agent.

As more trials are conducted, I believe that inhibition of menin may lead to benefits across all subtypes of diabetes. I applaud Biomea for developing a potential new treatment option that may be disease modifying for patients with diabetes.”



Ralph DeFronzo, M.D.

ENDOCRINOLOGIST, PROFESSOR OF MEDICINE UTHSCSA

“Great foray into precision medicine. We need to be addressing patients in a much more individualized manner. By addressing insulin-deficient diabetes patients with icovamenib, we have seen post treatment that the beta cell pool is being restored and producing a higher level of insulin, as measured by C-peptide.

This indicates a fundamental and potentially lasting impact on the disease and validates the mechanism of action of menin inhibition.”



Melanie Davies, M.D.

DIABETOLOGIST, PROFESSOR OF DIABETES MEDICINE AT THE UNIVERSITY OF LEICESTER

KEY OPINION LEADERS HIGHLIGHT ICOVAMENIB'S POTENTIAL TO TRANSFORM DIABETES TREATMENT



“We do not have an agent today that addresses one of the root cause of diabetes - beta cell dysfunction - icovamenib would be the first.

Patients are achieving lasting benefits without continuous chronic dosing, suggesting that icovamenib may be disease modifying. I am very impressed.”



Alice Cheng, M.D.

ENDOCRINOLOGIST, ASSOCIATE
PROFESSOR OF MEDICINE
UNIVERSITY OF TORONTO

“The icovamenib data are quite interesting because of the continued effects despite having stopped it for 14 weeks.

Usually, one would expect to see the HbA1c levels climb towards baseline when the medication is stopped, but with icovamenib, the HbA1c levels decreased, which is quite intriguing and unprecedented.”



Julio Rosenstock, M.D.

DIRECTOR VELOCITY CLINICAL
RESEARCH AT MEDICAL CITY
DALLAS AND CLINICAL PROFESSOR
OF MEDICINE, UNIV. OF TEXAS
SOUTHWESTERN MEDICAL CENTER

“Icovamenib is a very interesting molecule that acts quite differently than anything I have seen before. We are observing glucose controlled and beta cell-specific proliferation and an increase in stimulated C-peptide secretion leading to patient benefits that continued after the icovamenib dosage ended.

I am very excited to further explore the many opportunities that the covalent inhibition of menin will provide to patients.”



**Rohit Kulkarni,
M.D., Ph.D.**

PROFESSOR OF MEDICINE AT
HARVARD MEDICAL SCHOOL

ADA 2026

Icovamenib in Type 1 Diabetes

Icovamenib, a Menin Inhibitor, Improves Endogenous Insulin Secretion in T1D: Results from the COVALENT-112 Study

Juan Pablo Frías, MD; Jeffrey Kim, PhD
Biomea Fusion, 1599 Industrial Road, San Carlos, CA 94070 USA

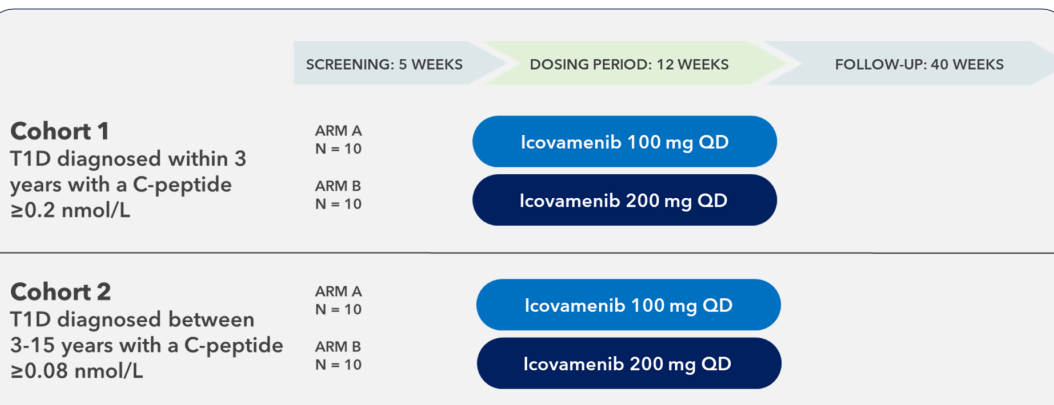


Background

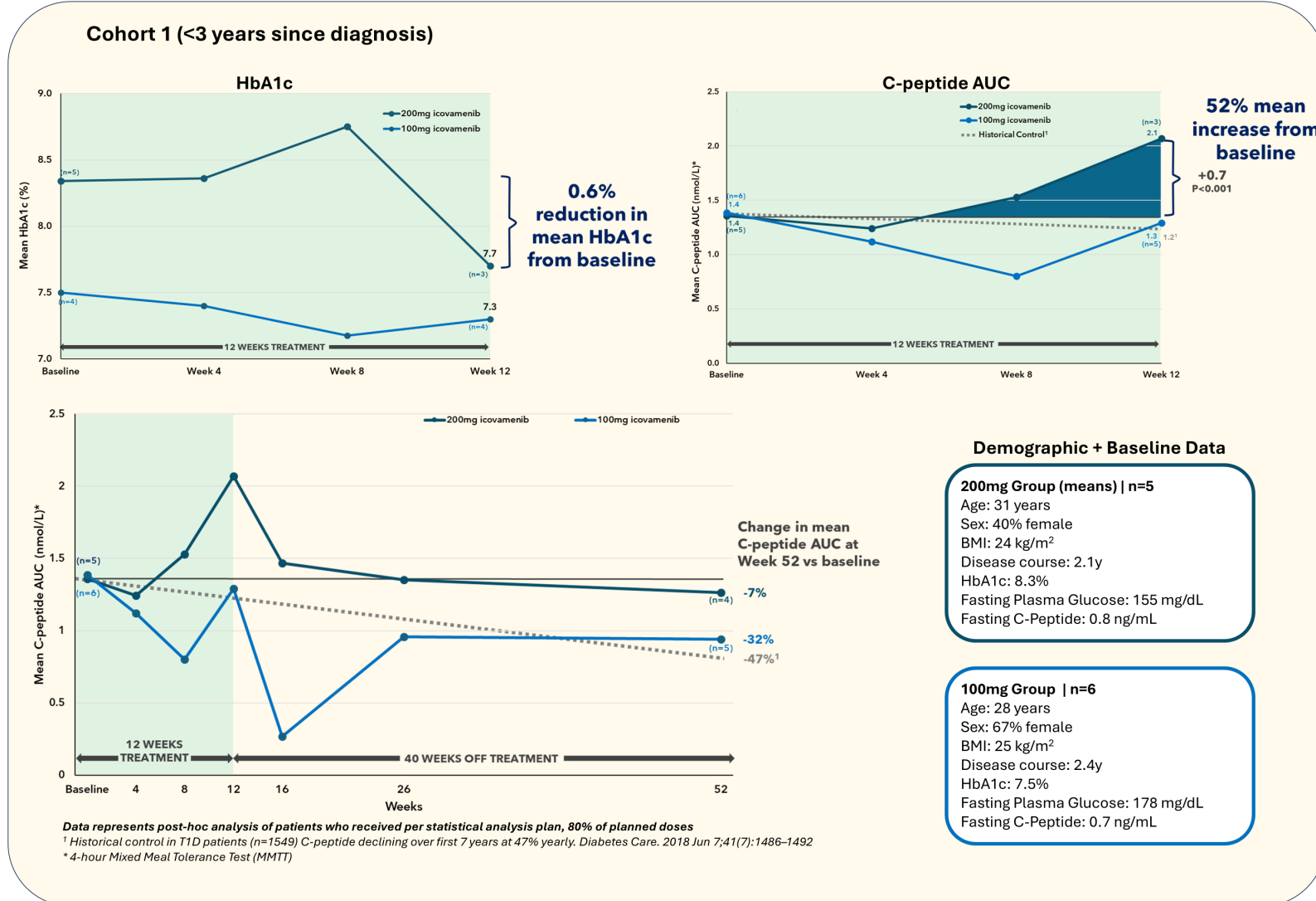
- Type 1 diabetes (T1D)** is characterized by progressive autoimmune loss of functional pancreatic beta-cell mass, leading to declining endogenous insulin secretion and chronic hyperglycemia
- Current Stage 3 T1D management remains centered on insulin replacement and diabetes technologies, which improve glycemic control but do not address beta-cell loss
- Disease-modifying approaches in Stage 3 T1D have primarily focused on preserving residual beta-cell function; while some have slowed C-peptide decline, they have not consistently demonstrated durable restoration or improvement of endogenous insulin secretion
- Therapies capable of restoring or sustainably improving beta-cell function remain a major unmet need
- Menin** is a scaffold protein that regulates gene expression and cell signaling in a tissue-specific manner. In pancreatic beta-cells, menin negatively regulates beta-cell proliferation and mass, supporting menin inhibition as a potential approach to enhance residual beta-cell function
- Icovamenib**, formerly BMF-219, is an orally administered investigational small molecule currently in Phase 2 clinical development for the treatment of T2D and T1D. Icovamenib targets menin and has been shown preclinically in both animal and ex vivo human islet studies to induce transient reductions in menin protein levels, thereby modulating pathways associated with insulin secretion and glycemic control
- COVALENT-112** evaluated icovamenib in adults with T1D to assess effects on endogenous insulin secretion
 - Enrollment, dosing exposure, and study completion were impacted by a temporary FDA clinical hold related to liver enzyme elevations, which was subsequently resolved

COVALENT-112: Study Overview

- COVALENT-112 (NCT06152042) is a phase 2 trial that was designed to examine beta-cell function (as measured by C-peptide change and glucose and lipid metabolism in participants with T1D treated with icovamenib
- COVALENT-112 was conducted in the US and Canada
- Enrollment, dosing exposure, and the final evaluable population in COVALENT-112 were affected by a temporary FDA clinical hold related to liver enzyme elevations, which was subsequently resolved



Results | HbA1c & C-peptide



Results | Cohort 1 Cytokine Profile

Cytokine	Week 12			Week 26			Week 52		
	pg/mL change	status	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. Cytokine profiling showed no evidence of systemic immune activation in Cohort 1 participants receiving 200 mg icovamenib
- All cytokines remained classified as Non-Inflammatory through Week 52
- 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
- These findings suggest that increased 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

Safety

Event	Cohort 1		Cohort 1 Total (N=17)	Cohort 2		Cohort 2 Total (N=19)
	Arm A 100 mg QD (N=8)	Arm B 200 mg QD (N=9)		Arm A 100 mg QD (N=9)	Arm B 200 mg QD (N=10)	
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

Summary

- Icovamenib was associated with preservation of endogenous insulin secretion among evaluable participants, with a directional response favoring 200 mg over 100 mg
- In Cohort 1 participants diagnosed with T1D <3 years, 200 mg icovamenib increased C-peptide AUC by ~52% at Week 12 versus baseline
- At Week 52, C-peptide AUC was ~7% below baseline, compared with a ~47% decline in historical placebo
- Cytokine profiling showed no evidence of systemic immune activation, with inflammatory markers stable or reduced through Week 52
- Overall, these findings suggest that menin inhibition may enhance or preserve residual β-cell function in T1D without a measurable systemic inflammatory cytokine response

References

- Butler T. et al. Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models. *Diabetes*, 2022 Jun 1; 71 (Supplement_1): 851-P.
- Somanath P. et al. Oral Menin Inhibitor, BMF-219, Displays a Significant and Durable Reduction in HbA1c in a Type 2 Diabetes Mellitus Rat Model. *Diabetes*, 2022 Jun 1; 71 (Supplement_1): 113-LB.
- Frías J. et al. BMF-219: A Novel Therapeutic Agent to Re-Establish Functional Beta Cells and Provide Long-Term Glycemic Control. *Metabolism-Clinical and Experimental*, 2024; 0088.
- Rodriguez J. et al. Durable Glycemic Control With BMF-219 During Off-treatment Period At Week 26: A Phase 1/2 Trial Of BMF-219 In Patients With Type 2 Diabetes. *Diabetes Technol Ther*, 2024; 26:S2: PD064.

Cohort 2 (3-15 years since diagnosis)

Demographic + Baseline Data

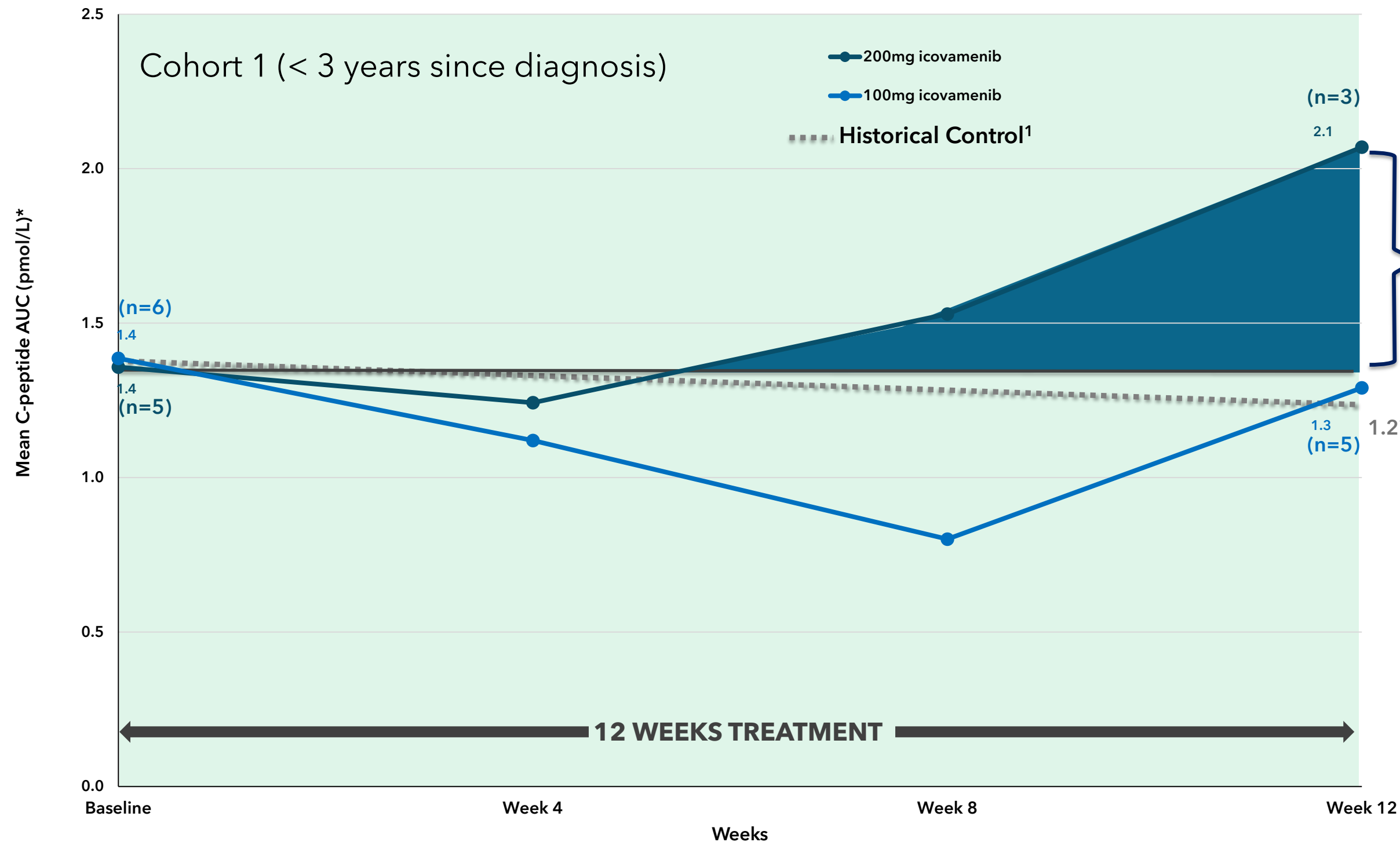
200mg Group (means) n=4 Age: 38 years Sex: 25% female BMI: 26 kg/m ² Disease course: 7y HbA1c: 7.3% Fasting Plasma Glucose: 120 mg/dL Fasting C-Peptide: 0.3 ng/mL	100mg Group n=5 Age: 37 years Sex: 60% female BMI: 25 kg/m ² Disease course: 10y HbA1c: 6.8% Fasting Plasma Glucose: 117 mg/dL Fasting C-Peptide: 0.4 ng/mL
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Key Findings

- Cohort 2 included participants with 3-15 years since T1D diagnosis, a population with potentially lower residual beta-cell reserve than those earlier in disease course.
- C-peptide AUC was relatively stable during the dosing period in both icovamenib dose groups.
- At Week 52, C-peptide AUC changed by -3.2% with 200 mg and -29.4% with 100 mg versus baseline.
- These findings suggest that longer-standing T1D may require additional dose and/or duration optimization to support durable preservation of endogenous insulin secretion.

Readout at Week 12

52% mean increase in C-peptide during the 12 weeks treatment period of icovamenib



52% mean increase from baseline

+0.7
P<0.001

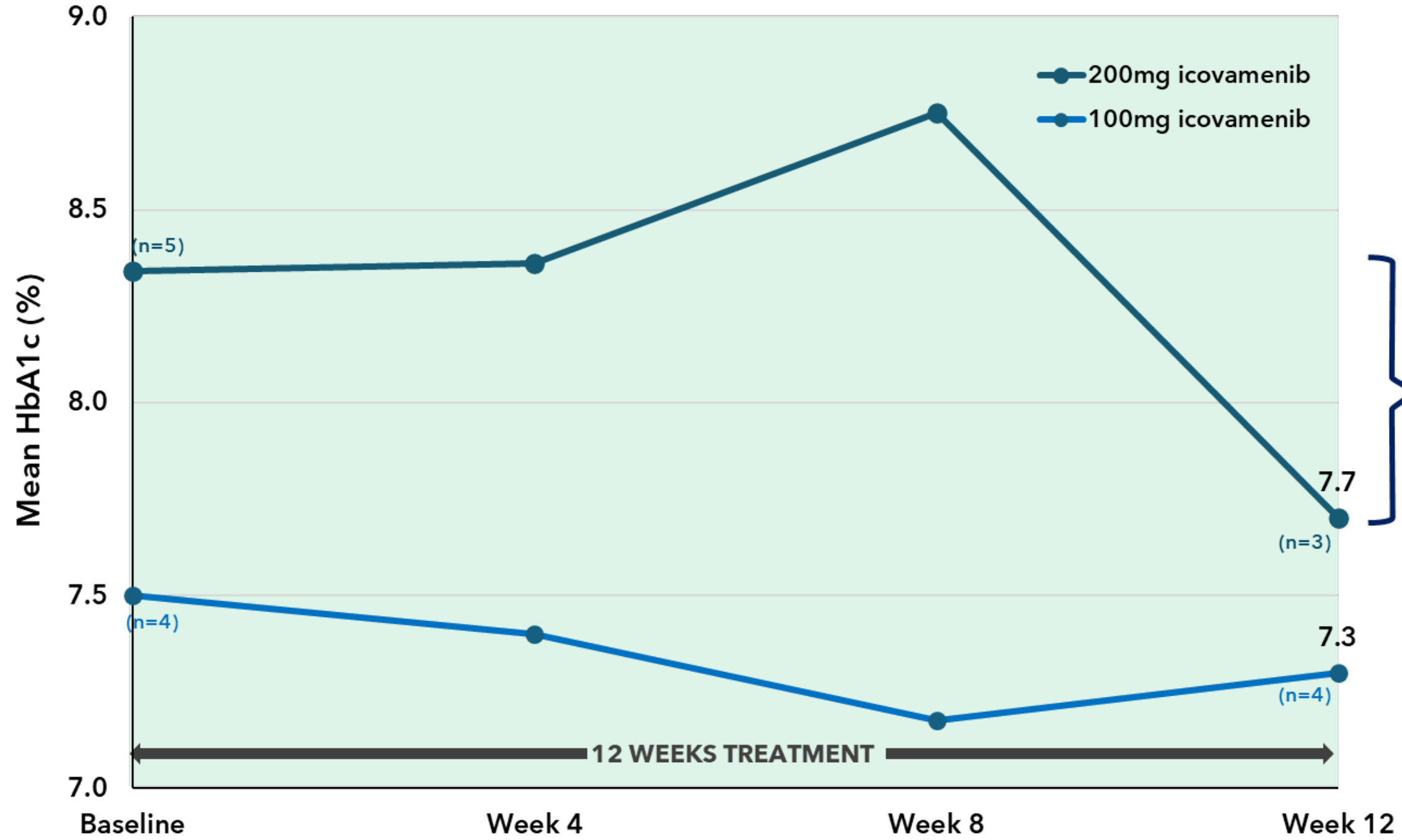
Data represents post-hoc analysis of patients who received per statistical analysis plan, 80% of planned doses

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)

Readout at Week 12

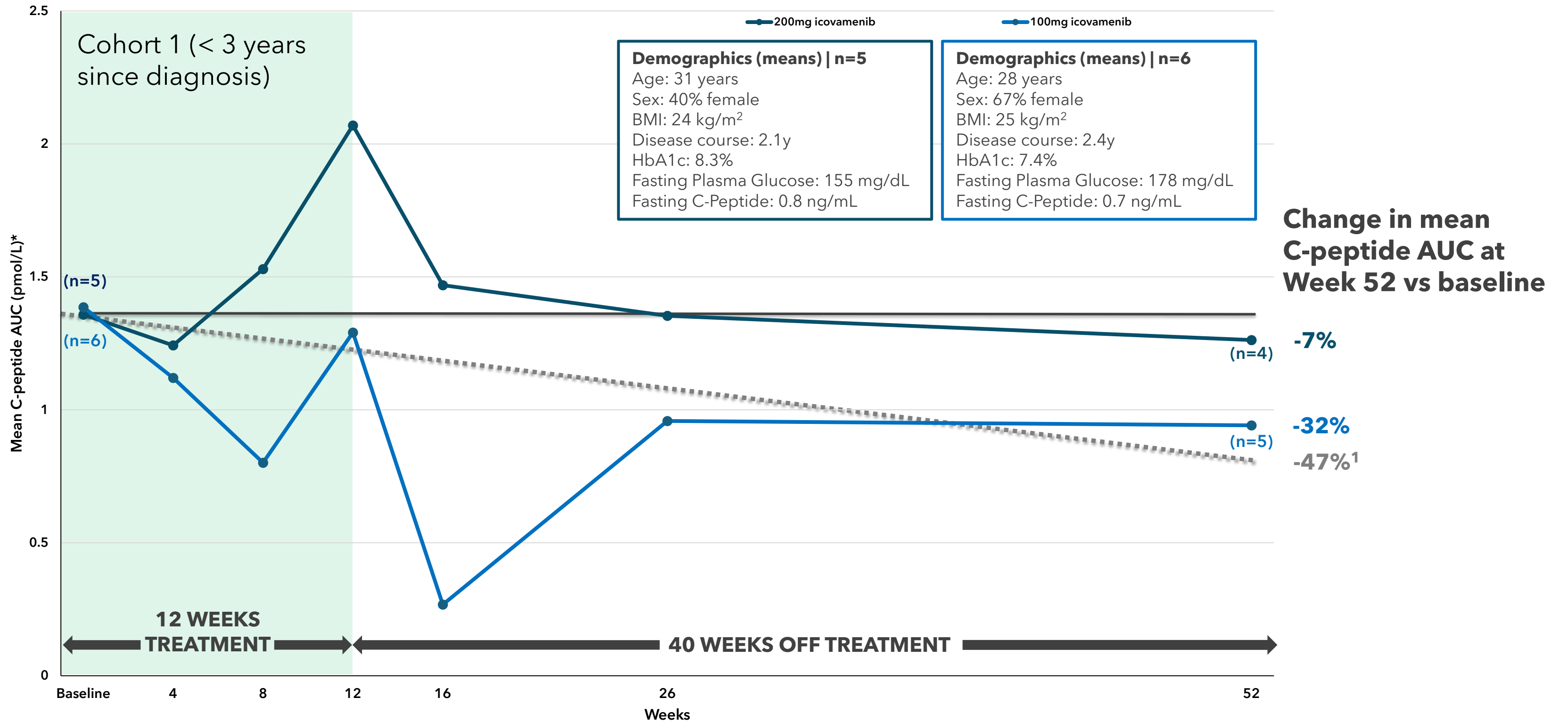
Reduction of HbA1c during the 12 weeks treatment period of icovamenib



0.6%
reduction in
mean HbA1c
from baseline

Readout at week 52

Baseline C-peptide levels sustained through week 52 with minimal decline (only -7.1%) observed post 12 weeks of 200mg daily icovamenib



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)

Cytokine Profiling of Cohort 1 (<3 year 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
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- Small Week 12 increases in IL-1 β , 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
- **These findings suggest that increased 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**

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)
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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

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- Overall, these findings suggest that menin inhibition may enhance or preserve residual β -cell function in T1D without a measurable systemic inflammatory cytokine response

ADA 2026

Icovamenib Supports Metabolic Health



Menin Inhibitor Icovamenib Activates Mechanisms That Support Metabolic Health

Nida Tanataweethum, Kung-Hsien Ho, Li Zhang and Mini Balakrishnan
Biomea Fusion, Inc., San Carlos, CA

Poster # 2871-LB

We Aim to Cure™

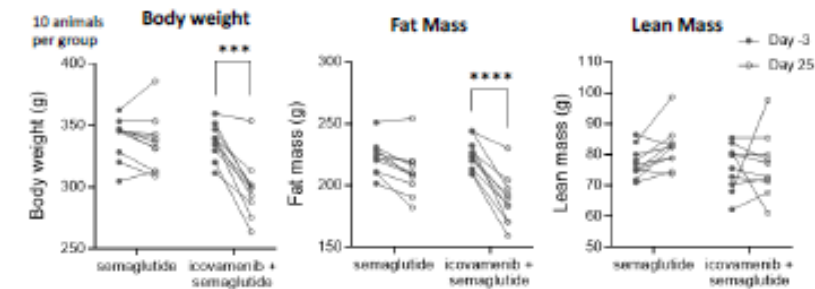
Background

- Icovamenib is an investigational, menin-targeted small-molecule oral drug candidate, currently in phase II clinical development for the treatment of type 1 diabetes (T1D) and type 2 diabetes (T2D).
- In T2D patients failing standard of care, a 12-week course of icovamenib resulted in durable HbA1c reduction and C-peptide increase through 52 weeks¹.
- Findings from non-clinical studies including studies in rodent models and ex vivo human islets indicate that icovamenib promotes glucose lowering through at least two distinct mechanisms: 1) increasing beta cell numbers and/or mass, and 2) enhancing the incretin effect (via increasing GLP-1 receptor and insulin expression).
- Menin interacts with transcription factors and chromatin-modifying complexes to modulate gene transcription, signaling pathways and cellular processes involved in glycemic control as well as metabolism.

Rationale

- Menin is a negative regulator of GIP (via inhibition of PI3K/AKT signaling), GLP-1 (via β -catenin), and GLP-1 receptor (via PRMT5) expression^{2,3,4}.
- Menin modulates signaling pathways critical for muscle health. Menin-depleted mice display increased intercostal muscle mass and enhanced myogenesis⁵.
- In STZ and ZDF rat models, icovamenib treatment induced modest appetite suppression and body weight reductions along with reductions in plasma triglyceride levels^{6,7}.
- In ZDF rats, the combination of icovamenib and low dose semaglutide induced greater body weight reduction driven by fat mass loss with preservation of lean mass⁸.

Combination Treatment of Icovamenib and Low Dose Semaglutide in ZDF Rats Induced Greater Body Weight Reduction, Driven by Fat Loss With Preservation of Lean Mass⁷



- References:
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 - Muhammad AB, Xing B, Liu C, et al. *Am J Physiol Endocrinol Metab* 2017; 313: E148-E156; doi:10.1152/ajpendo.00241.2016
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Figure 1: Icovamenib Enhanced GLP-1 Expression

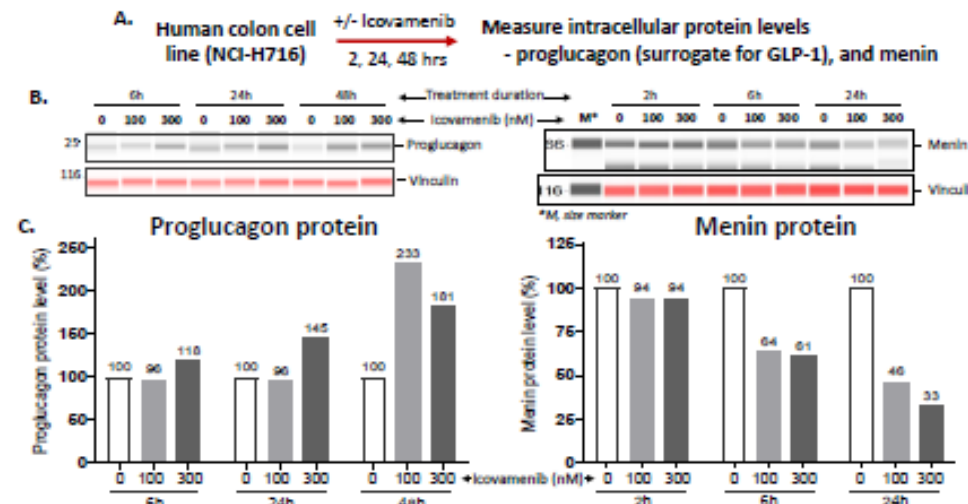


Figure 1. Icovamenib increases intracellular proglucagon expression in the human colon cell line NCI-H716. The human colon cell line NCI-H716 retains enteroendocrine characteristics and serves as an intestinal L cell model for studying GLP-1 expression and secretion. A) Schematic of the assay setup. Cells were cultured in the presence of icovamenib (100 nM or 300 nM) or vehicle and harvested at the specified time-points. Cell lysates were analyzed for proglucagon (surrogate for GLP-1) and menin protein levels by automated Western using JESS (ProteinSimple). B) Results from a representative experiment are shown. Vinculin served as the loading control. C) Bar charts depict the quantified results for intracellular levels of proglucagon (left) and menin (right) protein. The % protein in the icovamenib-treated samples are plotted relative to the protein level in the vehicle (DMSO)-treated samples.

Figure 2: Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes

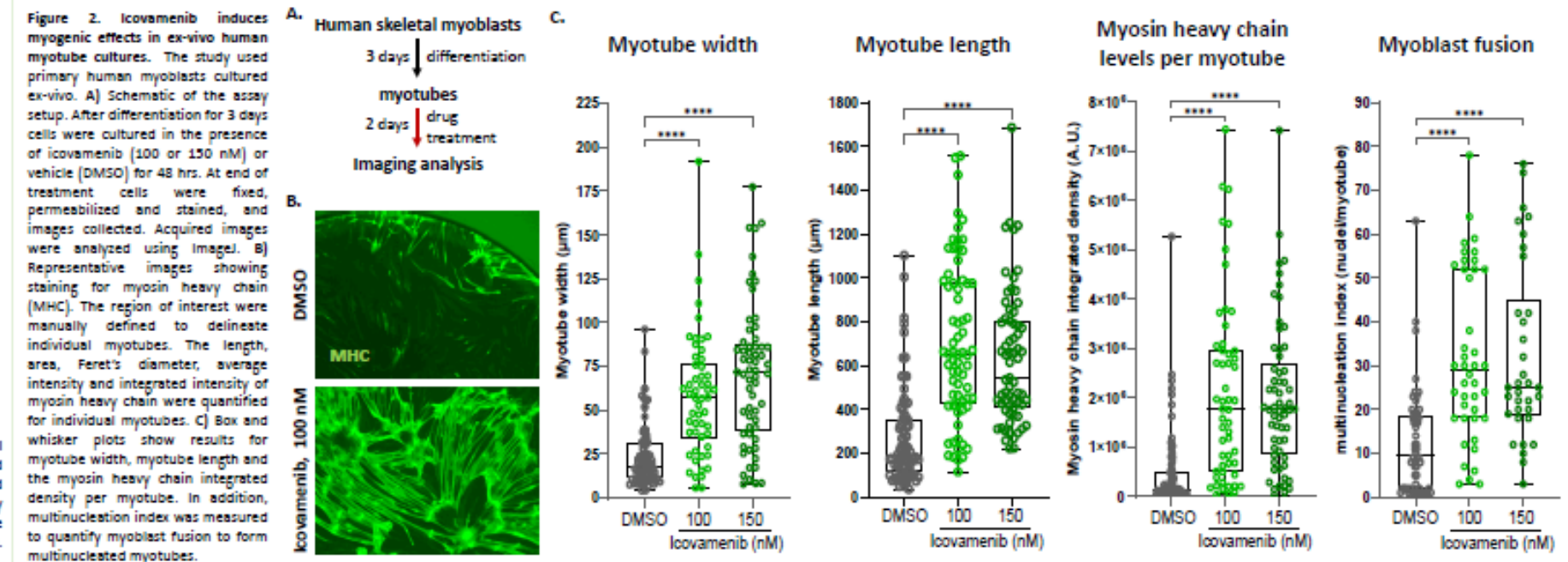


Figure 2. Icovamenib induces myogenic effects in ex-vivo human myotube cultures. The study used primary human myoblasts cultured ex-vivo. A) Schematic of the assay setup. After differentiation for 3 days cells were cultured in the presence of icovamenib (100 or 150 nM) or vehicle (DMSO) for 48 hrs. At end of treatment cells were fixed, permeabilized and stained, and images collected. Acquired images were analyzed using ImageJ. B) Representative images showing staining for myosin heavy chain (MHC). The region of interest were manually defined to delineate individual myotubes. The length, area, Feret's diameter, average intensity and integrated intensity of myosin heavy chain were quantified for individual myotubes. C) Box and whisker plots show results for myotube width, myotube length and the myosin heavy chain integrated density per myotube. In addition, multinucleation index was measured to quantify myoblast fusion to form multinucleated myotubes.

Figure 3: Icovamenib Promoted Lipolysis and Fat Browning in Human Adipose Tissue

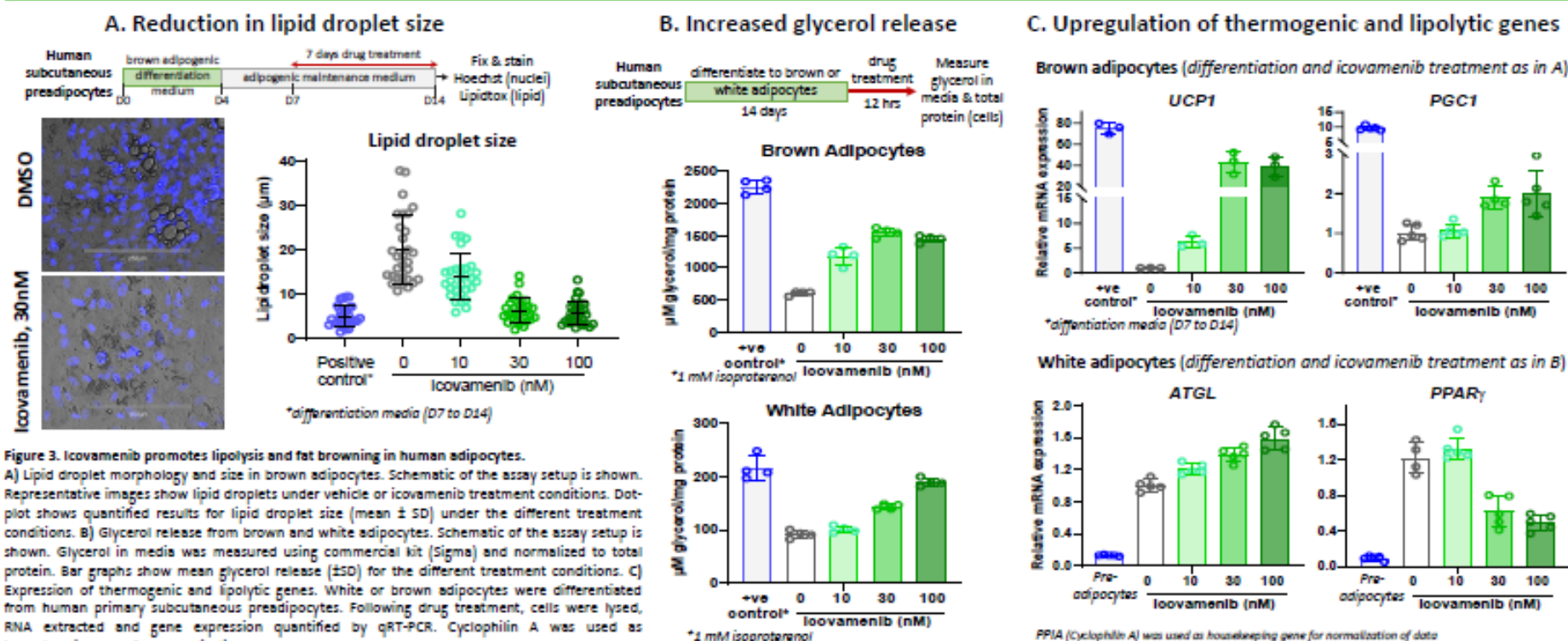


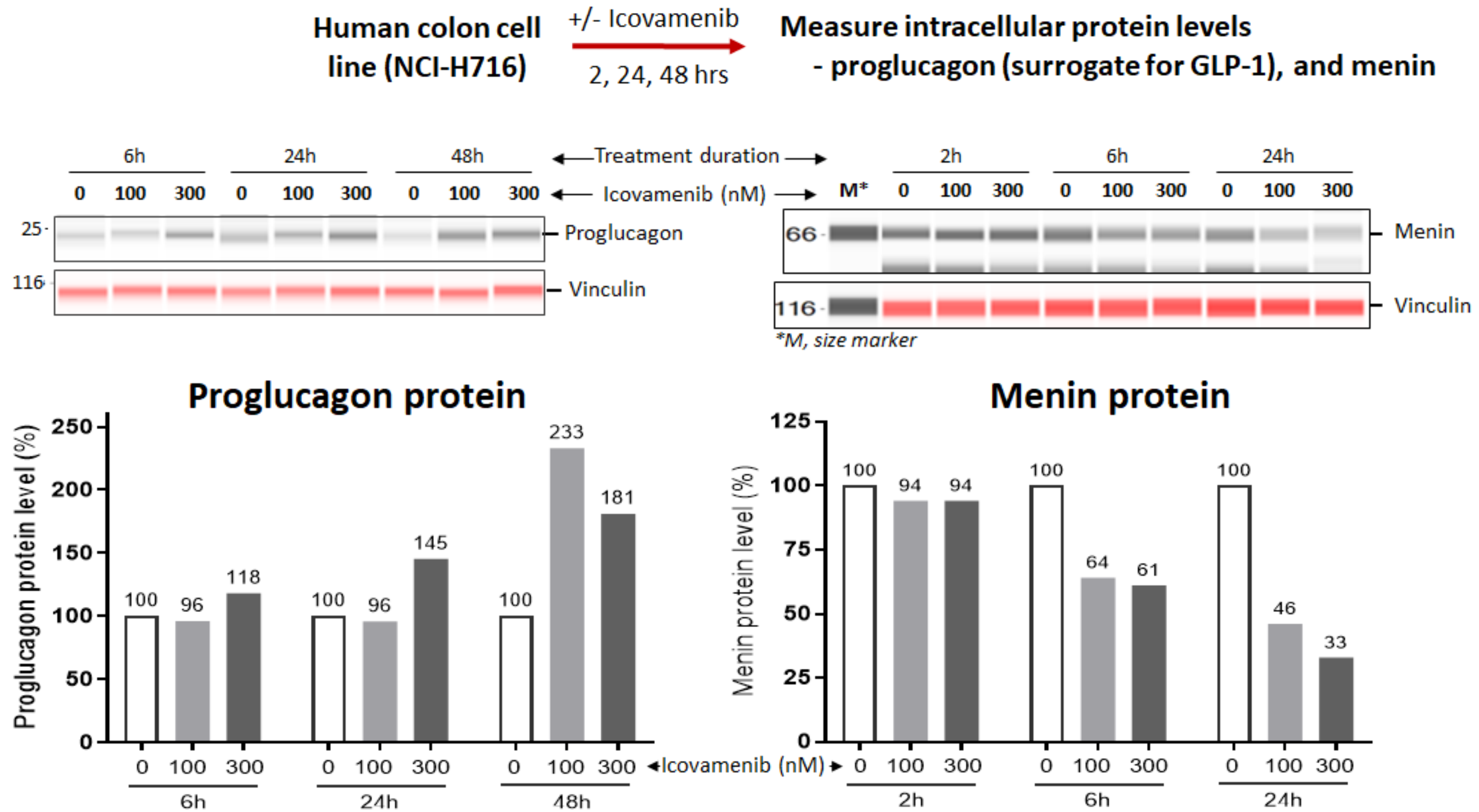
Figure 3. Icovamenib promotes lipolysis and fat browning in human adipocytes. A) Lipid droplet morphology and size in brown adipocytes. Schematic of the assay setup is shown. Representative images show lipid droplets under vehicle or icovamenib treatment conditions. Dot-plot shows quantified results for lipid droplet size (mean \pm SD) under the different treatment conditions. B) Glycerol release from brown and white adipocytes. Schematic of the assay setup is shown. Glycerol in media was measured using commercial kit (Sigma) and normalized to total protein. Bar graphs show mean glycerol release (\pm SD) for the different treatment conditions. C) Expression of thermogenic and lipolytic genes. White or brown adipocytes were differentiated from human primary subcutaneous preadipocytes. Following drug treatment, cells were lysed, RNA extracted and gene expression quantified by qRT-PCR. Cyclophilin A was used as housekeeping gene for normalization.

Conclusions

The overall findings provide insights into icovamenib's potential to activate mechanisms that support metabolic health, including enhancing glycemic control, fat reduction and muscle preservation.

- Icovamenib induced dose-dependent increase in GLP-1 expression in the human colon cell line as well as GLP-1 receptor expression in human islets⁹, properties that can promote incretin effects.
- In primary human skeletal myoblast-derived myotubes, icovamenib induced myogenic effects evidenced by:
 - dose-dependent increase in myotube width and length
 - upregulation of myosin heavy chain protein levels, and
 - increased myoblast fusion to form multinucleated myotubes
- Icovamenib promoted adipocyte browning and lipolysis evidenced by:
 - reduction in lipid droplet size
 - increased glycerol release, and
 - modulation of UCP1, PGC1, ATGL and PPAR γ , key molecular regulators in triglyceride hydrolysis and energy metabolism
- Collectively these findings suggest that icovamenib activates complimentary biological pathways promoting metabolic health and support icovamenib's potential for treating obesity in addition to diabetes. These observations warrant further evaluation of icovamenib as part of combination therapy approaches with GLP-based agents.

Icovamenib Enhanced Intracellular Proglucagon Expression in a Human Colon L-cell Model



Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes

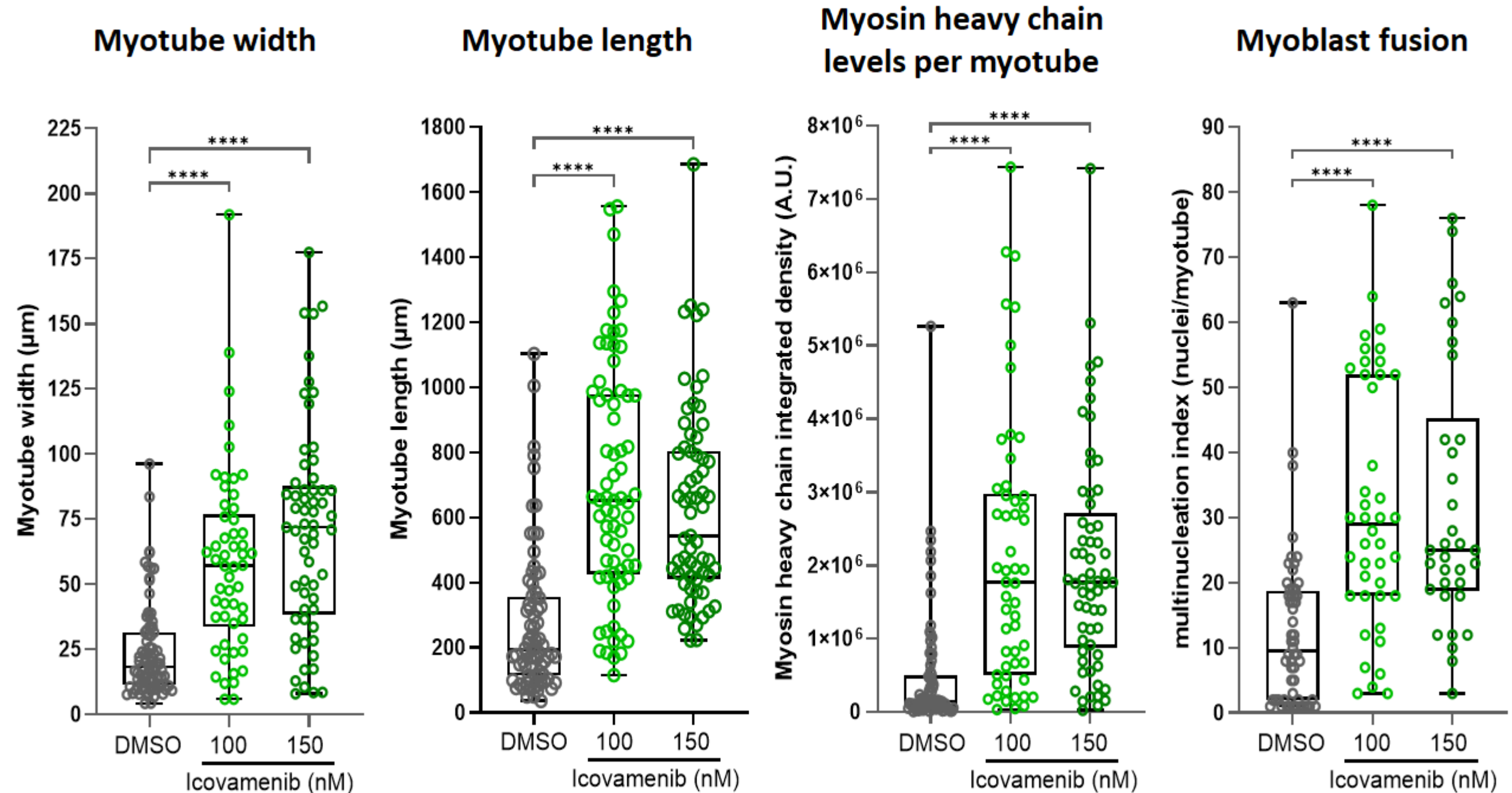
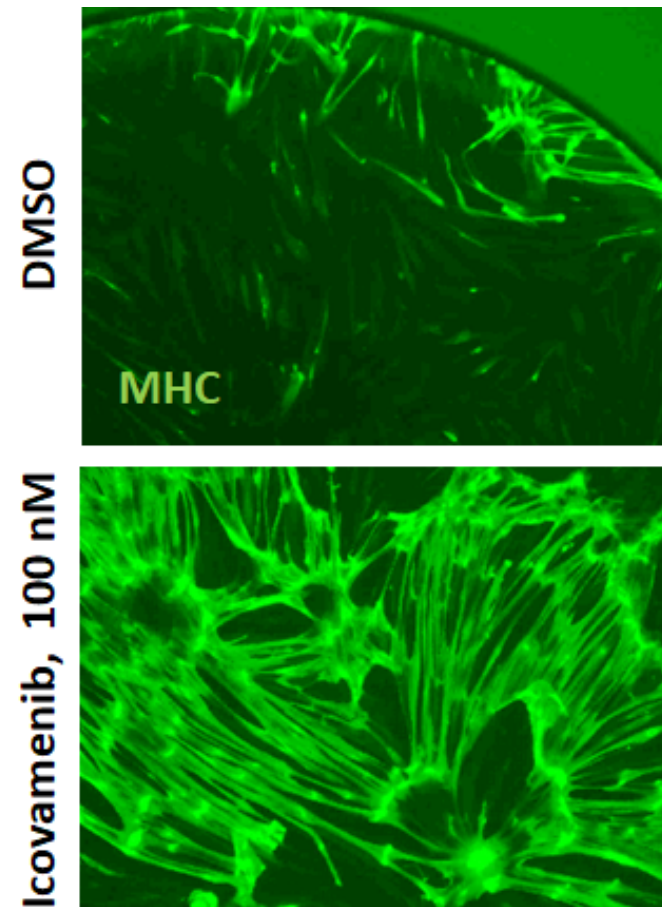
Human skeletal myoblasts

3 days ↓ differentiation

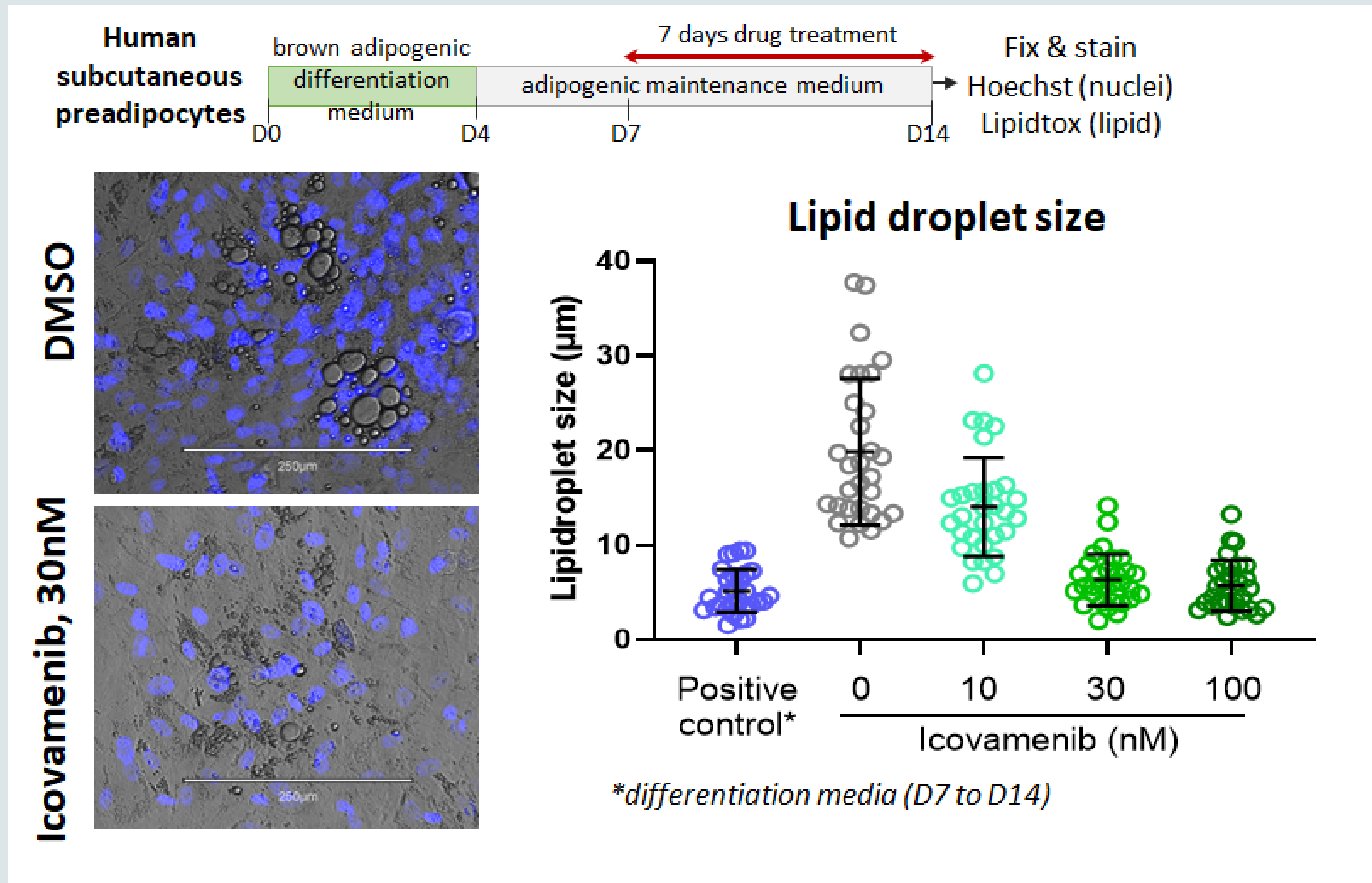
myotubes

2 days ↓ drug treatment

Imaging analysis

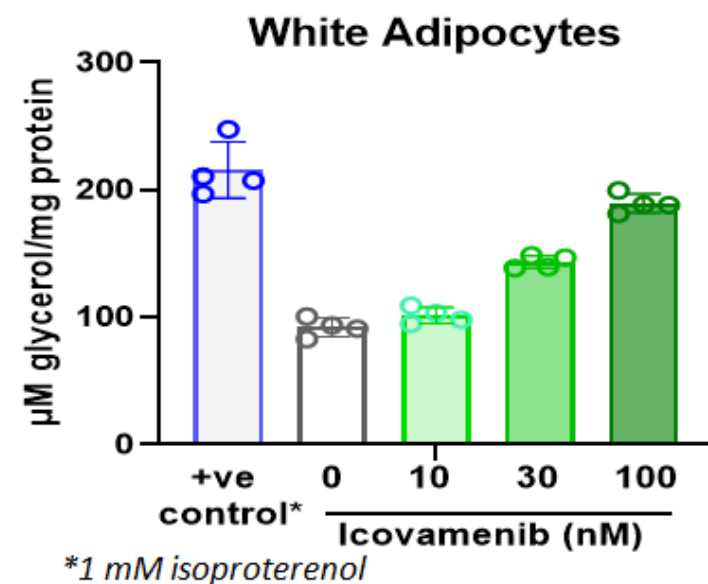
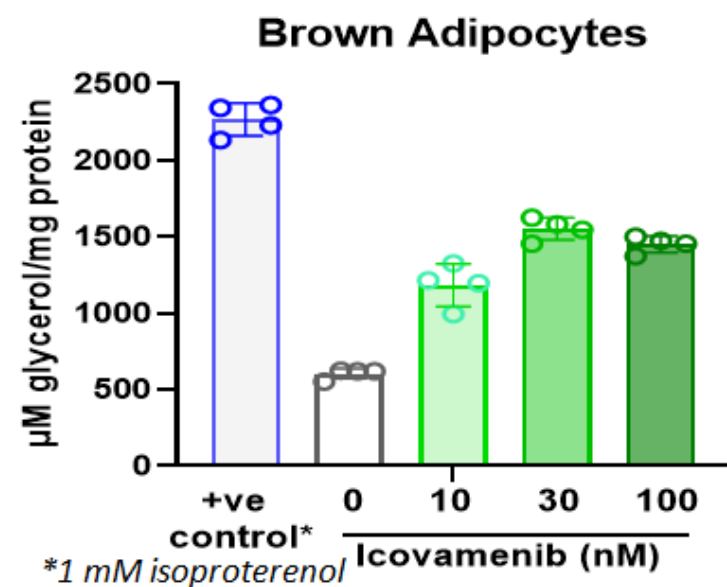
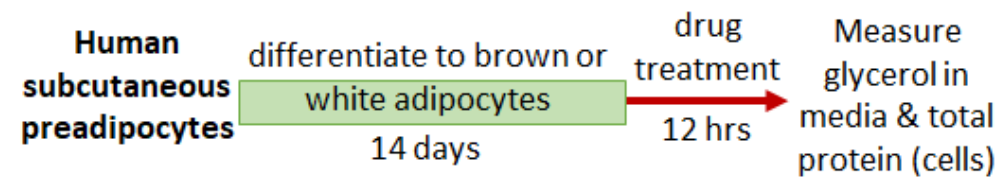


Icovamenib Promoted Lipolysis in Primary Human Adipocytes



Icovamenib Promoted Effects Indicative of Lipolysis and Fat Browning in Primary Human Adipocytes

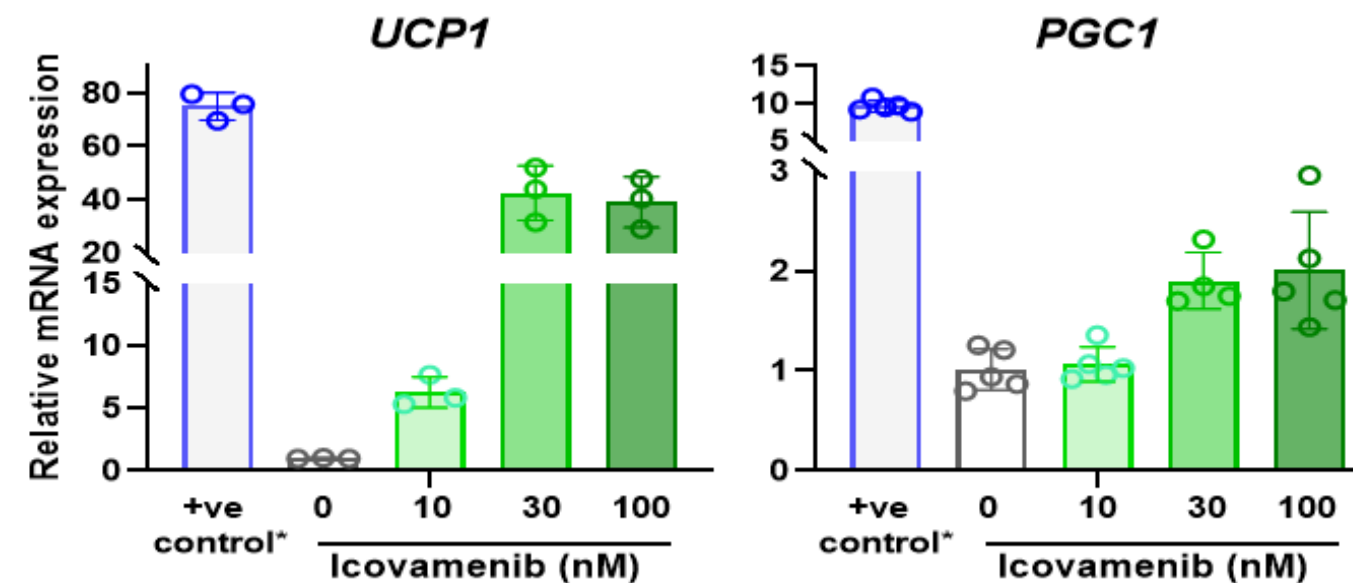
Enhanced Glycerol Release



Upregulation of thermogenic and lipolytic genes

Human Brown Adipocytes

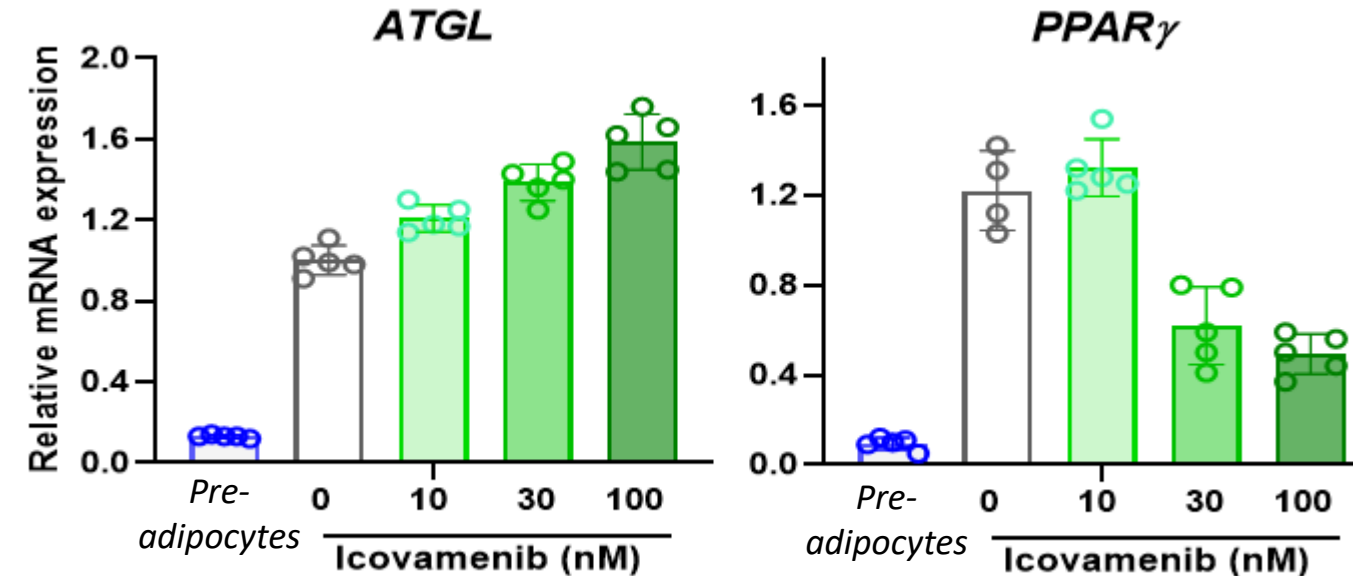
(differentiated from primary subcutaneous preadipocytes)



*differentiation media (D7 to D14)

Human White Adipocytes

(differentiated from primary subcutaneous preadipocytes)



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

Conclusions

The overall findings provide insights into icovamenib's potential to activate mechanisms that support metabolic health, including enhancing glycemic control, fat reduction and muscle preservation:

- ❑ Icovamenib induced dose-dependent increase in GLP-1 expression in the human colon cell line as well as GLP-1 receptor expression in human islets¹, properties that can promote incretin effects.
- ❑ In primary human skeletal myoblast-derived myotubes, icovamenib induced myogenic effects evidenced by:
 - dose-dependent increase in myotube width and length
 - upregulation of myosin heavy chain protein levels, and
 - increased myoblast fusion to form multinucleated myotubes
- ❑ Icovamenib promoted adipocyte browning and lipolysis evidenced by:
 - reduction in lipid droplet size
 - increased glycerol release, and
 - modulation of UCP1, PGC1, ATGL and PPAR γ , key molecular regulators in triglyceride hydrolysis and energy metabolism
- ❑ Collectively these findings suggest that icovamenib activates complimentary biological pathways promoting metabolic health and support icovamenib's potential for treating obesity in addition to diabetes. These observations warrant further evaluation of icovamenib as part of combination therapy approaches with GLP-1 based agents.

1. Balakrishnan M. et al. *Metabolism* 2025;168. doi:10.1016/j.metabol.2025.156226

ADA 2026

Icovamenib in Type 2 Diabetes with GLP-1 RA

Glycemic Improvements with Icovamenib in Adults with T2D Receiving Background GLP-1 Therapy: Subgroup Analysis from the COVALENT-111 Study

2026-LB-2857

We Aim to Cure™

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Background

Type 2 Diabetes (T2D) and Beta-Cell Dysfunction

- T2D is characterized by hyperglycemia driven by a progressive loss of beta-cell mass and insulin secretory capacity
- At diagnosis, beta-cell function is often reduced by >50%, with further decline over the disease course¹
- Most standard therapies improve glycemia but do not address the underlying loss of insulin-producing beta cells
- As beta-cell function worsens, many patients ultimately require lifelong insulin therapy, which can be associated with hypoglycemia risk, weight gain, and patient burden related to injections and monitoring
- Although GLP-1 receptor agonists improve glycemia and provide important metabolic benefits, many individuals with T2D remain above glycemic targets despite GLP-1 RA-based therapy

Menin: A Negative Regulator of Beta-Cell Regeneration

- Menin is a scaffold protein that regulates gene expression through multiple protein complexes
- In beta cells, menin acts as a key repressor of proliferation and adaptive expansion, maintaining them in a quiescent state
- Hyperglycemia and metabolic stress strengthen this menin-driven repression, creating a biological brake on beta-cell recovery

Icovamenib: A Selective Oral Menin Inhibitor

- Icovamenib is an orally administered investigational small molecule currently in Phase 2 clinical development for the treatment of T2D and T1D
- Icovamenib targets menin and has been shown preclinically in both animal and ex vivo human islet studies to induce transient reductions in menin protein levels, thereby modulating pathways associated with insulin secretion and glycemic control
- In diabetic rodent models, short-course icovamenib led to sustained, treatment-free glycemic improvements^{2,3}
- In human islet microtissues, icovamenib induced dose- and duration-dependent beta-cell proliferation under hyperglycemic conditions⁴

Clinical Rationale

- COVALENT-111 results showed short-term icovamenib dosing (4-12 weeks) to lead to continued HbA1c improvements for months after treatment cessation, together with increases in C-peptide, consistent with enhanced beta-cell function⁵
- This subgroup analysis evaluated whether icovamenib provided additional glycemic benefit in adults with T2D who were receiving stable background GLP-1 RA therapy at baseline

Safety | Treatment Emergent Adverse Events

Parameter	Pooled Placebo (N=4)	Icovamenib Combined arms (N=12)	Arm A icovamenib (N=3)	Arm B icovamenib (N=3)	Arm C icovamenib (N=6)
Patients with ≥1 TEAE, N (%)	3 (75)	3 (25)	1 (33)	1 (33)	1 (17)
Treatment-Related SAEs, N (%)	1 (25)	1 (8)	1 (33)	0	0
SAEs*, N (%)	0	0	0	0	0
Treatment Discontinuation due to TEAE, N (%)	0	0	0	0	0
Study Discontinuation due to TEAE, N (%)	0	0	0	0	0
Deaths, N (%)	0	0	0	0	0
Diarrhea, N (%)	1 (25)	1 (8)	1 (33)	0 (0)	0 (0)
Nausea, N (%)	1 (25)	0	0	0	0
Hyperglycemia, N (%)	0	0	0	0	0
Headache, N (%)	0	0	0	0	0
AST/ALT increase, N (%)	2 (50)	5 (42)	1 (33)	1 (33)	3 (50)
Resolution of ALT/AST w/o interruption in study treatment, %	100	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
ALT, alanine aminotransferase; AST, aspartate aminotransferase

AST/ALT increase: In the icovamenib arms, 4 of the 5 events were Grade 1 and 1 event was Grade 2 (Arm C)

- Icovamenib was generally well tolerated in participants receiving background GLP-1 RA therapy
- No serious adverse events or discontinuations due to adverse events were reported in this subgroup
- No new safety signals were identified. The safety profile was consistent with the overall COVALENT-111 study population

COVALENT-111 (Expansion Phase): Study Overview & Design

Study Design

- 52-week, randomized, double-blind, placebo-controlled

Key Eligibility Criteria

- Adults (18-65 years) with T2D (<7 years)
- HbA1c 7.0-10.5%
- BMI 25-40 kg/m²
- Treated with up to 3 antihyperglycemic agents (excluding insulin and SFUs)

Per Protocol Population* N=161

- Icovamenib N=105
- Placebo N=56
- Icovamenib + GLP-1RA (background) N=12
- Placebo + GLP-1RA (background) N=4

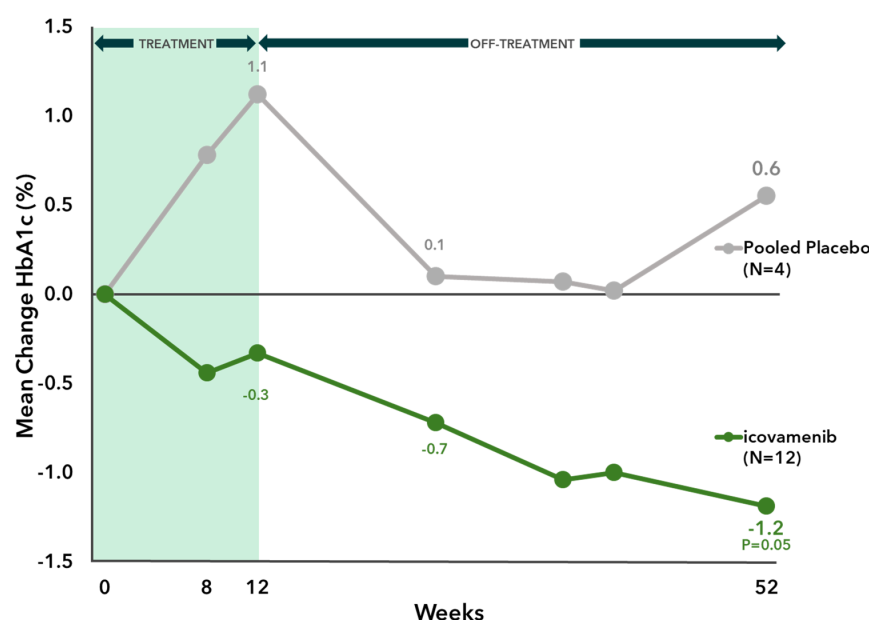
Primary Endpoints

- Change in HbA1c from baseline at Week 26
- Safety and tolerability at Week 52

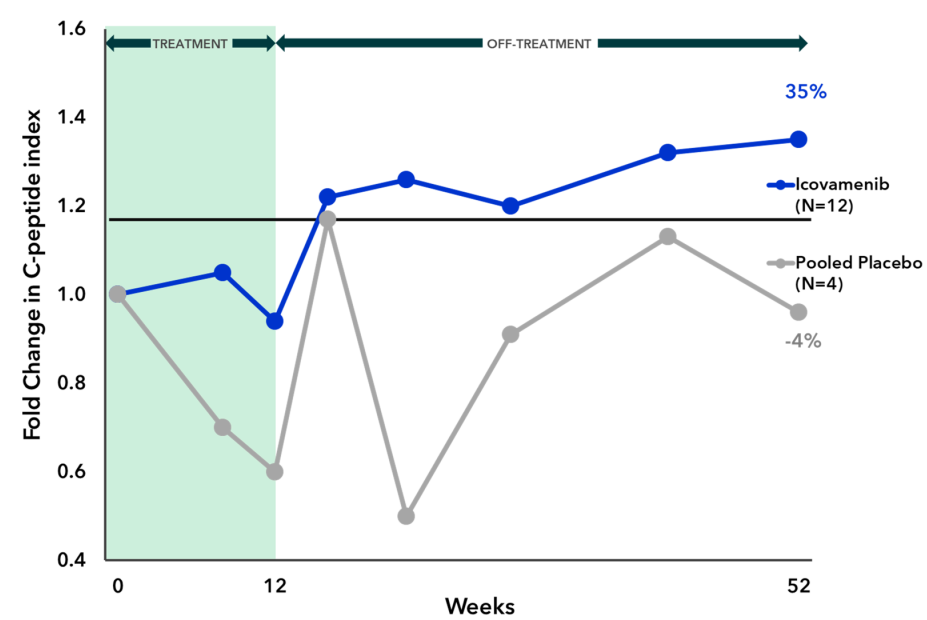
Characteristic	Icovamenib (n=12)	Placebo (n=4)
Age, years	53 ± 9	58 ± 9
T2D duration, years	5.4 ± 0.8	4.8 ± 2.6
HbA1c, %	8.4 ± 0.9	7.9 ± 0.3
BMI, kg/m ²	35.1 ± 3.3	32.5 ± 3.5

*Reduction in study population impacted by FDA hold and major protocol deviations related to quality and study conduct at certain clinical trial sites

Short-term Dosing Resulted in Lasting Benefit Through 52 Weeks



Patients on GLP-1 based therapy not achieving HbA1c target at baseline demonstrated durable and clinically meaningful persistent decline in HbA1c through Week 52 (9 months after last dose)



Icovamenib increased insulin secretion (C-peptide index) in GLP-1 RA treated patients (9 months post last dose)

Conclusions

- In adults with T2D receiving background GLP-1 RA therapy, icovamenib demonstrated durable HbA1c improvement through Week 52, 40 weeks after treatment discontinuation
- At Week 52, HbA1c decreased by 1.2% with icovamenib versus an increase of 0.6% with placebo, corresponding to a clinically meaningful 1.8% placebo-adjusted reduction, comparable to leading therapies
- An increase in C-peptide index compared to placebo points to the mechanism driving the improved glycemia
- Icovamenib was generally well tolerated, with no serious AEs, no AE-related discontinuations, and no new safety signals, supporting further evaluation as a beta-cell-directed therapeutic approach for T2D
- These findings suggest icovamenib may provide additional glycemic benefit when used alongside GLP-1-based therapy
- The results support further evaluation of icovamenib as a directed therapeutic approach for patients with T2D not achieving glycemic targets

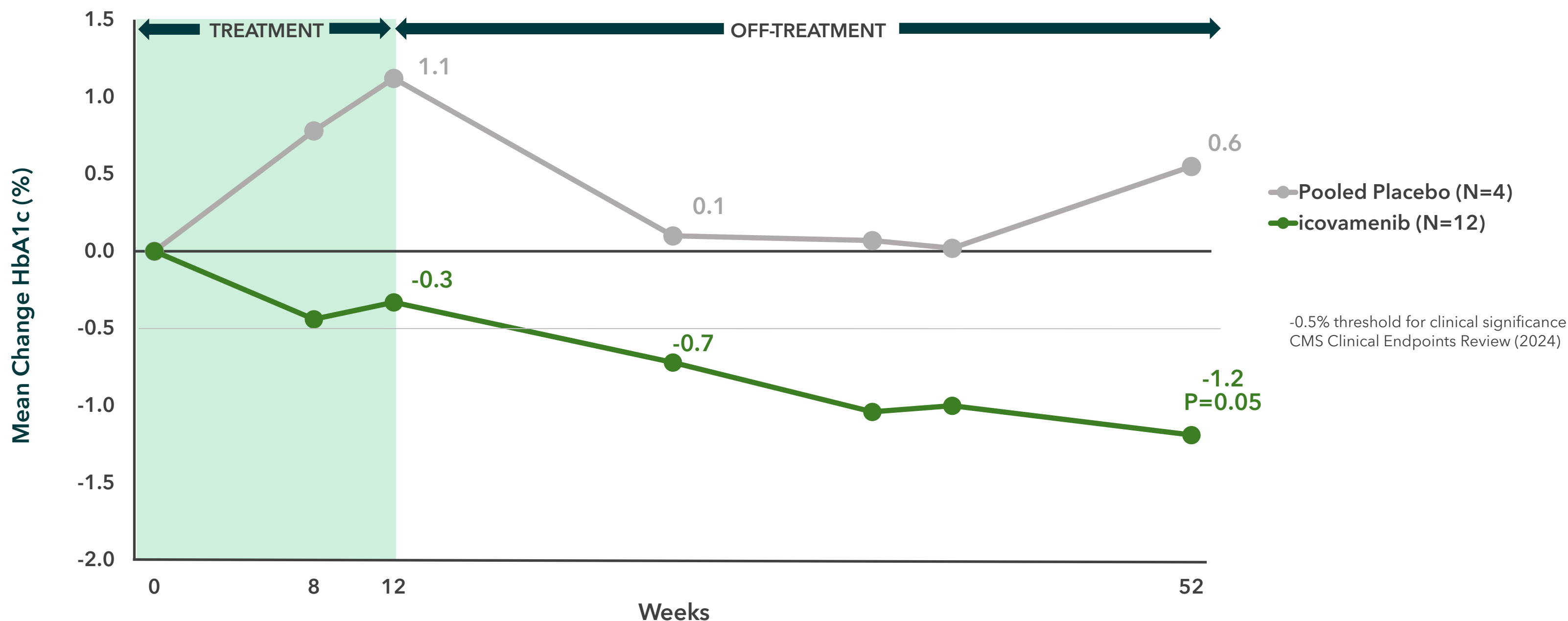
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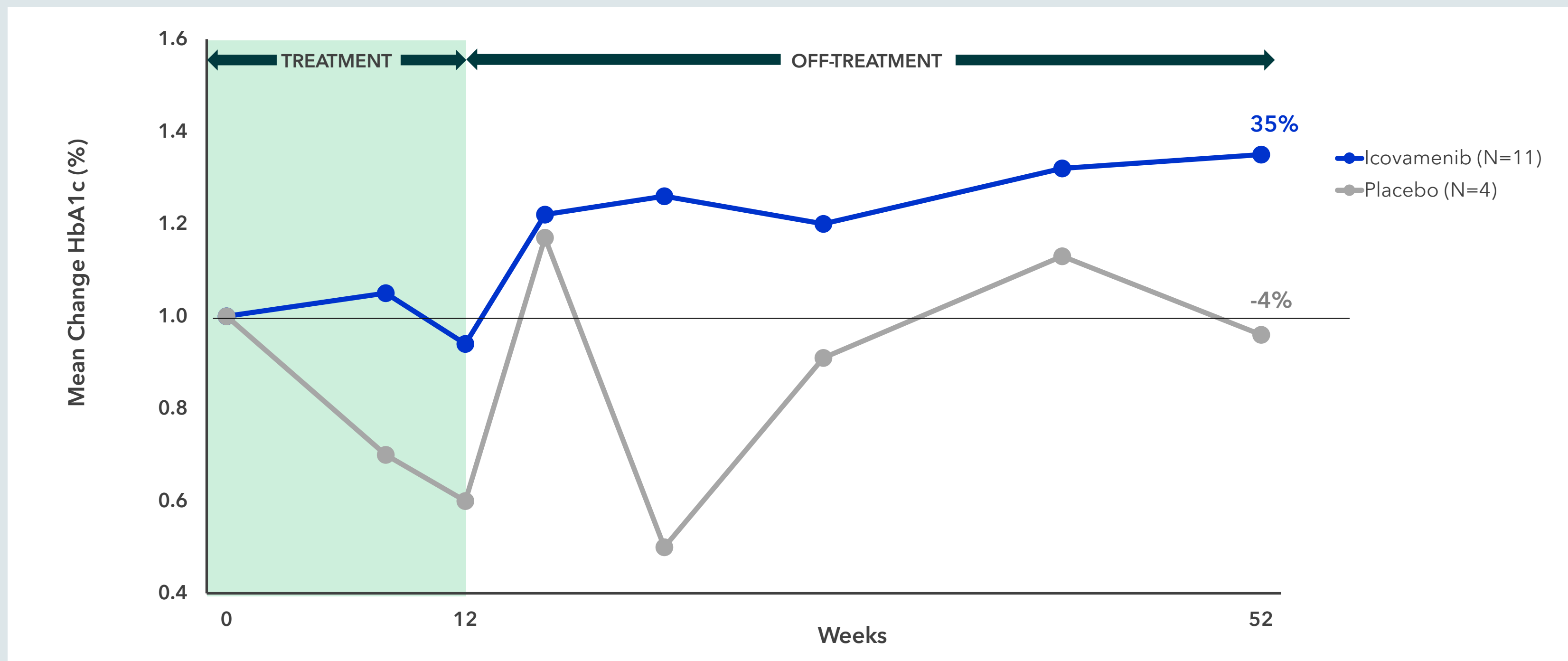
Baseline Characteristics of Patients on a GLP-1 RA-based therapy at enrollment

Characteristic	Icovamenib (n=12)	Placebo (n=4)
Age, years	53 ± 9	58 ± 9
T2D duration, years	5.4 ± 0.8	4.8 ± 2.6
HbA1c, %	8.4 ± 0.9	7.9 ± 0.3
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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	Pooled Placebo (N=4)	Icovamenib Combined arms (N=12)	Arm A icovamenib (N=3)	Arm B icovamenib (N=3)	Arm C icovamenib (N=6)
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Key Findings

- In adults with T2D receiving background GLP-1 RA therapy, icovamenib demonstrated durable HbA1c improvement through Week 52, 40 weeks after treatment discontinuation
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