Biomea Fusion Corporate Presentation

3Q 2026

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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]

1. www.breakthrought1d.org Scherer et al., Scientific Reports, 2020; 2. Nichols et al., Diabetes Care, 2015; 3.UKPDS Group. Lancet, 1998; 4. Prime Therapeutics & Magellan Rx Management, 2023 real-world claims analysis. 5. Neeland IJ, et al. Changes in lean body mass with glucagon-like peptide-1-based therapies and mitigation strategies. Diabetes Obes Metab. 2024.

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 in diabetes
- Potential best-in-class oral GLP-1 receptor agonist in obesity
- 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

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**

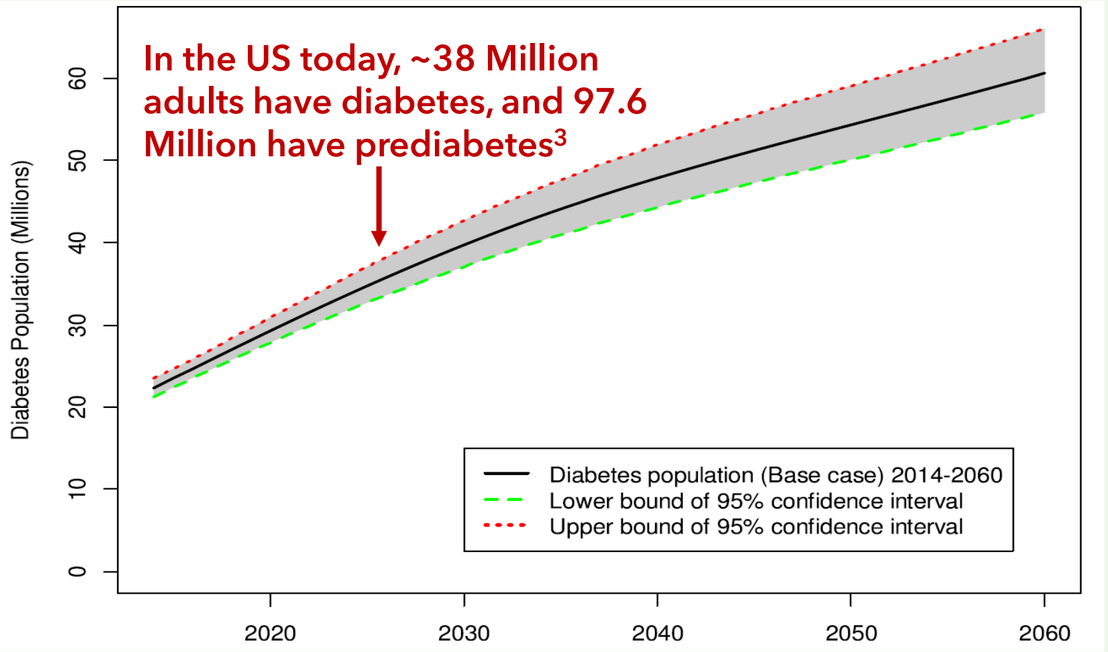
1.International Diabetes Federation. IDF Diabetes Atlas www.diabetesatlas.org (Based on company calculations)
2.NHANES analyses of glycemic control among U.S. adults with diabetes (JAMA; Diabetes Care);
3.SUSTAIN, AWARD, and SURPASS clinical trial programs for GLP-1 receptor agonists
4.Mayer-Davis et al., NEJM / CDC updates
5.National Center for Health Statistics August 2023. Accessed June 10, 2026

1 in 3 Americans will develop diabetes during their lifetime

In the U.S. **80% of people with diabetes will die from diabetes**.[1] Premature mortality caused by diabetes results in an estimated **12-14 years of life lost.**[2]

Diabetes creates one of the largest economic burdens on the U.S. health care system. **$1 out of every $4 in U.S. health care costs** is being spent on caring for people with diabetes[3].

There are over 60+ approved type 2 diabetes therapies, but these therapies **struggle to address the root cause of the disease.**



Over 800 million adults globally are living with diabetes[4]

Today diabetes remains poorly controlled in 50% of patients treated with standard of care agents[4]

1. Tabish Int J Health Sci. 2007 Jul;1(2):V–VIII.
2. National library of Medicine 1(2); 2007 Jul PMC3068646
3. CDC National Diabetes Statistics Report accessed January 2025
4. Zohu Lancet 2024; 404: 2077–93

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 Insulin[3]

25%

Of U.S. healthcare dollars go to treat those diabetes[4]

Obesity

>190M

People in U.S. are obese or overweight[5]

100M +

People in U.S. are obese[5]

5M+

People in U.S. discontinue GLP-1[6]

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

Icovamenib aims to delay need for insulin therapy
and reduce complications and disease burden

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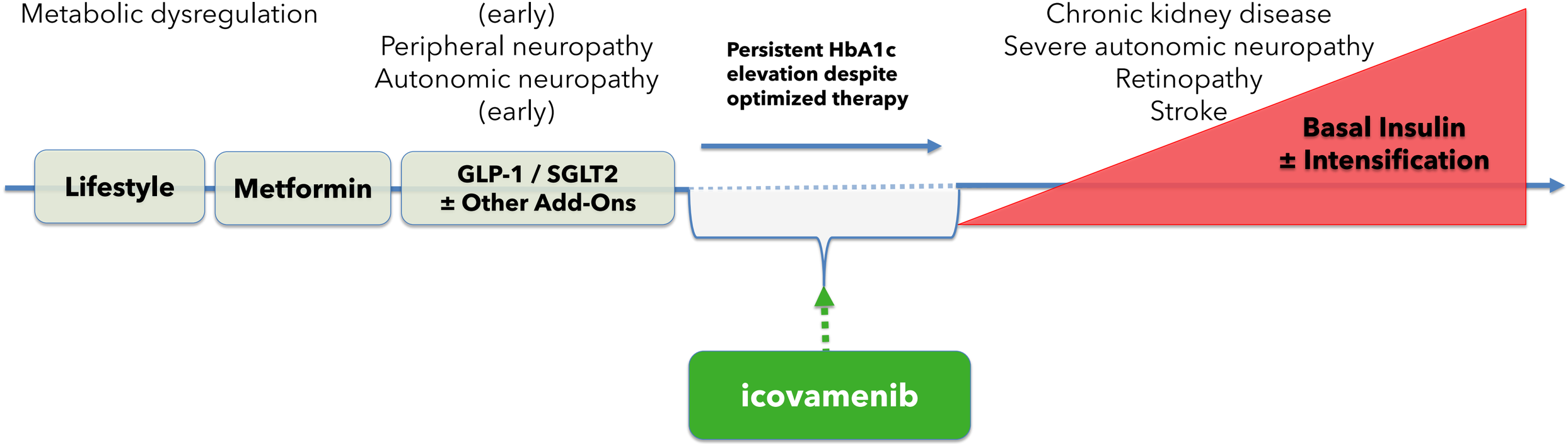
Early-Stage
β-cell stress
Insulin deficiency/resistance
Metabolic dysregulation

Mid-Stage
Microvascular disease
Diabetes nephropathy (early)
Peripheral neuropathy
Autonomic neuropathy (early)

Late-Stage
Macrovascular disease
Coronary artery disease
Chronic kidney disease
Severe autonomic neuropathy
Retinopathy
Stroke



In the U.S., >50% of patients with diabetes remain above HbA1c targets ≥7%[1]
Depending on the GLP-1 RA agent, 15-45% do not achieve HbA1c < 7% in clinical trials[2]

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

ICOVAMENIB

Potential first-in-class menin inhibitor for diabetes – PRECLINICAL RESULTS

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Menin is naturally inhibited during pregnancy and breastfeeding

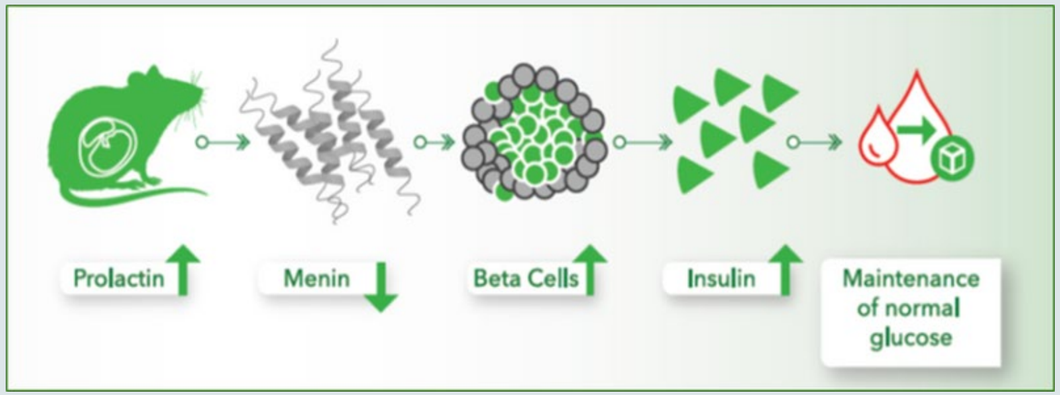
- allowing for adaptive beta cell mass increase & reduced diabetes risk

- 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



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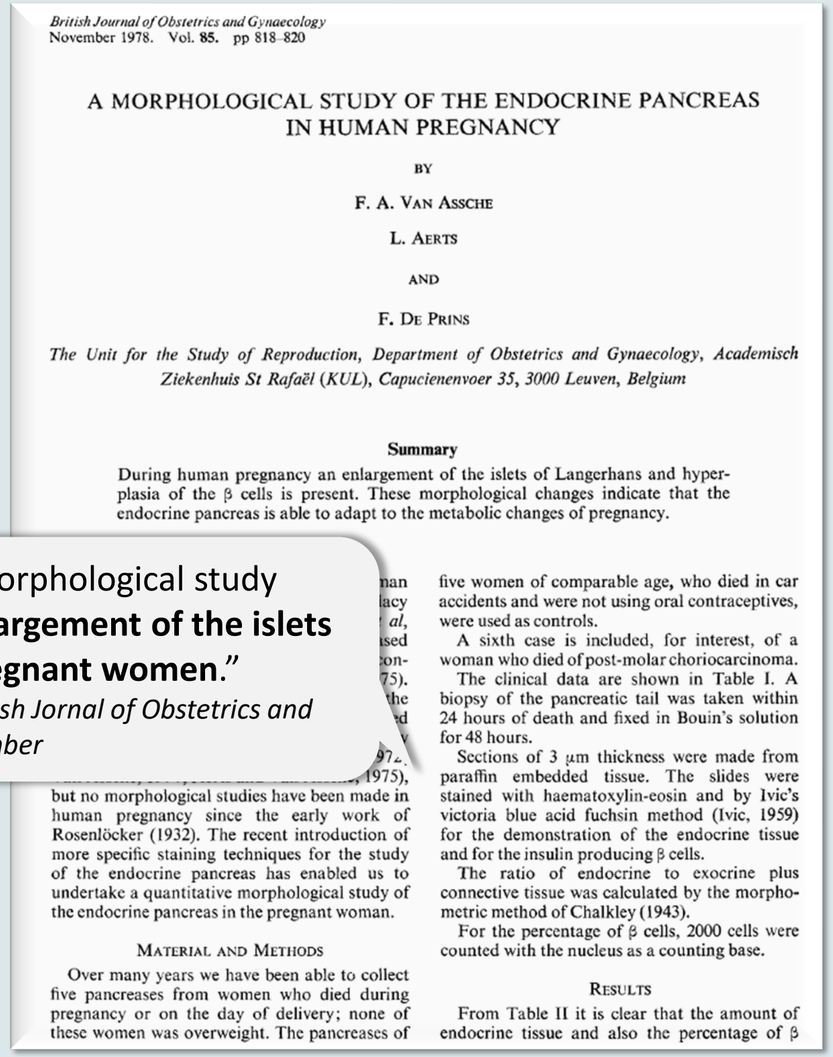
Beta Cells Proliferation During Pregnancy



British Journal of Obstetrics and Gynaecology
November 1978. Vol. 85. pp 818–820

A MORPHOLOGICAL STUDY OF THE ENDOCRINE PANCREAS IN HUMAN PREGNANCY

BY

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L. AERTS

AND

F. DE PRINS

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Summary

During human pregnancy an enlargement of the islets of Langerhans and hyperplasia of the β cells is present. These morphological changes indicate that the endocrine pancreas is able to adapt to the metabolic changes of pregnancy.

but no morphological studies have been made in human pregnancy since the early work of Rosenlöcker (1932). The recent introduction of more specific staining techniques for the study of the endocrine pancreas has enabled us to undertake a quantitative morphological study of the endocrine pancreas in the pregnant woman.

MATERIAL AND METHODS

Over many years we have been able to collect five pancreases from women who died during pregnancy or on the day of delivery; none of these women was overweight. The pancreases of five women of comparable age, who died in car accidents and were not using oral contraceptives, were used as controls.

A sixth case is included, for interest, of a woman who died of post-molar choriocarcinoma.

The clinical data are shown in Table I. A biopsy of the pancreatic tail was taken within 24 hours of death and fixed in Bouin's solution for 48 hours.

Sections of 3 μm thickness were made from paraffin embedded tissue. The slides were stained with haematoxylin-eosin and by Ivic's victoria blue acid fuchsin method (Ivic, 1959) for the demonstration of the endocrine tissue and for the insulin producing β cells.

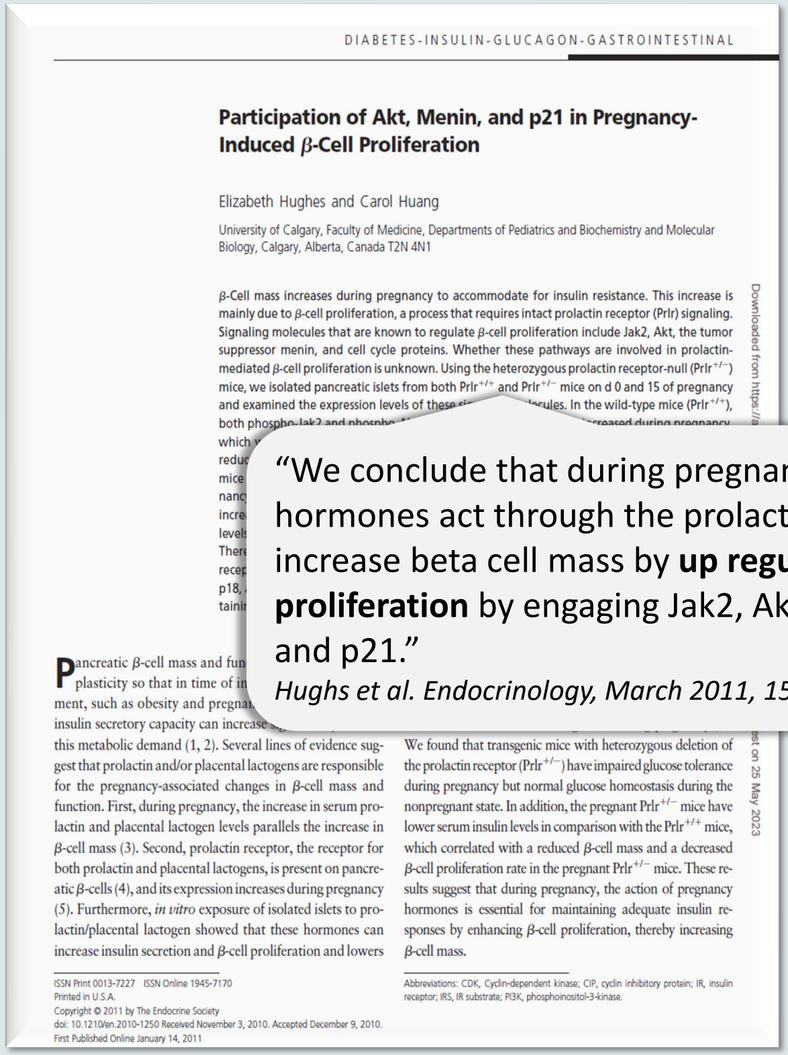
The ratio of endocrine to exocrine plus connective tissue was calculated by the morphometric method of Chalkley (1943).

For the percentage of β cells, 2000 cells were counted with the nucleus as a counting base.

RESULTS

From Table II it is clear that the amount of endocrine tissue and also the percentage of β

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



Participation of Akt, Menin, and p21 in Pregnancy-Induced β-Cell Proliferation

Elizabeth Hughes and Carol Huang

University of Calgary, Faculty of Medicine, Departments of Pediatrics and Biochemistry and Molecular Biology, Calgary, Alberta, Canada T2N 4N1

β-Cell mass increases during pregnancy to accommodate for insulin resistance. This increase is mainly due to β-cell proliferation, a process that requires intact prolactin receptor (Prlr) signaling. Signaling molecules that are known to regulate β-cell proliferation include Jak2, Akt, the tumor suppressor menin, and cell cycle proteins. Whether these pathways are involved in prolactin-mediated β-cell proliferation is unknown. Using the heterozygous prolactin receptor-null ($Prlr^{+/-}$) mice, we isolated pancreatic islets from both $Prlr^{+/+}$ and $Prlr^{+/-}$ mice on d 0 and 15 of pregnancy and examined the expression levels of these si… …lecules. In the wild-type mice ($Prlr^{+/+}$), both phospho-Jak2 and phospho-… …creased during pregnancy, which … reduc… mice … nanc… incre… level… There… recep… p18, … tainir…

Pancreatic β-cell mass and fun… plasticity so that in time of in… ment, such as obesity and pregna… insulin secretory capacity can increase … this metabolic demand (1, 2). Several lines of evidence suggest that prolactin and/or placental lactogens are responsible for the pregnancy-associated changes in β-cell mass and function. First, during pregnancy, the increase in serum prolactin and placental lactogen levels parallels the increase in β-cell mass (3). Second, prolactin receptor, the receptor for both prolactin and placental lactogens, is present on pancreatic β-cells (4), and its expression increases during pregnancy (5). Furthermore, *in vitro* exposure of isolated islets to prolactin/placental lactogen showed that these hormones can increase insulin secretion and β-cell proliferation and lowers

We found that transgenic mice with heterozygous deletion of the prolactin receptor ($Prlr^{+/-}$) have impaired glucose tolerance during pregnancy but normal glucose homeostasis during the nonpregnant state. In addition, the pregnant $Prlr^{+/-}$ mice have lower serum insulin levels in comparison with the $Prlr^{+/+}$ mice, which correlated with a reduced β-cell mass and a decreased β-cell proliferation rate in the pregnant $Prlr^{+/-}$ mice. These results suggest that during pregnancy, the action of pregnancy hormones is essential for maintaining adequate insulin responses by enhancing β-cell proliferation, thereby increasing β-cell mass.

ISSN Print 0013-7227 ISSN Online 1945-7170
Printed in U.S.A.

doi: 10.1210/en.2010-1250 Received November 3, 2010. Accepted December 9, 2010.
First Published Online January 14, 2011

Abbreviations: CDK, Cyclin-dependent kinase; CIP, cyclin inhibitory protein; IR, insulin receptor; IRS, IR substrate; PI3K, phosphoinositol-3-kinase.

"We conclude that during pregnancy, placental hormones act through the prolactin receptor to increase beta cell mass by **up regulating beta cell proliferation** by engaging Jak2, Akt, **menin**/p18, and p21."
Hughs et al. Endocrinology, March 2011, 152(3):847–855

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]*
[3]Division of Endocrinology, Department of Medicine, and [4]School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI; and [5]William 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 rev… that secondary factors other tha… for diabetes to develop; the 2 a… sity is associated with periphe… of the pathophysiology of typ… hyperglycemia there must be … sulin to meet this increased d… to the pancreatic β-cell, wher… to circulating nutrients and o…

Pancreatic β-cells are foun… 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…

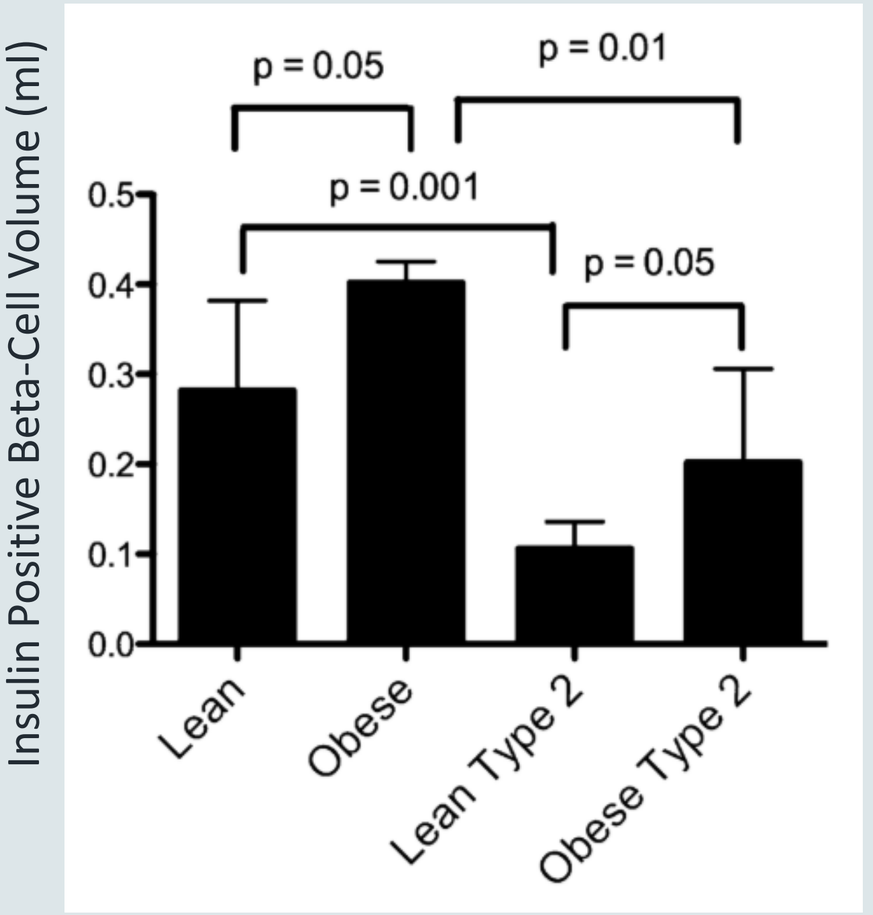
metabolic demand is dependent on numerous factors, including proper sensing of nutrient and hormonal signals, adequate insulin synthesis and secretion, and the overall number of functional β-cells. Although all of these factors are important, this review will focus on the regulation of β-cell … ber. The number of β-cells in a pancreas can … ways by using histologic analysis. To-… less than ~1.1% (3). More than 25 y ago, a study of autopsy specimens revealed 2 key points about β-cell mass in humans (4). First, β-cell mass is increased in nondiabetic obesity, and second, there is decreased β-cell mass in both lean and obese patients diagnosed with type 2 diabetes (Fig. 1).

[1] D.B.D. is supported by National Institute of … (NIDDK) DK083442. M.B. is supported by the N… 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.

 Adv. Nutr. 5: 278–288, 2014; doi:10.3945/an.113.005488.

"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

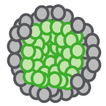


Icovamenib's mechanism of action

Icovamenib promotes selective and partial reduction in menin levels

Lowering menin levels releases the break on beta cell proliferation and GLP-1 and GLP-1 receptor expression

Induction of beta cell proliferation



Pancreatic islet

Increased expression of
- **GLP-1**
- **GLP-1 receptor**

IMPROVED BETA CELL MASS & FUNCTION FOR TYPE 1 AND TYPE 2 DIABETES

- ↑ Increase in insulin/C-peptide
- ↓ Decrease in blood glucose (HbA1c)

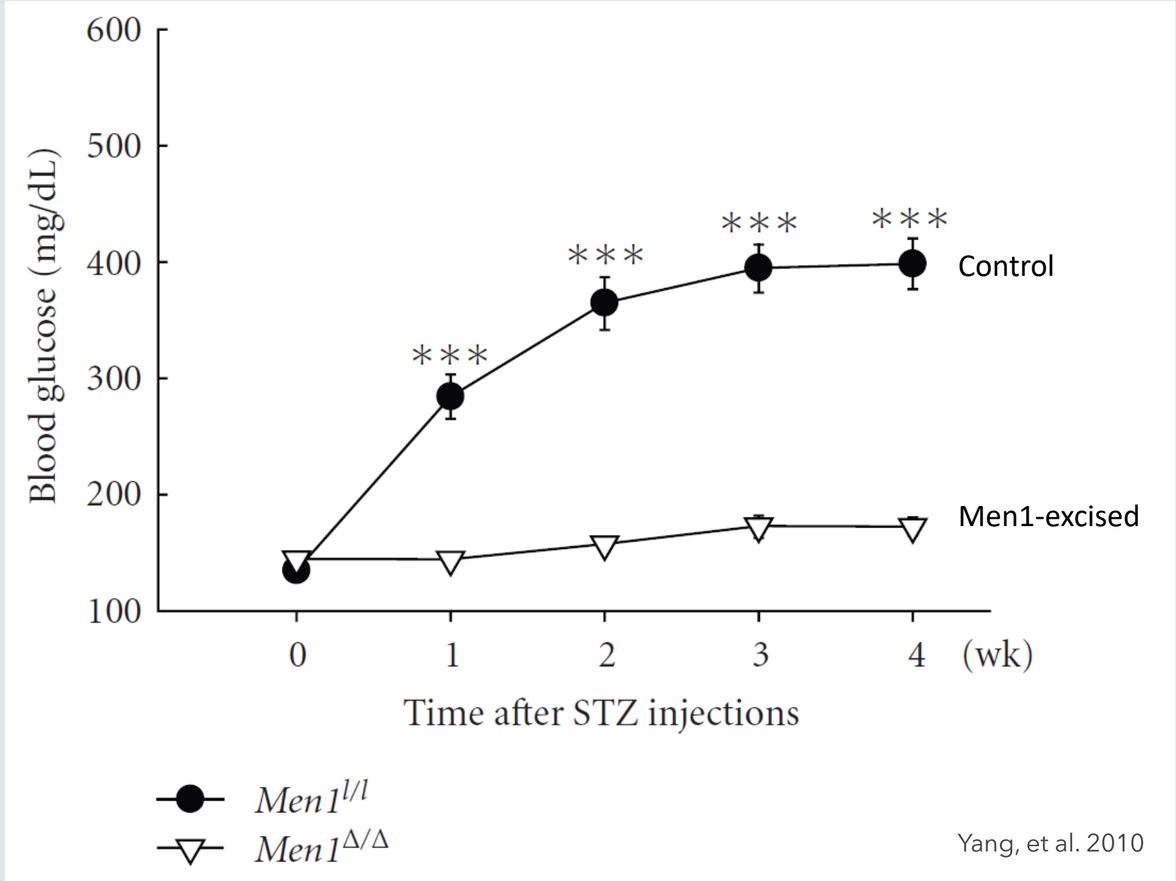
IMPROVED INCRETIN EFFECTS

- ↑ Synergistic with GLP-1 based therapies
- ↑ Improved beta cell function
- ↓ Decrease in blood glucose (HbA1c)
- ↓ Potential for weight loss
- ↑ Potential for lean mass/muscle preservation

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.

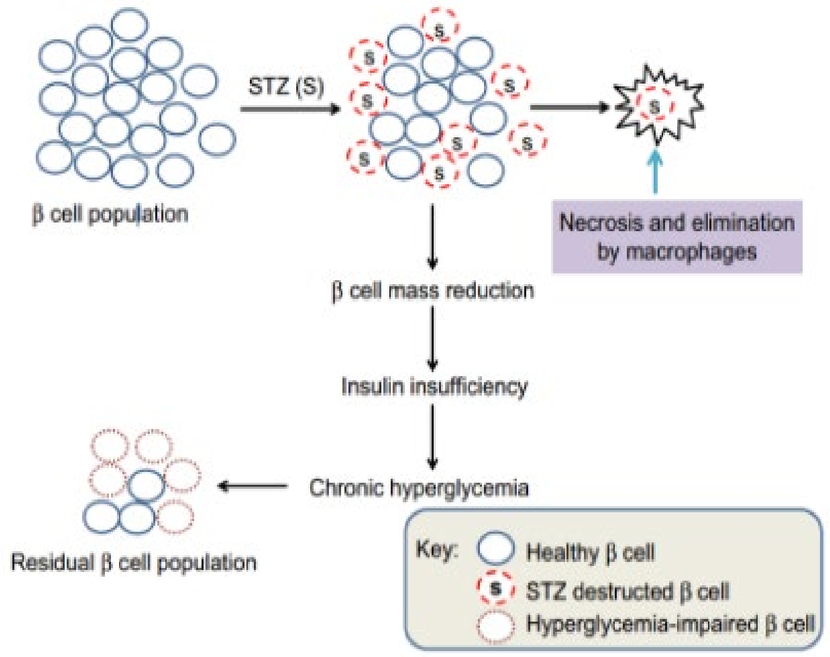


Men1-excised mice did not develop hyperglycemia in the STZ model, which was observed in the control group

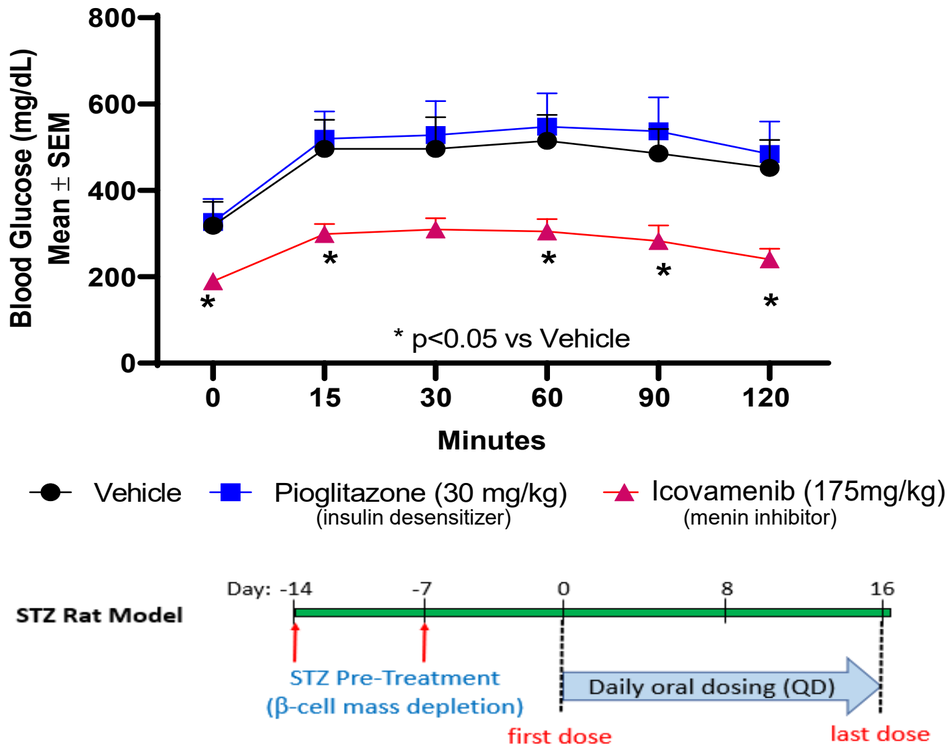
ICOVAMENIB | PRECLINICAL

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



ORAL GLUCOSE TOLERANCE TEST (DAY 17)



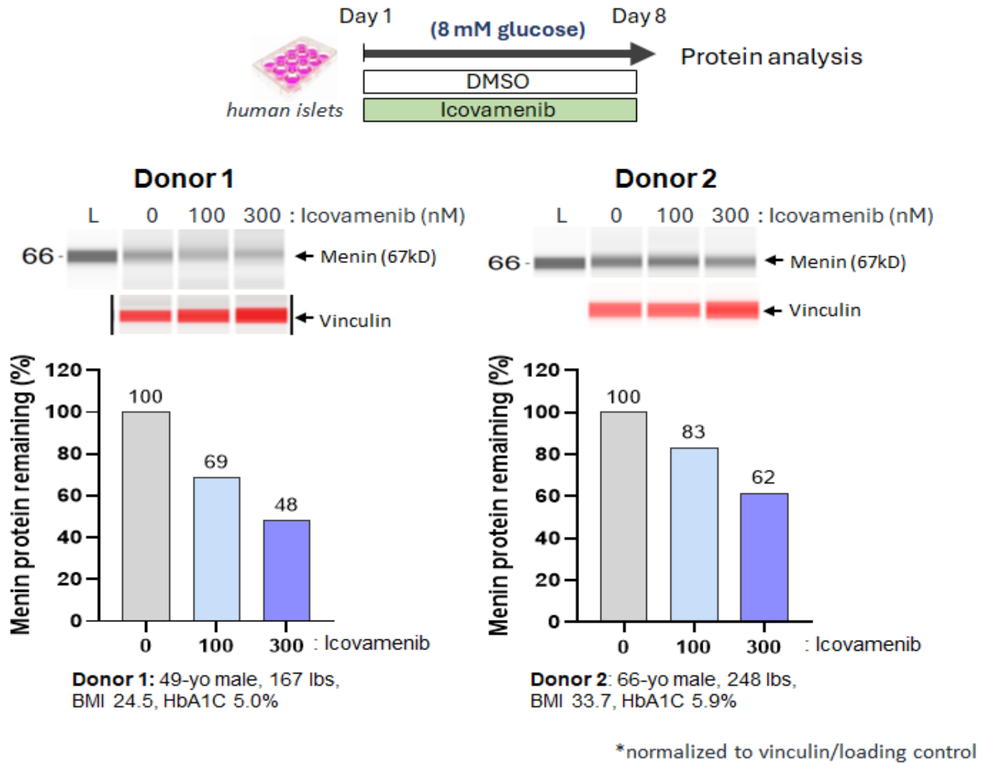
STZ=Streptozotocin, an antibiotic that produces pancreatic islet beta cell destruction and is widely used experimentally to produce a model in diabetes

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

ICOVAMENIB | PRECLINICAL

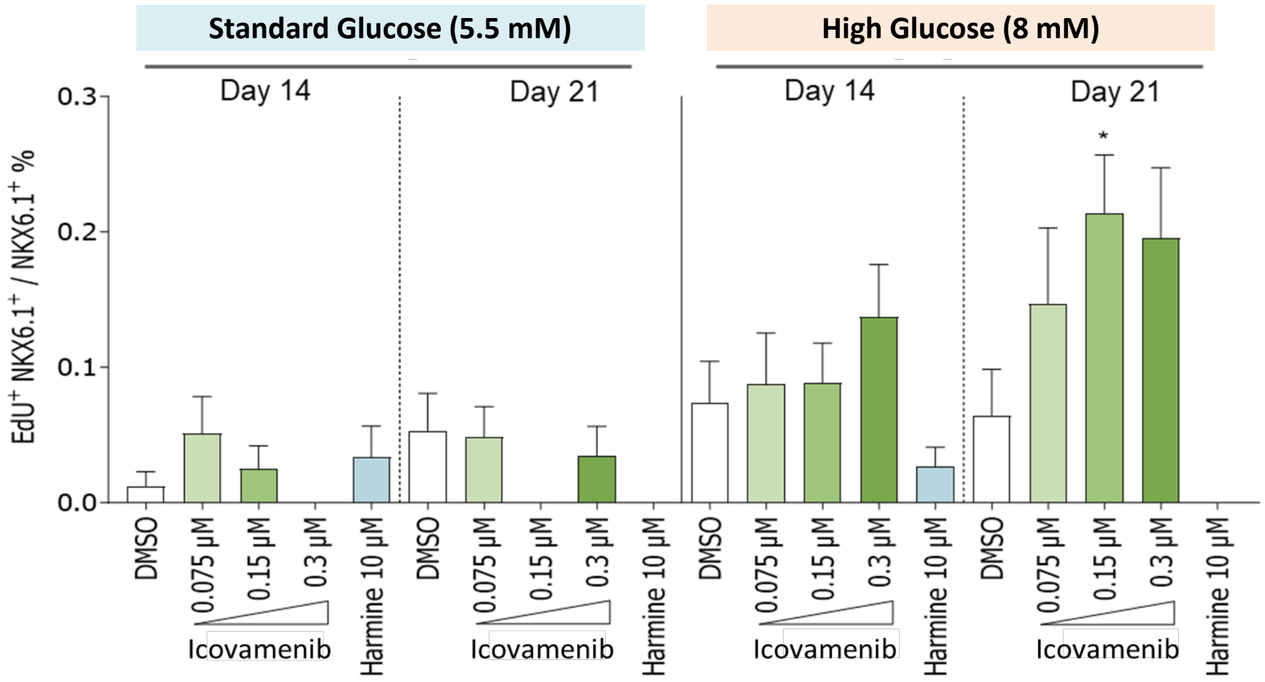
Icovamenib downregulated menin protein levels & promoted beta cell proliferation in ex vivo human islet cultures

MENIN LEVELS DOWNREGULATED



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

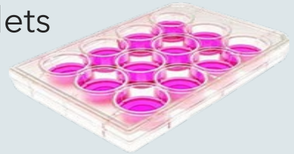
ICOVAMENIB CONDITIONALLY PROMOTED BETA CELL PROLIFERATION ONLY UNDER HYPERGLYCEMIC CONDITIONS



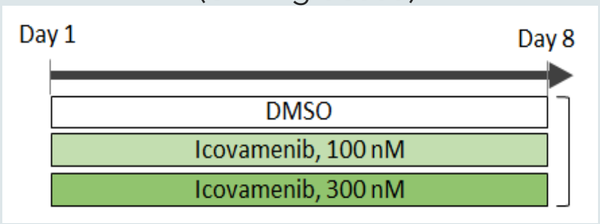
Frias, et al. (WCIRDC) Metabolism,Vol153, Supplement,2023,#88

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

Cadaver derived human islets

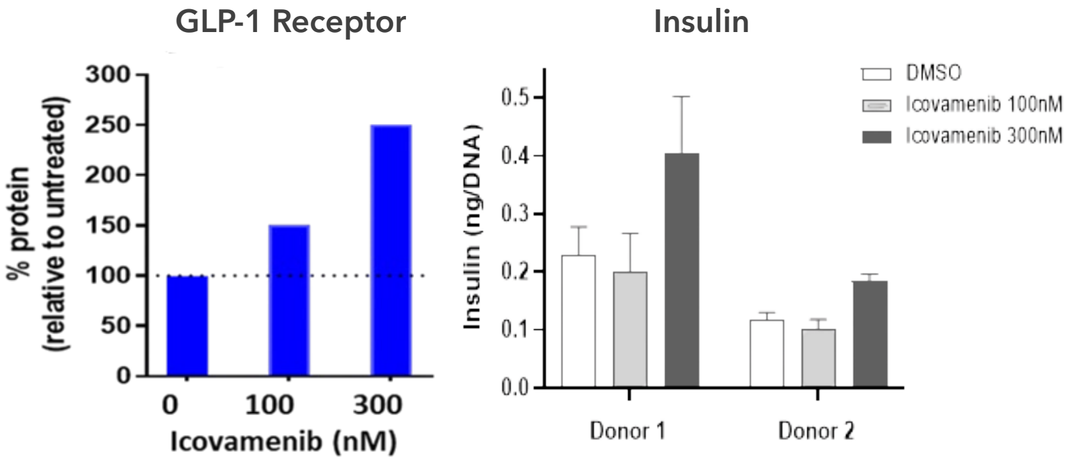


Culture 7 days under glucotox conditions (8mM glucose)



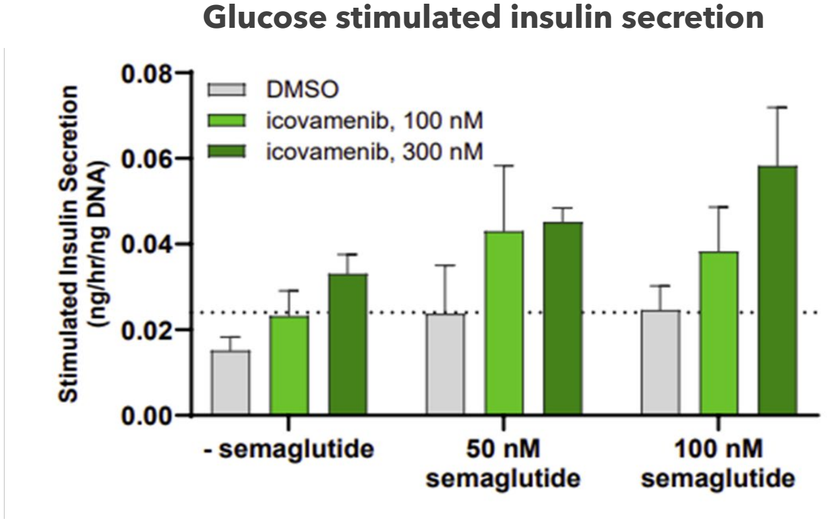
- Gene expression & Protein analysis
- Glucose Stimulated Insulin Secretion -/+ Semaglutide

ICOVAMENIB INCREASED GLP-1 RECEPTOR AND INSULIN PROTEIN LEVELS



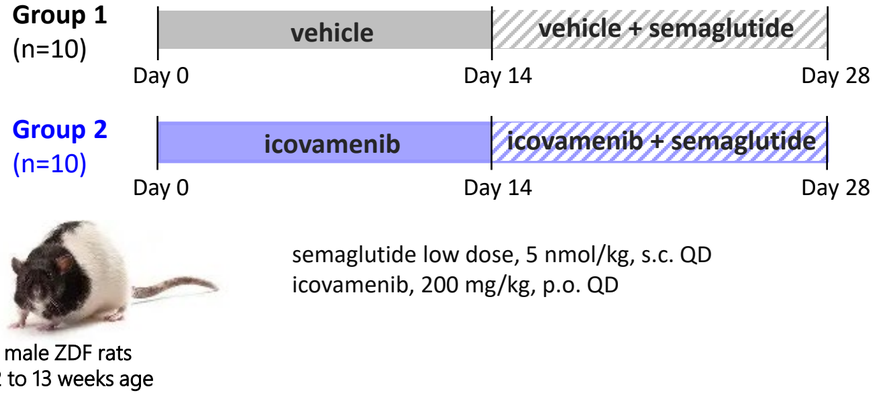
Balakrishnan, et al. (WCIRDC) Supplement,2025,156226. Oral presentation

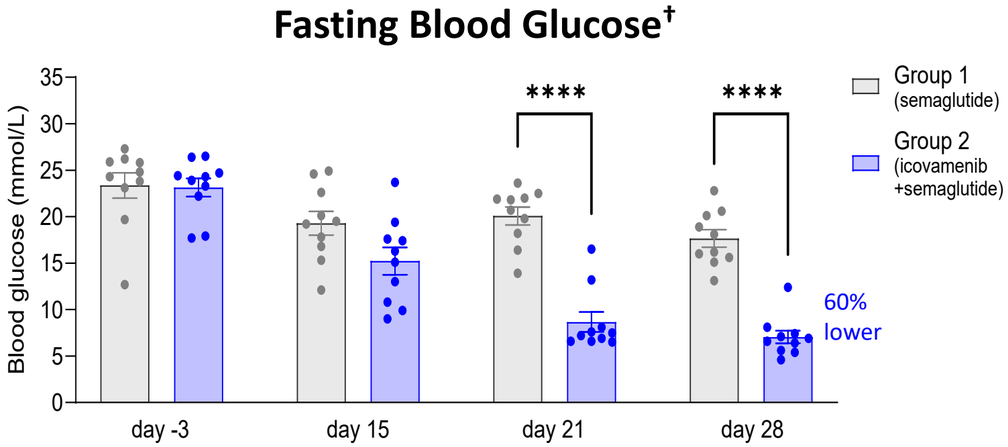
ICOVAMENIB ENHANCES THE RESPONSIVENESS OF HUMAN ISLETS TO GLP-1 RECEPTOR AGONISTS

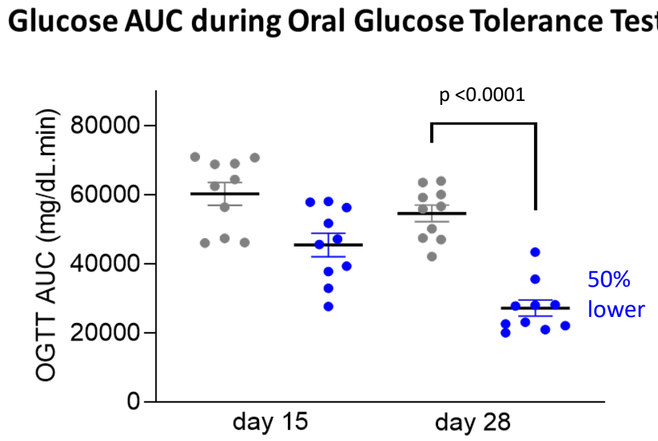


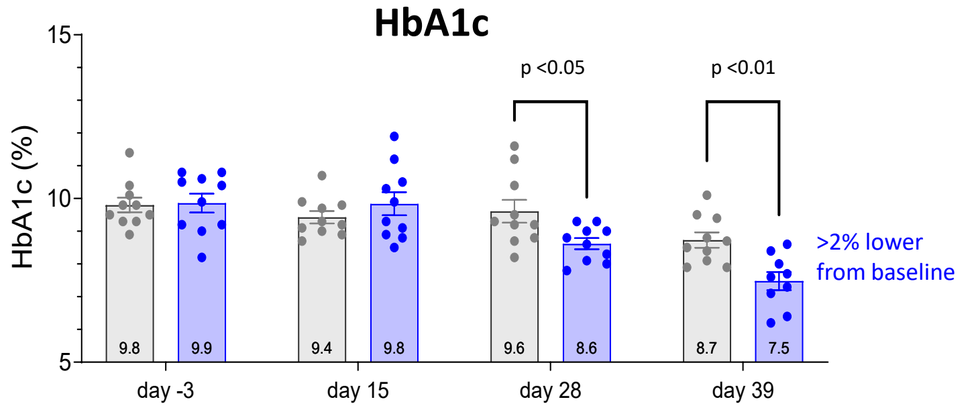
Somanath, et al. (EASD) Diabetologia 68 (Suppl 1), 1–754 (2025). Oral presentation #66

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









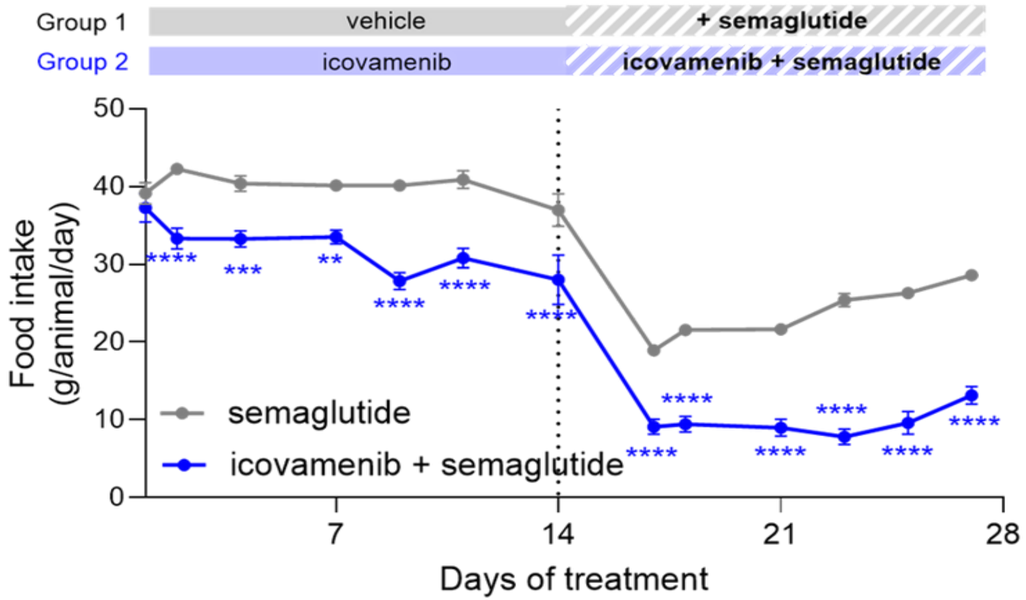
Plots represent mean ± SEM
Dots represent data for individual animal
† 6hr fasting on days -3 and 21, overnight fasting on days 15 and 28.

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

ICOVAMENIB WITH GLP-1RA

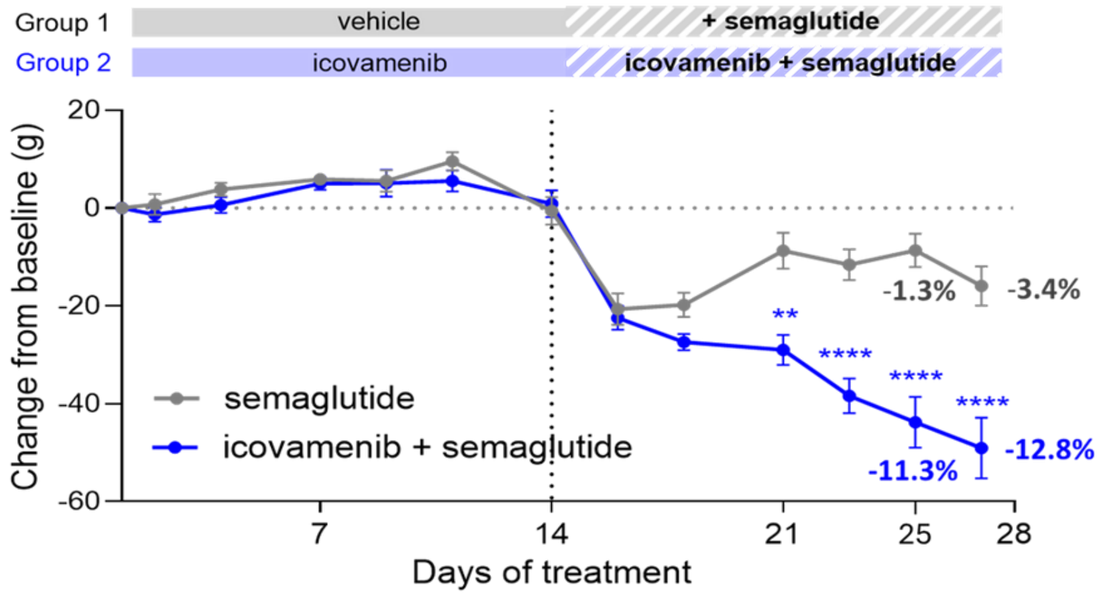
Combination Treatment of Icovamenib & Low-dose Semaglutide Reduces Food Intake & Body Weight

APPETITE SUPPRESSION



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

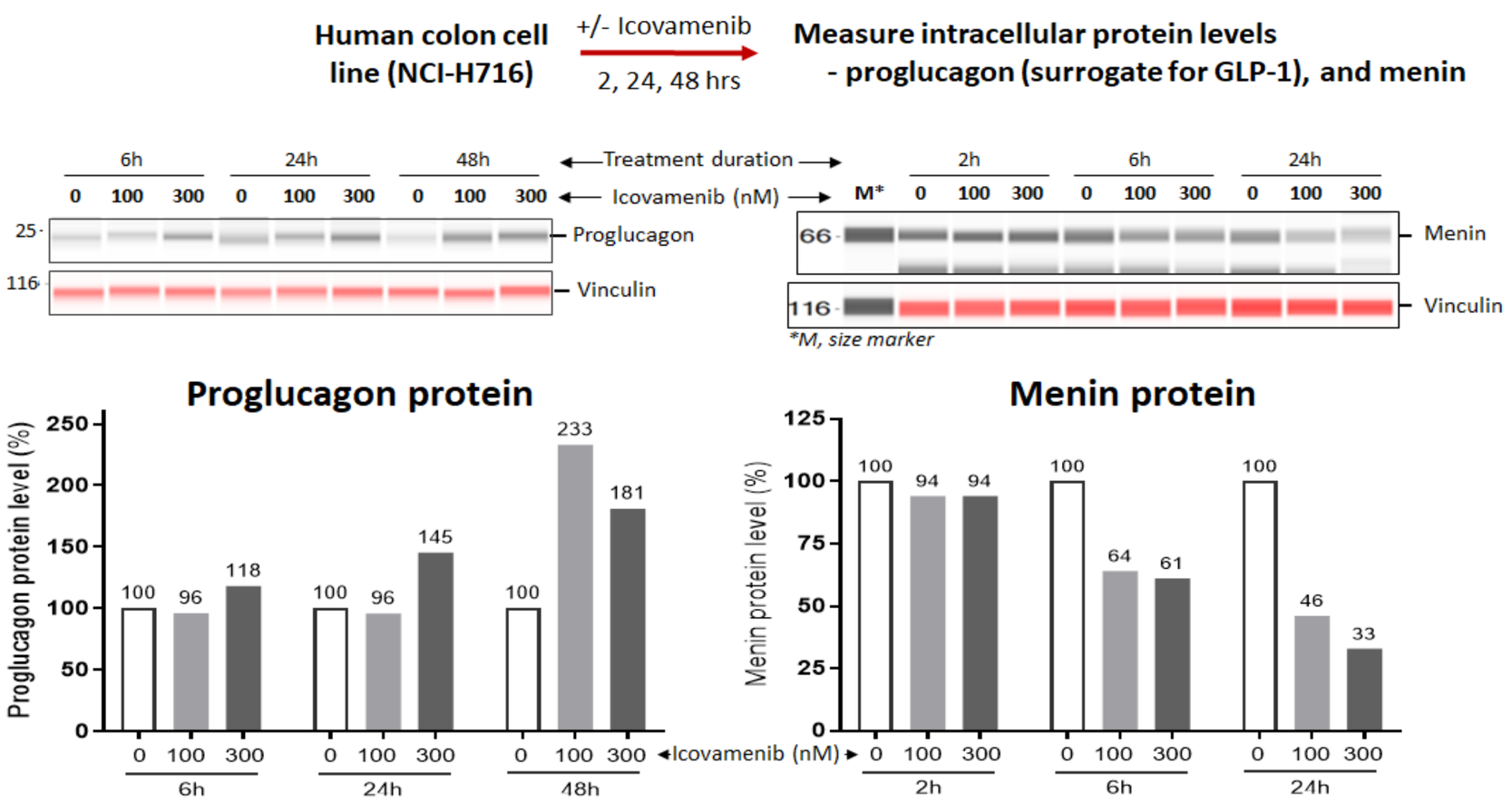
BODY WEIGHT REDUCTION



- ❑ 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 IN COLON CELLS

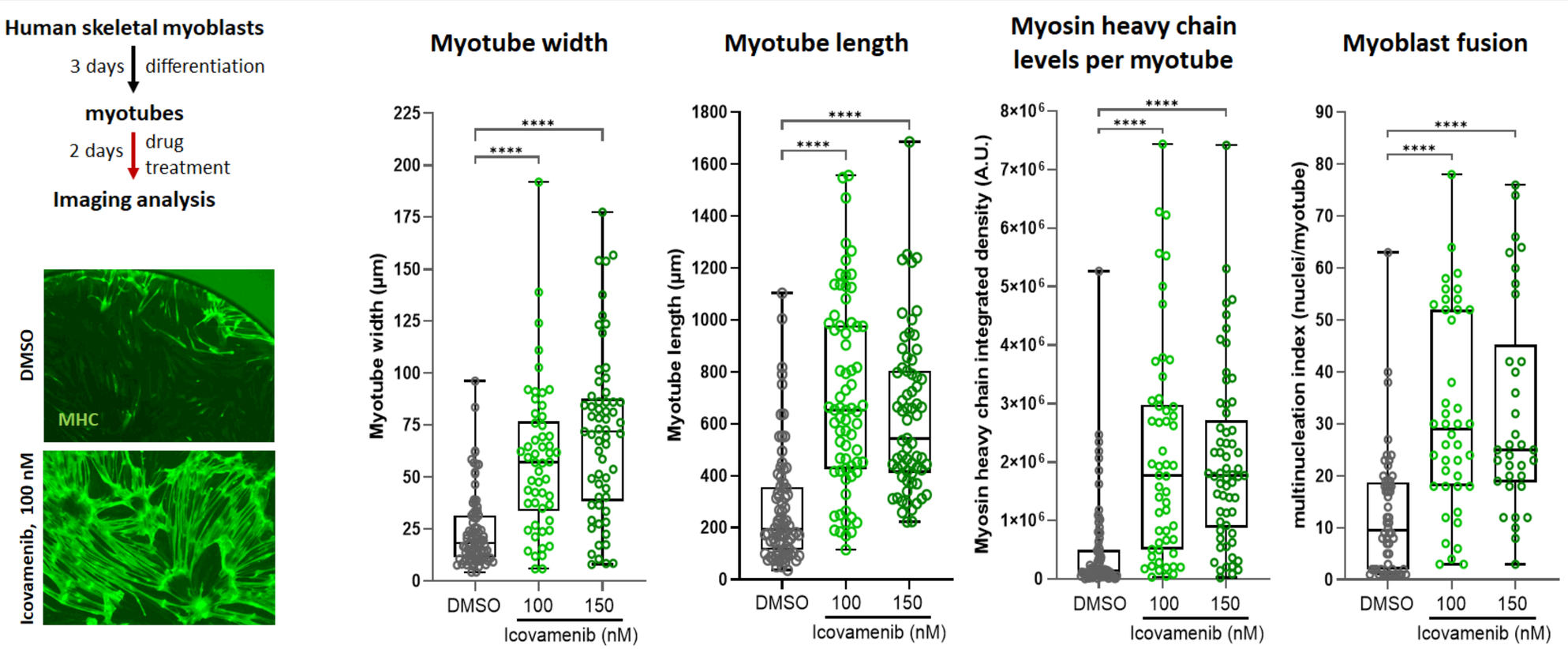
Icovamenib enhanced intracellular proglucagon expression in a human colon L-cell model



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

ICOVAMENIB IN MYOTUBES

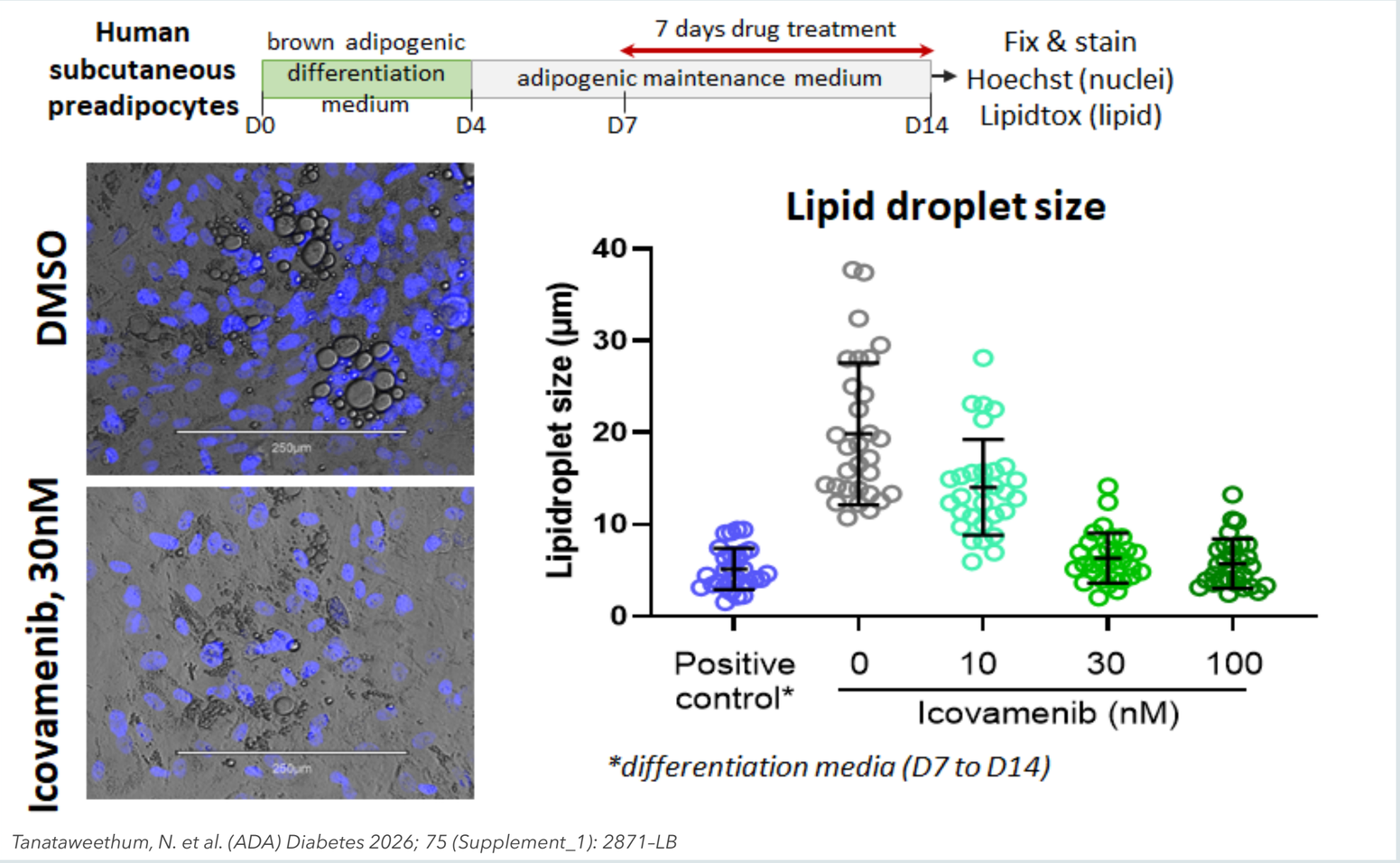
Icovamenib Induced Myogenic Effects in Human Skeletal Myoblast-derived Myotubes



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

ICOVAMENIB IN ADIPOCYTES

Icovamenib promoted lipolysis in primary human adipocytes

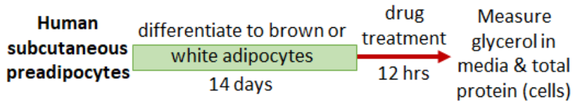


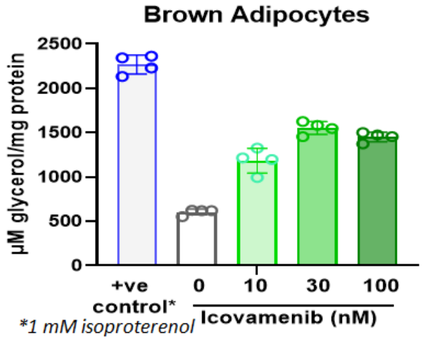
Tanataweethum, N. et al. (ADA) Diabetes 2026; 75 (Supplement_1): 2871–LB

ICOVAMENIB IN ADIPOCYTES

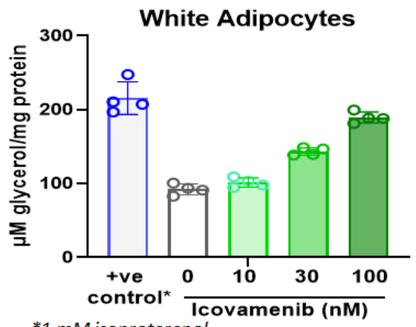
Icovamenib promoted effects indicative of lipolysis and fat browning in primary human adipocytes

Enhanced Glycerol Release



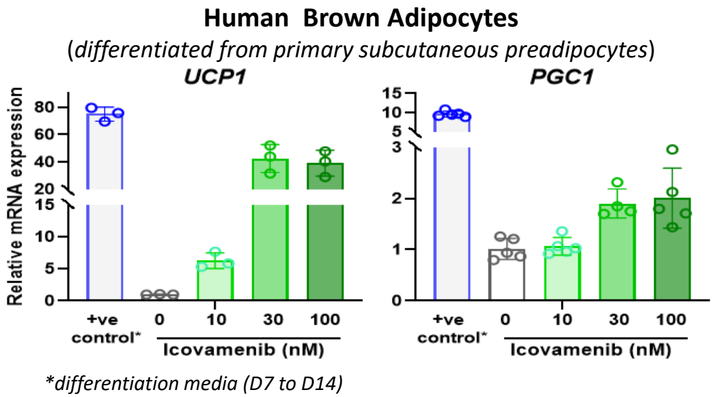


*1 mM isoproterenol

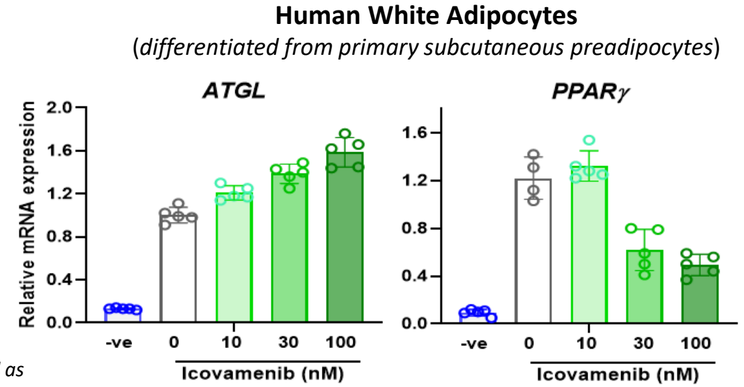


*1 mM isoproterenol

Upregulation of thermogenic and lipolytic genes



*differentiation media (D7 to D14)

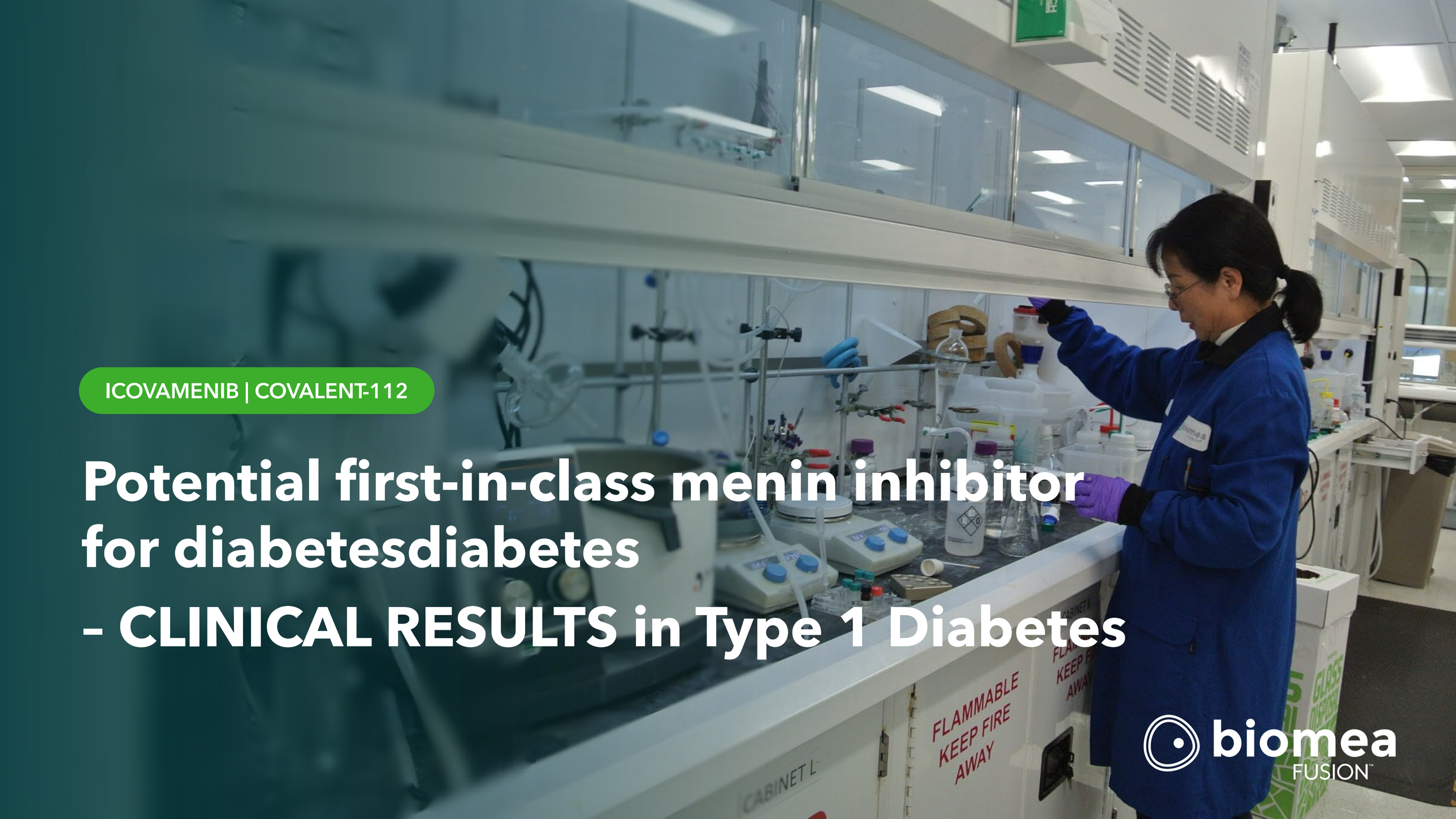


PPIA (Cyclophilin A) was used as housekeeping gene for normalization of data

Pre-adipocytes

Pre-adipocytes

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



ICOVAMENIB | COVALENT-112

Potential first-in-class menin inhibitor for diabetesdiabetes – CLINICAL RESULTS in Type 1 Diabetes

biomea FUSION™

Current T1D therapies are designed to preserve and protect icovamenib is developed to RESTORE beta cell function

CURRENT TREATMENT LANDSCAPE

Focus on immune modulation and preservation

- Immune modulation to slow autoimmune destruction
- Preserve remaining beta-cell function [1]
- Most effective when started shortly after diagnosis (<90 days, new-onset T1D) [2]
- Slows decline in C-peptide over time [3]

GOAL: Slow disease progression

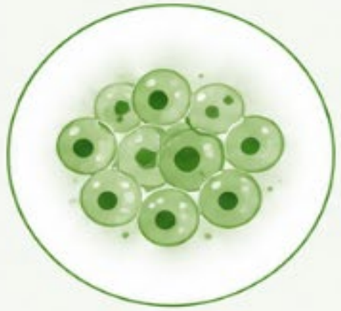
CURRENT STANDARD

NEXT GENERATION

PRESERVE → RESTORE

BIOMEA VISION

Beyond preservation: Restore beta-cell function and mass



- Restore beta-cell function and mass
- Increase endogenous insulin production
- Expand treatment window beyond early, new-onset T1D
- Potential for durable benefit after finite dosing

GOAL: Restore endogenous insulin secretion

RESTORE

Restore beta-cell function and mass

EXPAND

Expand the treatment window beyond early diagnosis

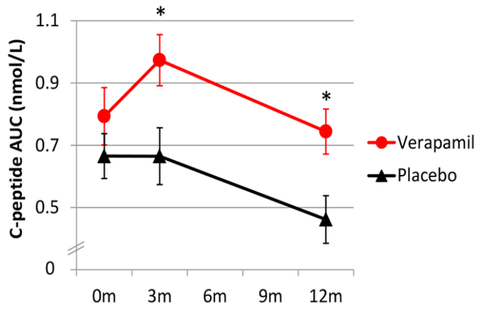
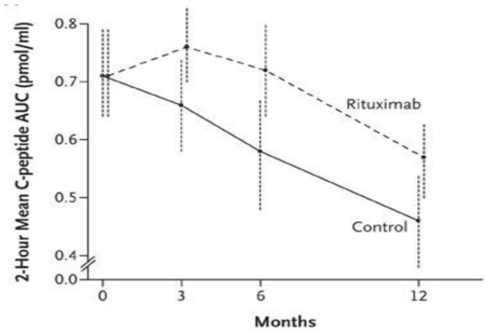
SUSTAIN

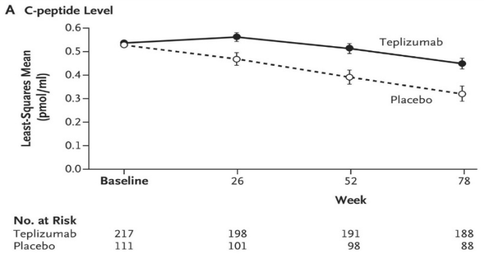
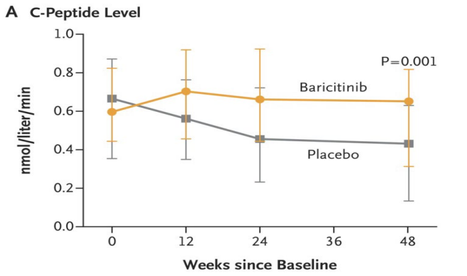
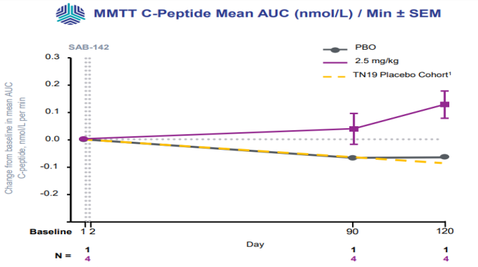
Enable durability and persistence of benefit beyond treatment

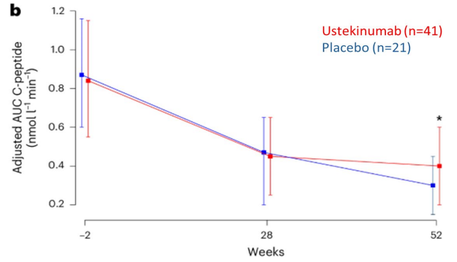
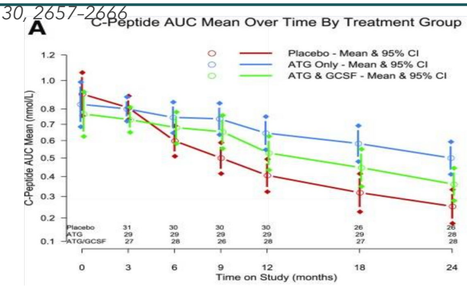
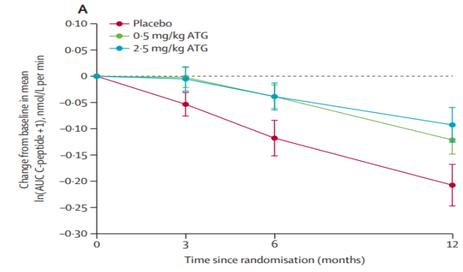
Icovamenib is being developed to move beyond slowing beta-cell decline toward restoring endogenous insulin secretion through beta-cell regeneration.

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

DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Verapamil	 *Nature. 2018 Aug;24(8):1108-1112*
Rituximab	 *NEJM. 2009 361:2143–2152*

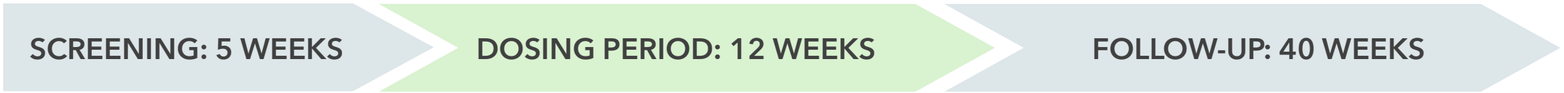
DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Teplizumab (Tzield)	 *ESPE Yearbook of Paediatric Endocrinology (2024) 21 10.2*
Baricitinib	 *N Engl J Med 2023;389:2140-2150*
SAB-142	 *SAB Bio website corporate presentation (March 10, 2026) https://www.sab.bio/*

DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Ustekinumab	 *Nature Medicine 2024 vol 30, 2657–2666*
ATG (TrialNet)	 *Diabetes Care 2018 Jul 16;41(9):1917–1925*
MELD-ATG	 *Lancet 2025 Sep 27;406(10510):1375-1388*

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

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

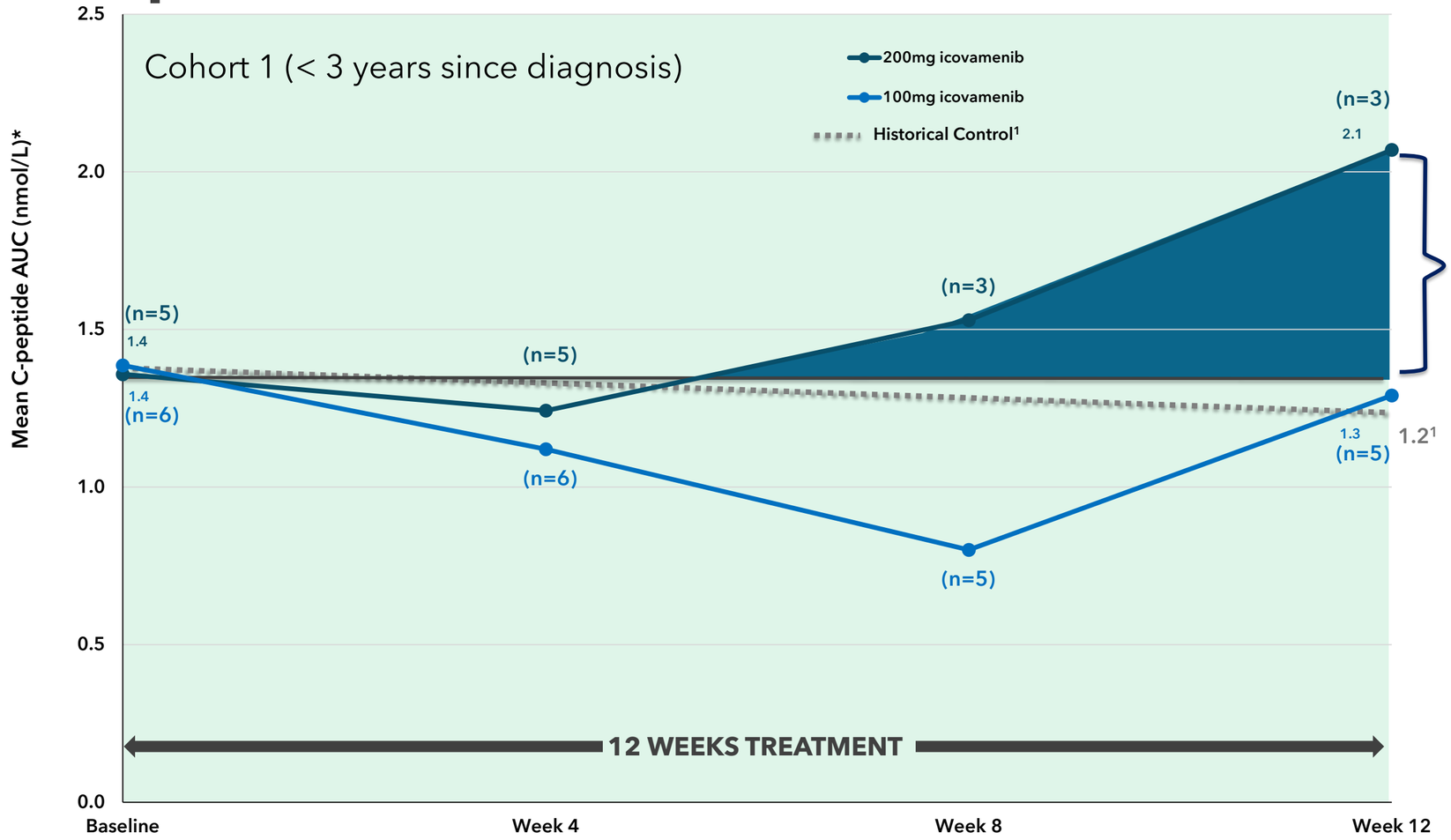
ARM A
N = 10
Icovamenib 100 mg QD

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.

ICOVAMENIB | COVALENT-112

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

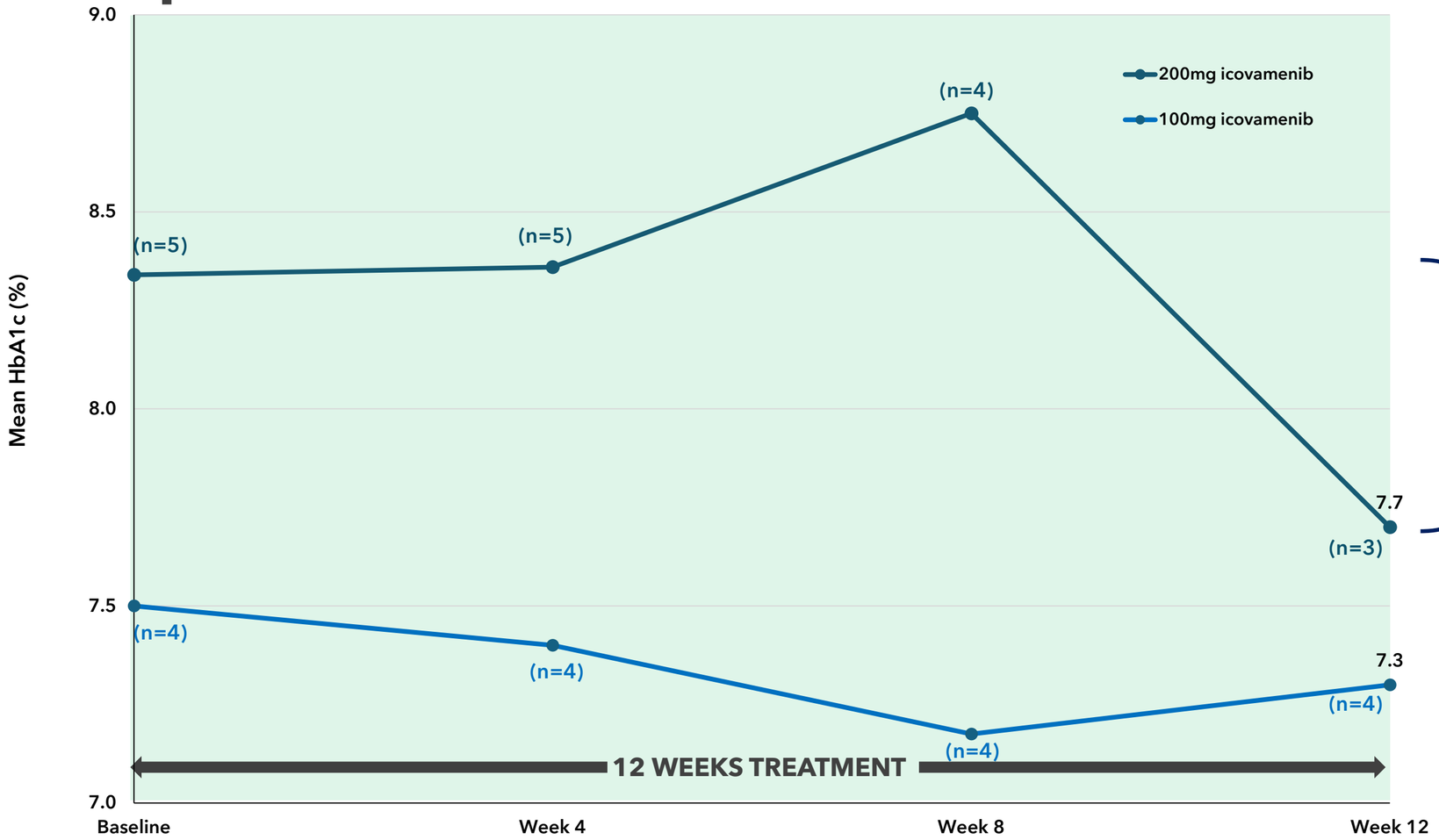
[1] Historical control in T1D patients (n=1549) C-peptide declining over first 7 years at 47% yearly. Diabetes Care. 2018 Jun 7;41(7):1486–1492

** 4-hour Mixed Meal Tolerance Test (MMTT)*

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

ICOVAMENIB | COVALENT-112

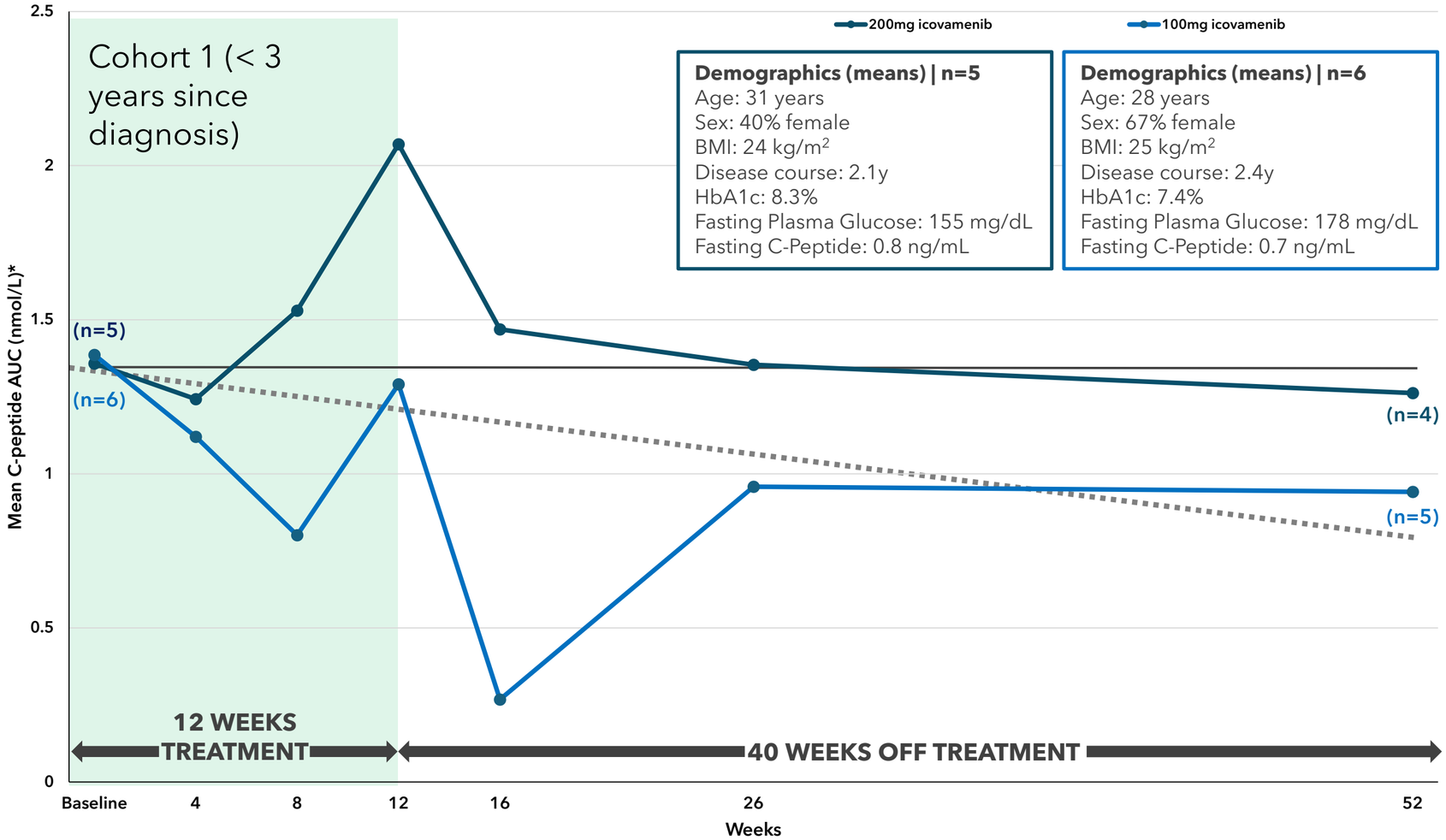
0.6% mean reduction in HbA1c during the 12 weeks treatment period of icovamenib



0.6% reduction in mean HbA1c from baseline

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

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



Change in mean C-peptide AUC at Week 52 vs baseline

-7%

-32%

-47%[1]

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.

biomea FUSION

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

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

Optimal dose and target population identified for T1D phase 2 program

T1D insights:

- Dose response: 200 mg demonstrated stronger clinical activity vs 100 mg
- Patients with T1D dosed ≤3 years / ≥0.2 nmol/L showed greater response vs those 3-15 years since 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

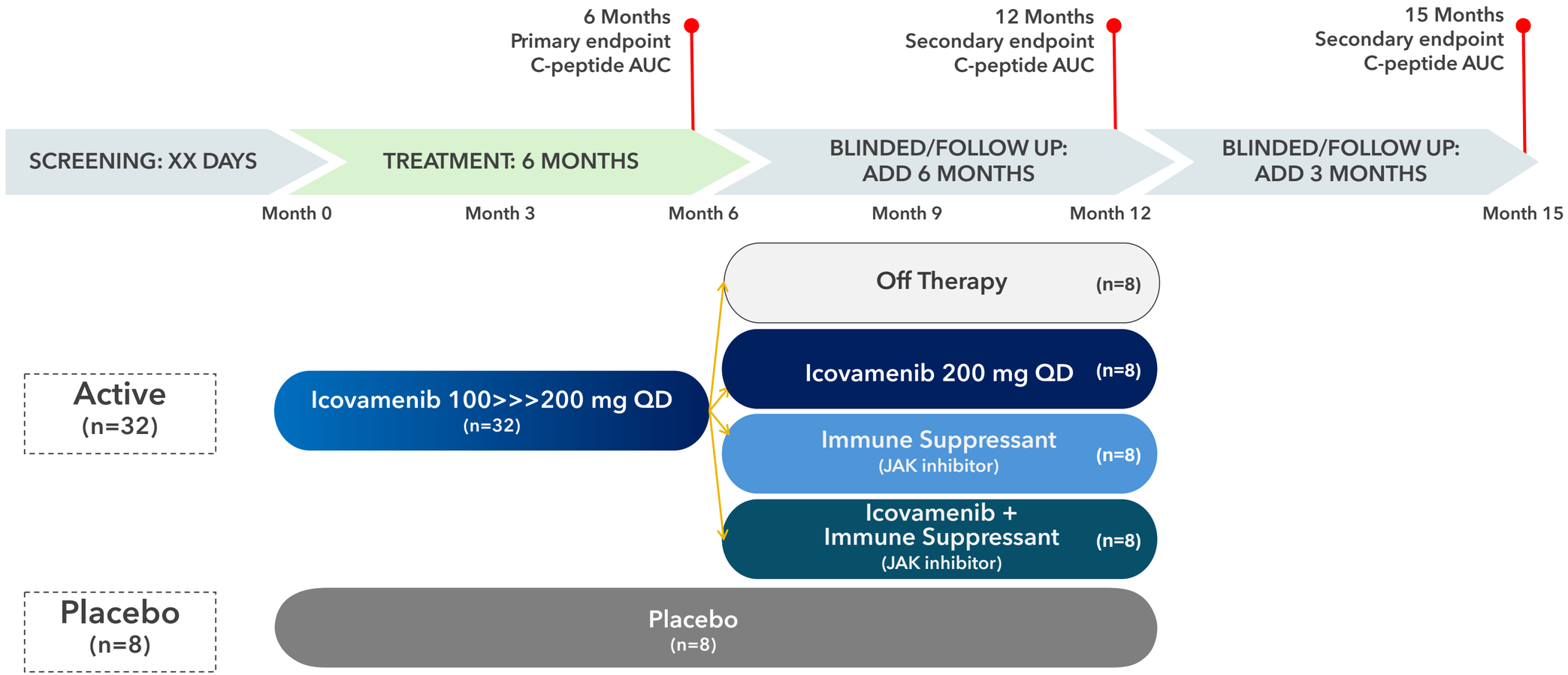
T1D development focus:

- Potential to further improve 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 for T1D clinical trial*

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.

Anschutz | 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)

Joslin Diabetes

David Baidal, MD

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

DRI Diabetes Research Institute FOUNDATION

Ralph A. DeFronzo, MD

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

UT Health San Antonio Long School of Medicine

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

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.

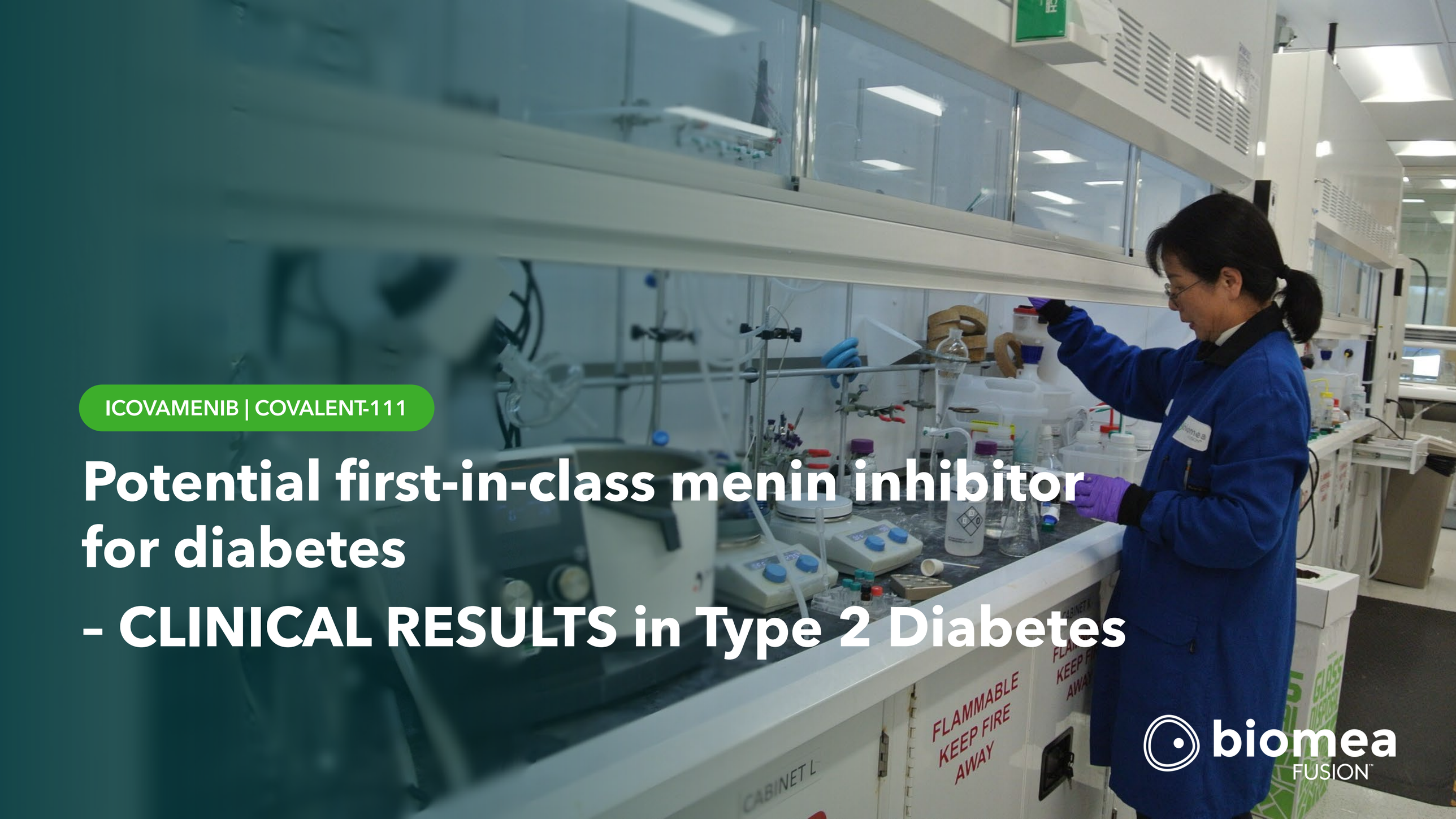
Jason Gaglia, MD, MMSc

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

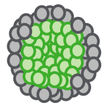
biomea FUSION™

Icovamenib's mechanism of action

Icovamenib promotes selective and partial reduction in menin levels

Lowering menin levels releases the break on beta cell proliferation

Induction of beta cell proliferation



Pancreatic islet

IMPROVED BETA CELL MASS & FUNCTION FOR TYPE 1 AND TYPE 2 DIABETES

- Increase in insulin/C-peptide
- Decrease in blood glucose (HbA1c)

Baseline demographics & characteristics

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

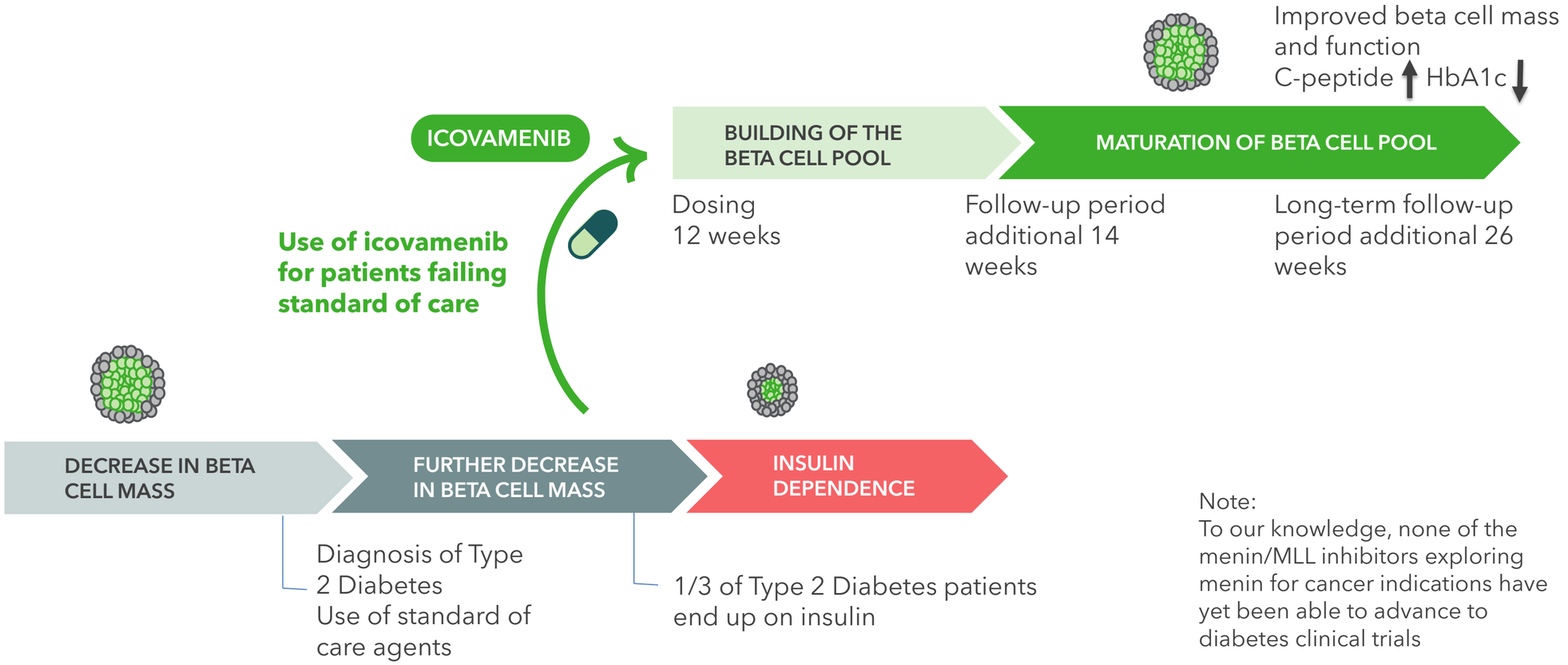
Parameter Mean (SD) or %	Arm A icovamenib (8 wks 100mg QD) (N=45)	Arm B icovamenib (12 wks 100 mg QD) (N=36)	Arm C icovamenib (8 wks 100 mg QD then 4 wks of 100 mg BID) (N=33)	Combined Arms icovamenib (N=114)	Combined Arms placebo (N=49)
Age (yr)	55 (7)	56 (6)	51 (10)	54 (8)	55 (7)
Duration of T2D Diagnosis (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 | COVALENT-111

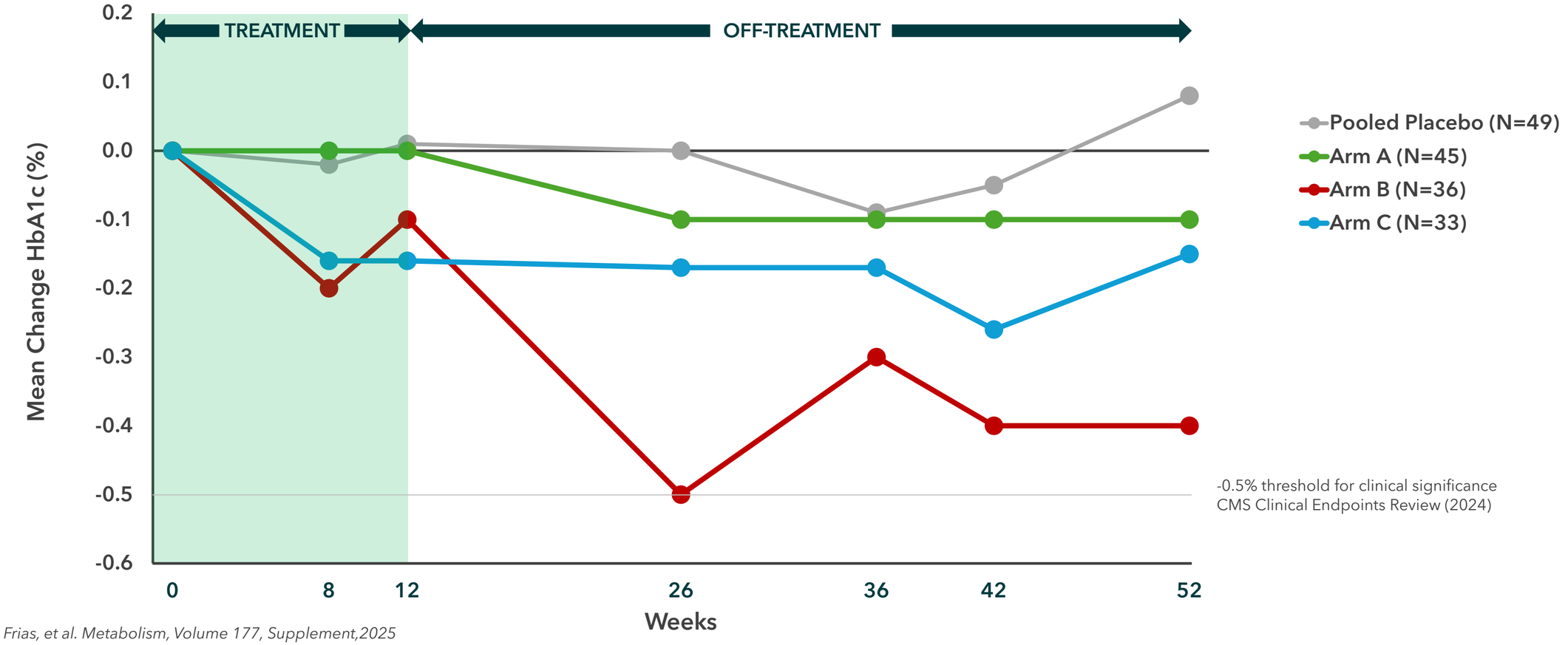
Icovamenib increased beta cell quantity, function & GLP-1 receptor expression following a short treatment period



Note:
To our knowledge, none of the menin/MLL inhibitors exploring menin for cancer indications have yet been able to advance to diabetes clinical trials

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

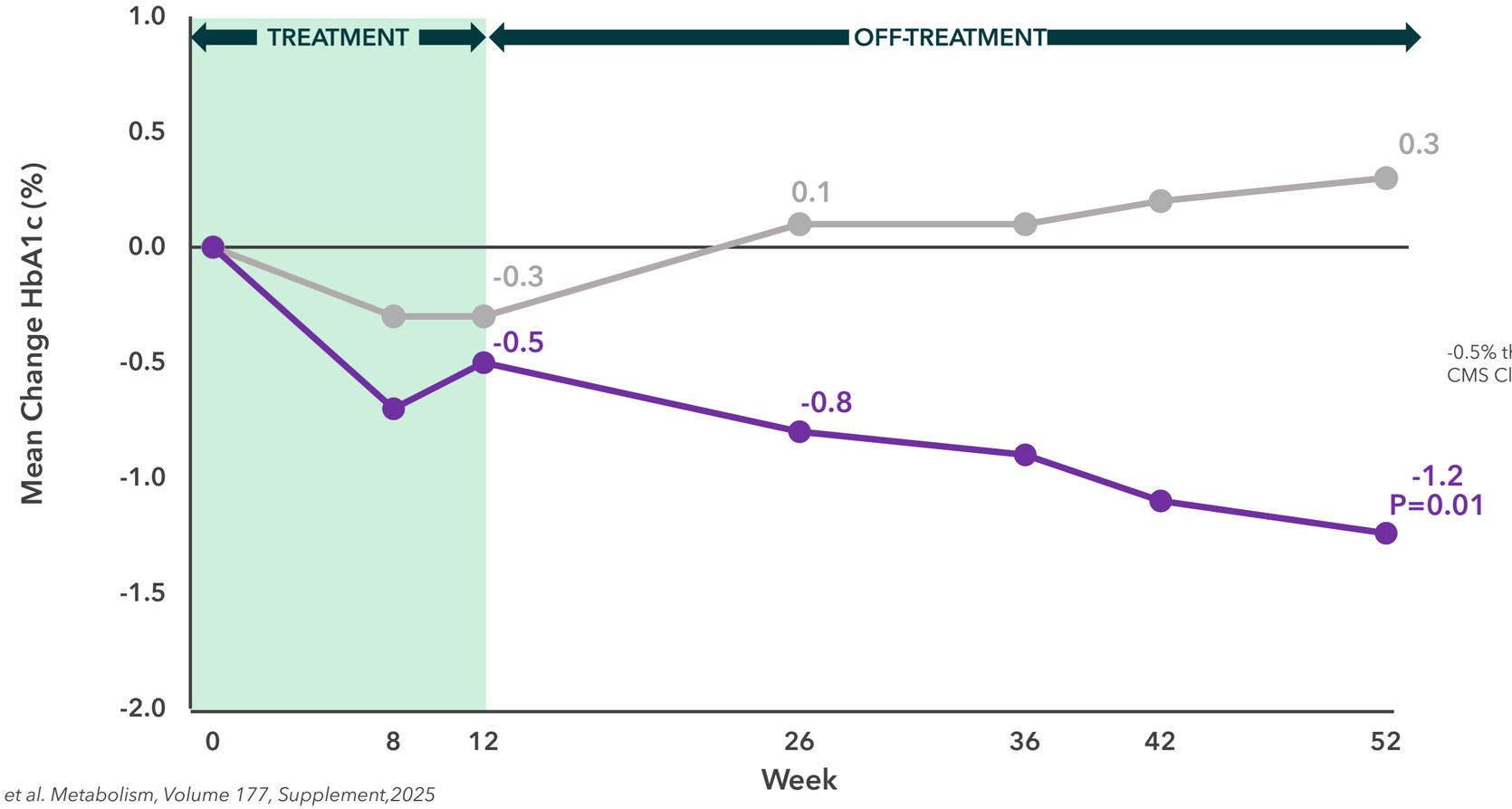


Frias, et al. Metabolism, Volume 177, Supplement,2025

All presented data utilized a while-on-treatment estimand with mixed model repeated measures (MMRM) analysis and was censored for use of rescue medication, defined as any modification in anti-diabetic therapy.

ICOVAMENIB | COVALENT-111

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

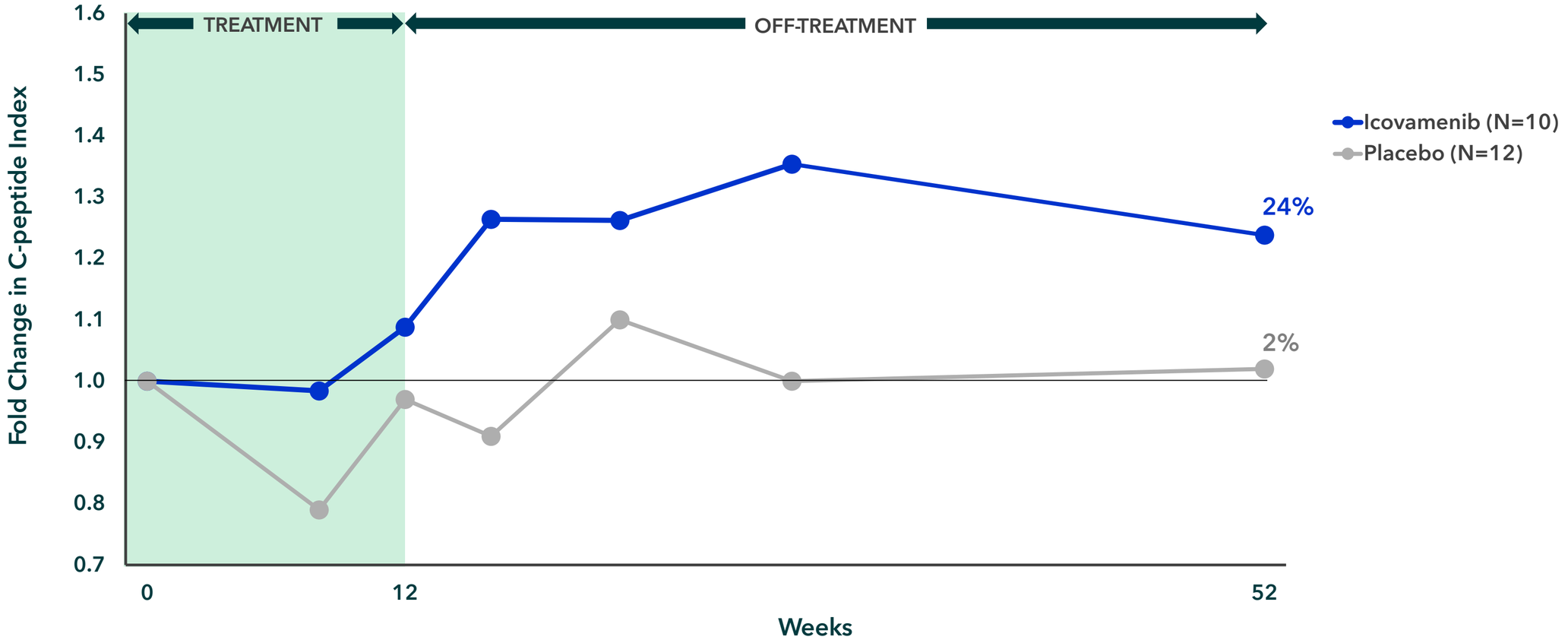


Frias, et al. Metabolism, Volume 177, Supplement,2025

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

ICOVAMENIB | COVALENT-111

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 | PRECLINICAL

Icovamenib's mechanism of action

Icovamenib promotes selective and partial reduction in menin levels

Lowering menin levels releases the break on beta cell proliferation and GLP-1 and GLP-1 receptor expression

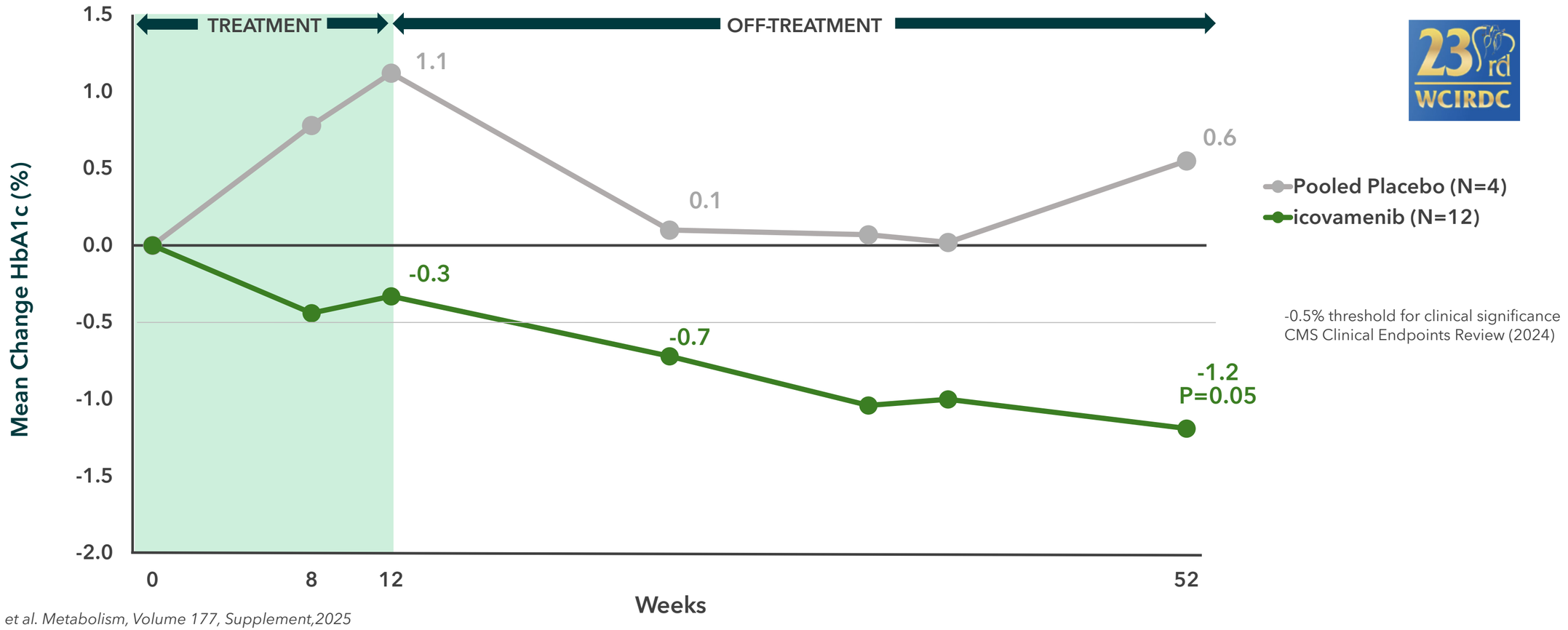
Increased expression of
- **GLP-1**
- **GLP-1 receptor**

IMPROVED INCRETIN EFFECTS

- Improved beta cell function
- Decrease in blood glucose (HbA1c)
- Synergistic with GLP-1 based therapies
- Potential for weight loss
- Potential for lean mass/muscle preservation

ICOVAMENIB | COVALENT-111

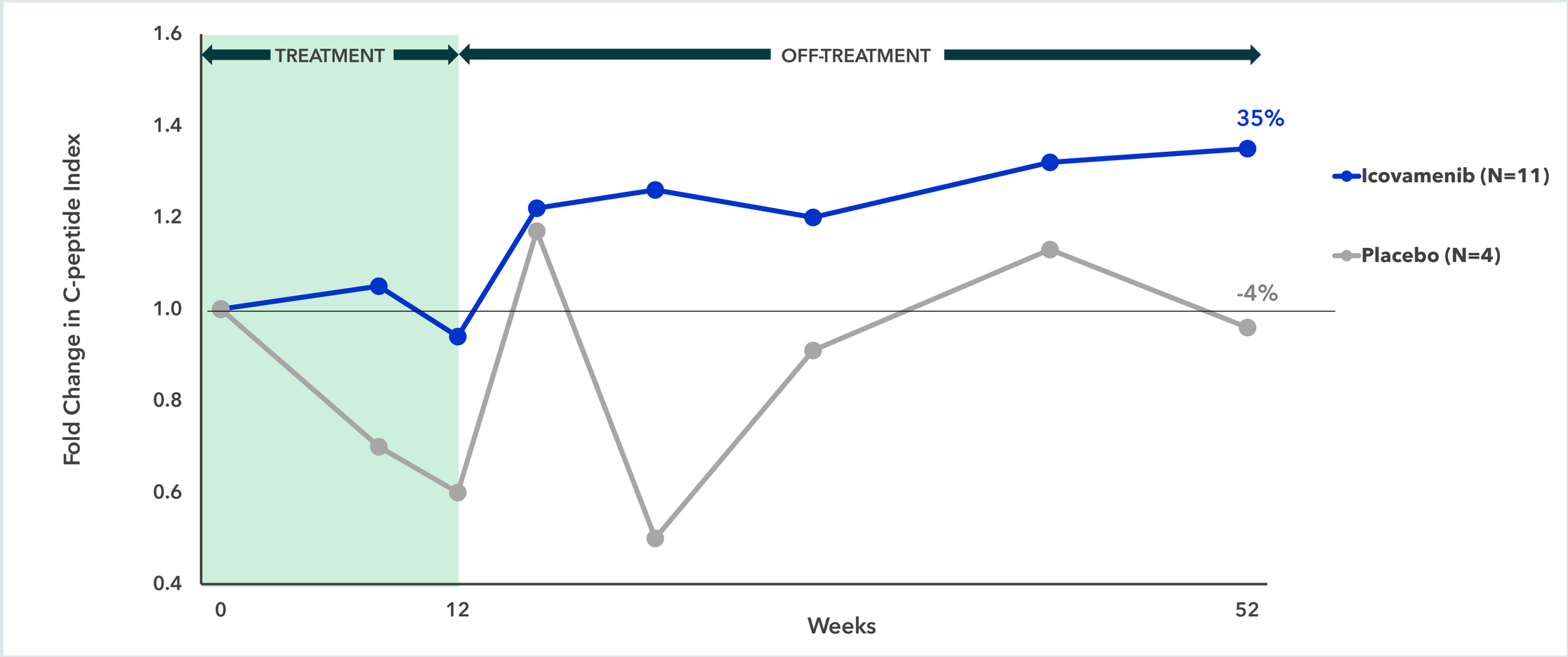
Patients on a GLP-1 based therapy at enrollment showed durable & clinically meaningful response in reduction of blood sugar (HbA1c)



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

ICOVAMENIB | COVALENT-111

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

ICOVAMENIB | COVALENT-111

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 ≥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 | COVALENT-111

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)
Icovamenib (menin inhibitor)	**12 weeks dosing**	**Oral**	**Week 52 (COVALENT-111)**	**-1.5% to -1.8%* (100 mg)**

Ozempic FDA Label; Mounjaro FDA Label; Jardiance FDA Label; Januvia FDA Label

*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.

ICOVAMENIB

Potential first-in-class oral menin inhibitor for diabetes

– ONGONG STUDIES in Diabetes

biomea FUSION™

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/m^2
- Background therapy maintained unless rescue required

COVALENT-212

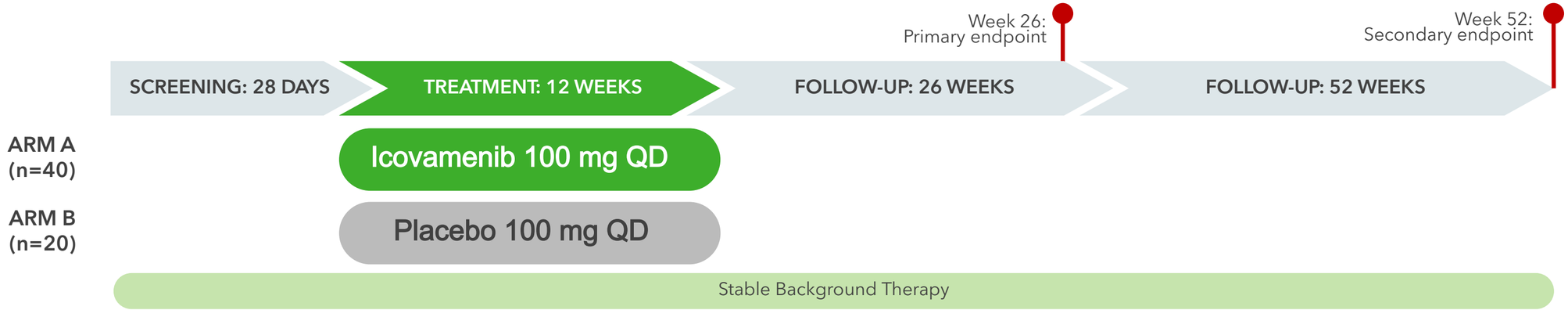
Phase II trial in type 2 diabetes patients failing standard of care while on a GLP-1 RA

- Adult participants with T2D who are not achieving glycemic targets despite GLP-1-based therapy
- HbA1c ≥7.5% and ≤9.5% and BMI 25 to 40 kg/m^2
- Background therapy maintained unless rescue required

ICOVAMENIB | COVALENT-211

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

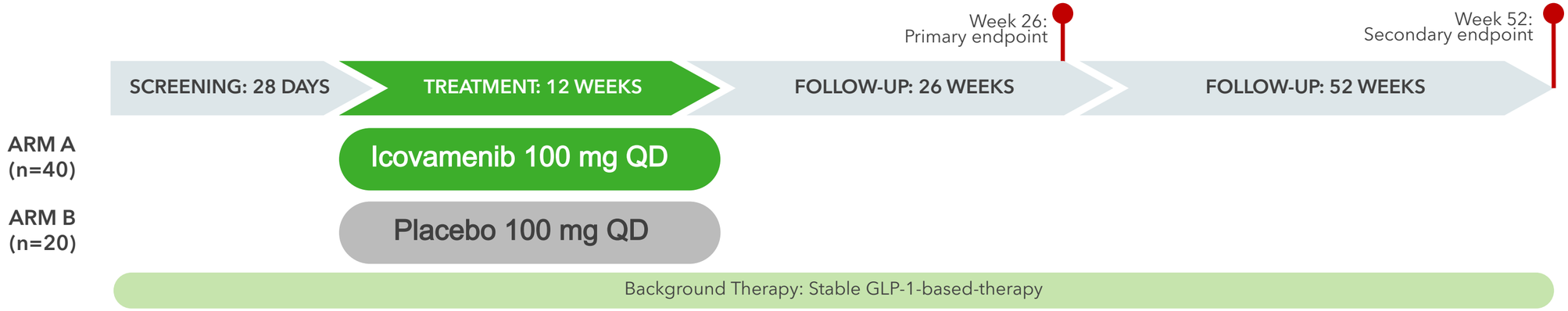
Objectives	Endpoints	Inclusion Criteria
To demonstrate that icovamenib 100 mg once daily for 12 weeks is superior to placebo for glycemic control at Week 26 and Week 52	• Mean change in HbA1c from baseline at Week 26 and 52 • Mean change in fasting plasma glucose (FPG) from baseline at Week 26 • Safety	• Adult participants with Type 2 Diabetes who were treated with 1-3 antidiabetic medications • HbA1c 7.5%-10.5% • BMI ≤ 32 kg/m2 • Background therapy maintained unless rescue required



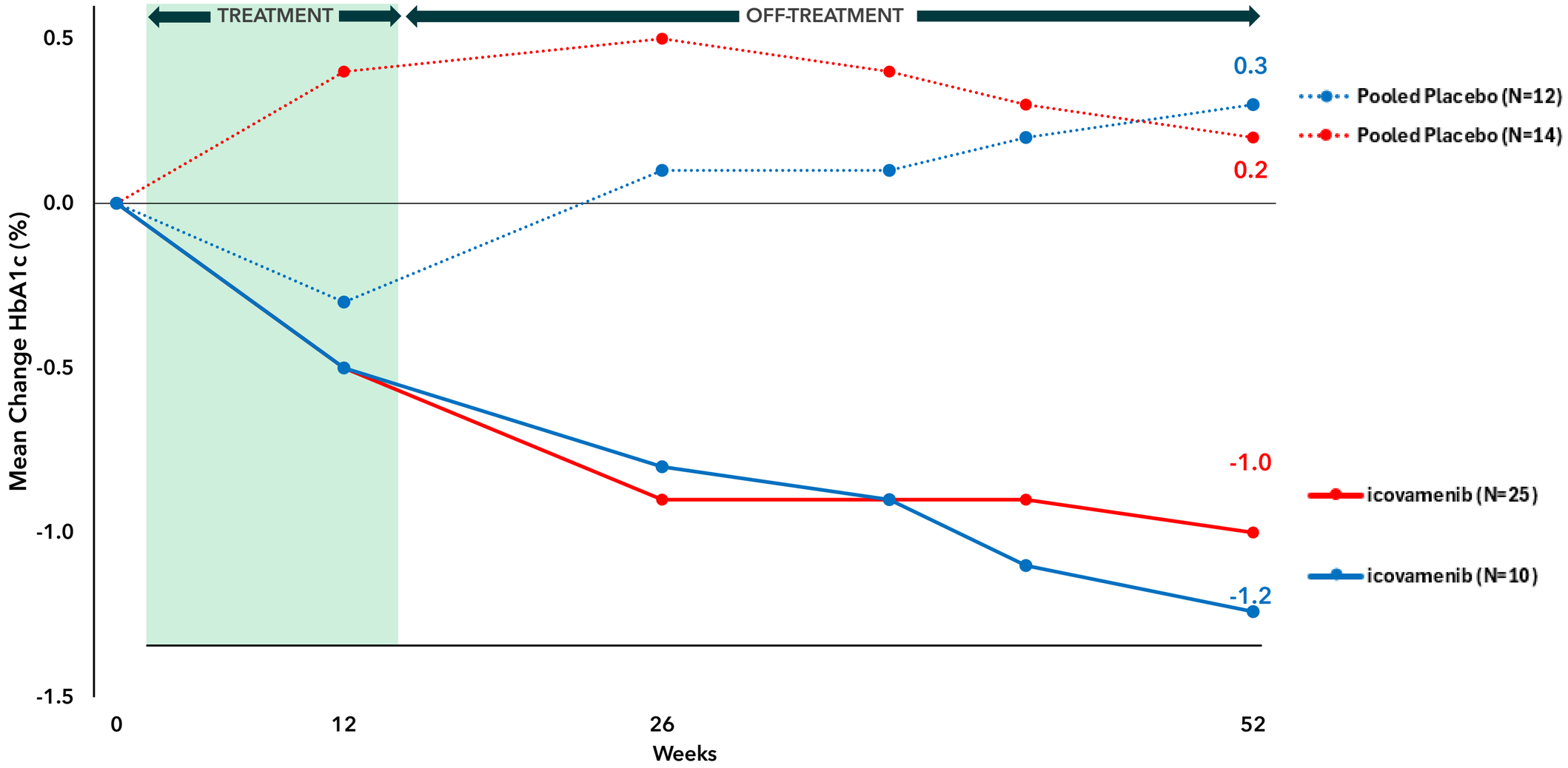
ICOVAMENIB | COVALENT-212

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

Objectives	Endpoints	Inclusion Criteria
To demonstrate that icovamenib 100 mg once daily for 12 weeks is superior to placebo for glycemic control at Week 26 and Week 52	• Mean change in HbA1c from baseline at Week 26 and 52 • Mean change in fasting plasma glucose (FPG) from baseline at Week 26 • Safety	• Adult participants with T2D who are not achieving glycemic targets despite GLP-1-based therapy • HbA1c ≥7.5% and ≤9.5% • BMI 25 to 40 kg/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

biomea FUSION™

BMF-650

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

THE CURRENT GLP-1 MARKET

Injectable GLP-1 RAs

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

First Generation Oral GLP-1 RAs

- **Long, complex titration** (typically 4-8+ steps, which can take 3-9 months depending on product)
- **High rates of GI side effects**
- **Many do not reach maintenance dose**
- **High discontinuation rates**

7 out of 10
Patients **discontinue** GLP-1 therapy due to side effects[1]

BMF-650
Designed for sustainable weight loss management

Next Generation Oral GLP-1 RA

- **Designed for improved GI tolerability**
  Potential for better tolerability and adherence
- **Built to improve persistence**
  Helping more patients stay on therapy
- **Chronic therapy in mind**
  Designed for sustainable weight loss management
- **Two-step titration**
  Faster path to maintenance dose
- **Oral administration**
  Convenience without injections

THE POJECTED 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

1.Real-world evidence across multiple GLP-RA studies (e.g. N Engl J Med 2021.385.896-907. JAMA Netw Open 2022.5e223433; Diabetes Obe Metab. 2023.25.1254-1264

BMF-650 | PRECLINICAL

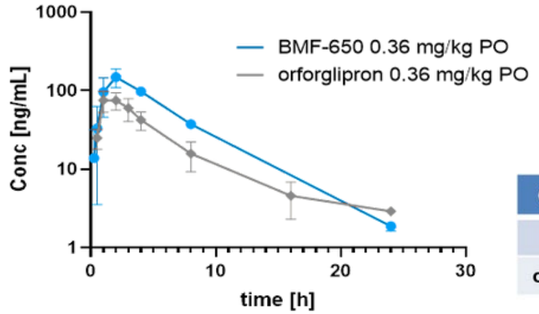
BMF-650 showed favorable in vitro on-target activity and off-target selectivity

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

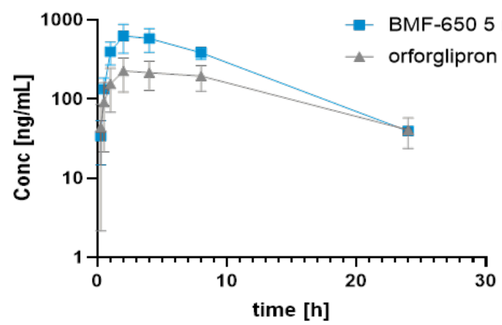
CYNOMOLGUS MONKEY PO PK



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

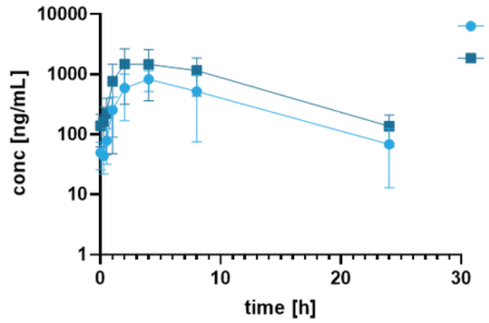
SPRAGUE-DAWLEY RAT PO PK



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



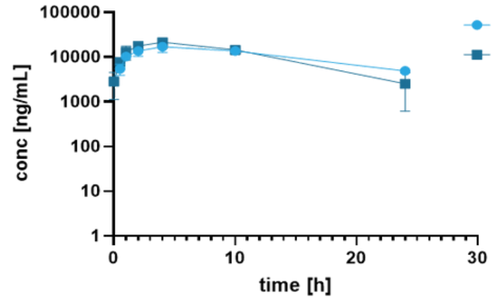
Dose Proportionate Exposure

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



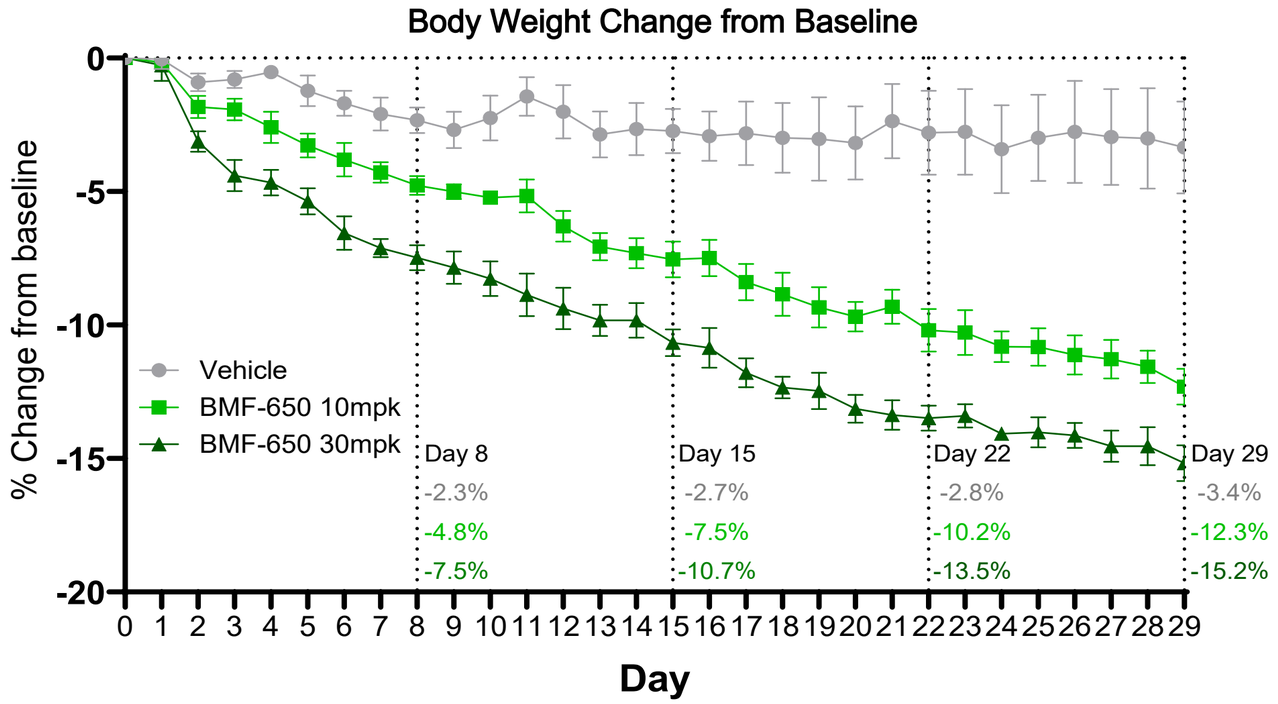
Continuous Exposure after multiple days

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

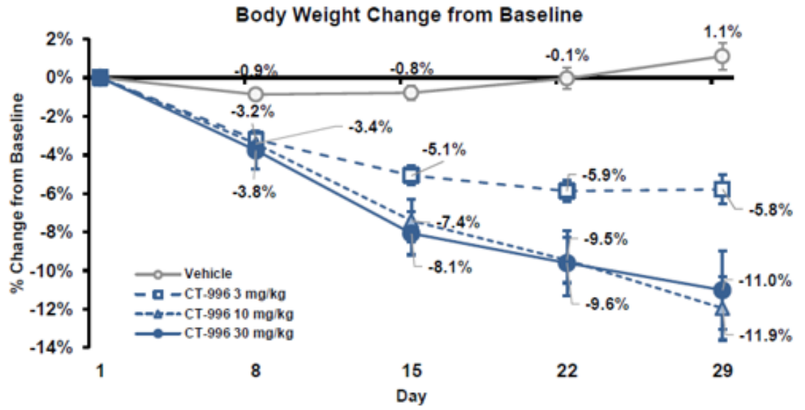


Figure 6. Effects of CT-996 on body weight in obese cynomolgus monkeys following once-daily oral administration. Weekly body weight percent change is represented as mean (± SE) from baseline. N = 6/group.

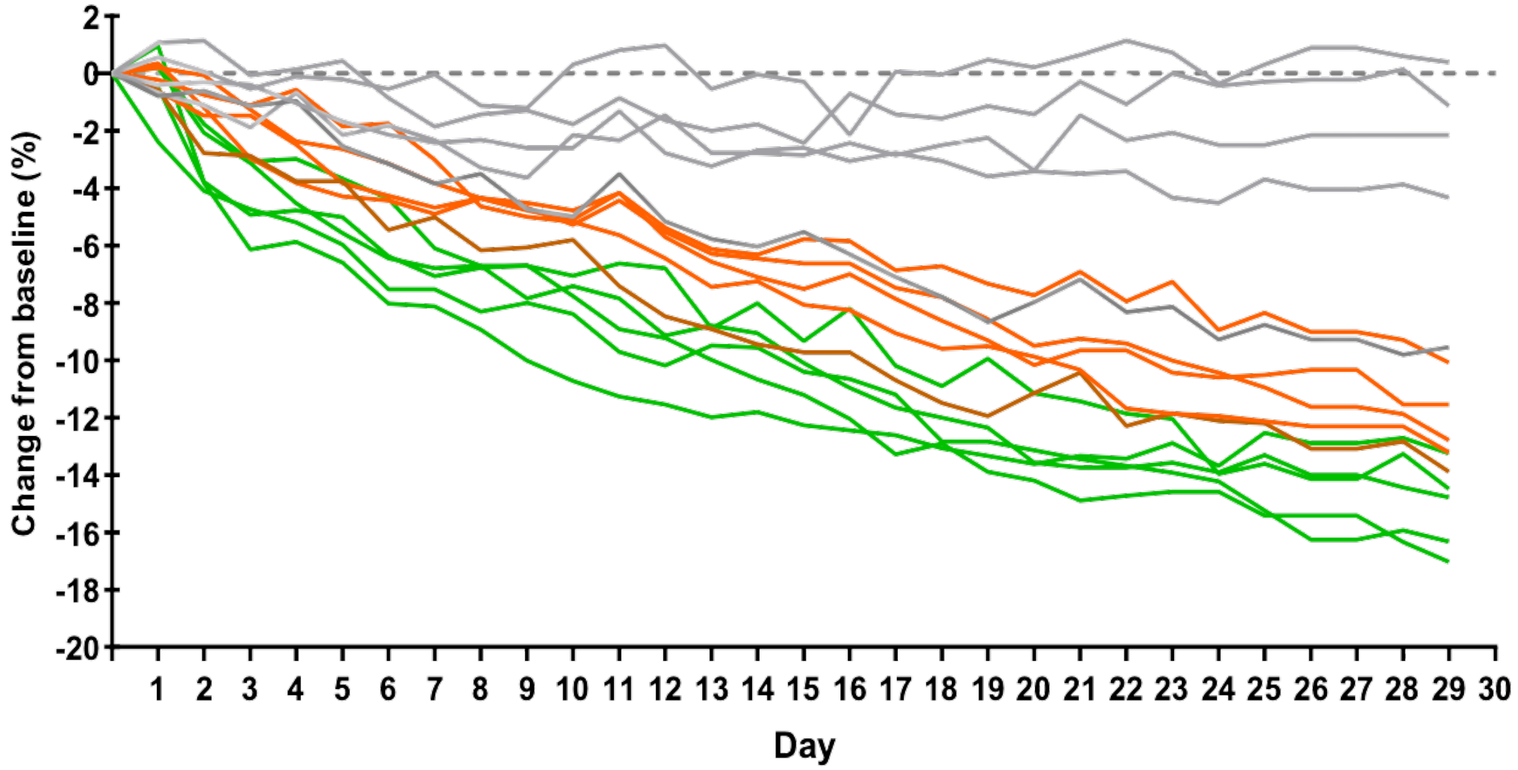
Literature data; Carmot Therapeutics (now part of the Roche group), ADA 2024.

Disclaimer: No head-to-head studies of BMF-650 and CT-996 have been conducted. Comparing results from different preclinical studies may be unreliable due to differences in study designs, study endpoints, and other parameters.

BMF-650 | PRECLINICAL

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

BODY WEIGHT CHANGE (individual obese monkey)



Mean reduction in body weight (Day 29)

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

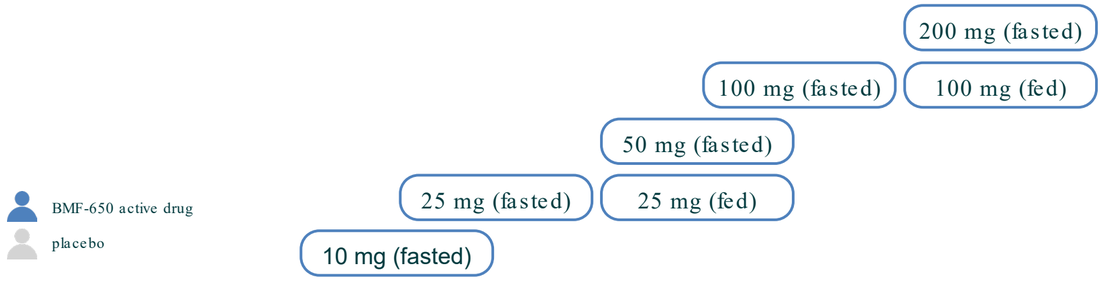
Wang, et al. Obesity 2025: 33 Sup 2 Poster #085

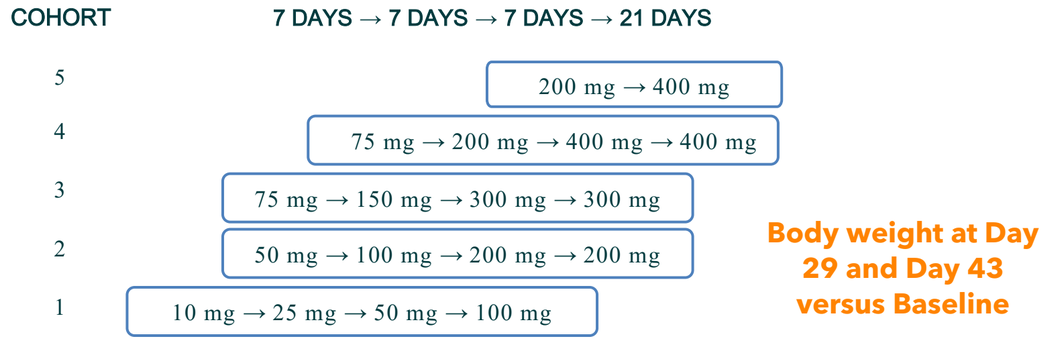
BMF-650 | GLP-131

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 	N=50 5 cohorts x 





Body weight at Day 29 and Day 43 versus Baseline

BMF-650 | PRECLINICAL

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 – IST | Phase 2 Study | n=40 | Enrollment anticipated to start 1Q 27

PLANNED T1D LEICESTER DIABETES CENTER | 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 | Start: 3Q 2026 | Enrollment anticipated to start 3Q 26

Icovamenib in Type 2 Diabetes

- Insulin deficient
- GLP-1 uncontrolled

COVALENT-211 in insulin deficient T2D | Phase 2 Study | n=60 | Start: 2Q 2026

COVALENT-212 in GLP-1 uncontrolled T2D | Phase 2 Study | n=60 | Start: 2Q 2026

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 1Q 2027

BMF-650 Phase 2
Initiation depending on Phase I results

THANK YOU

(NASDAQ: BMEA)

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

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biomea FUSION™

Slowing the clock on diabetes
Turning a healthcare crisis into a huge opportunity

The problem:
Diabetes is a global healthcare crisis, with over 800 million people affected worldwide. The disease is expanding at an estimated ~4% annually. In the United States, one in every four healthcare dollars is spent on people living with diabetes, totaling over $400 billion per year. More than 100 million Americans have prediabetes; approximately 40% will progress to diabetes, and ~60% are diagnosed only after reaching late-stage disease.

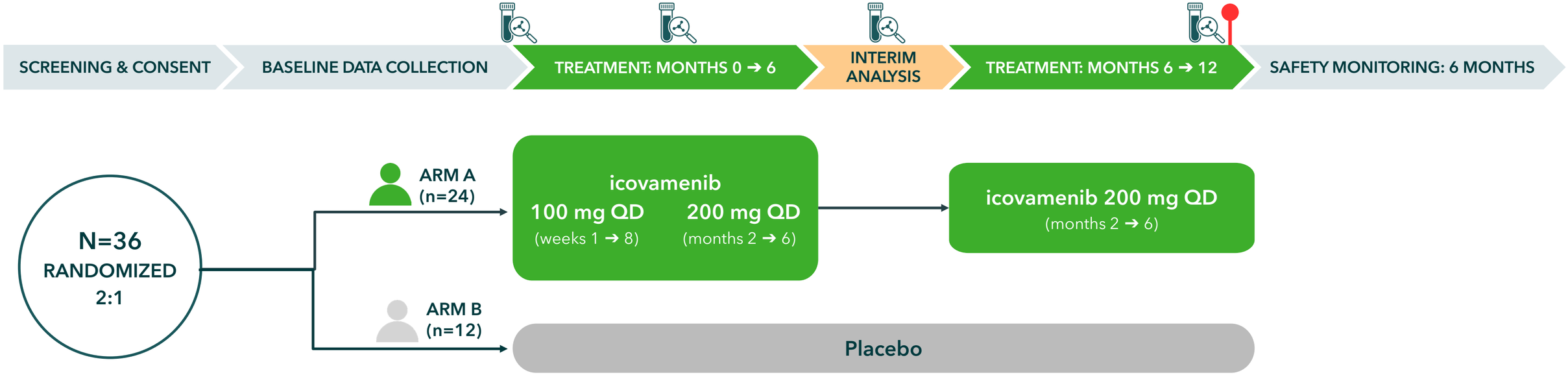
The economic impact:
Late-stage diabetes drives over 50% of healthcare related costs due to complications such as kidney failure, cardiovascular disease, amputations and visual loss. With late-stage diabetes the healthcare system is burden by additional $15,000 - $20,000 per patient. Assuming 10m US diabetes patients are in late stage, delaying the progression could save the system $150-200billion.

Our breakthrough:
We are developing a novel mechanism of action developed to restore beta-cell function and slow the progression of hyperglycemia. By rebuilding a functional beta-cell pool, the body may regain the ability to regulate its own insulin production. The true burden of diabetes is not early disease, but late-stage progression with irreversible organ damage. Slowing that clock by even a few years could generate societal returns exceeding the annual economic output of the entire pharmaceutical sector. Icovamenib would delay the need for unwieldy and often unreliable insulin therapy for years!

Our vision:
Keeping diabetes patients durably controlled, preventing progression to late-stage disease and avoiding the devastating complications that drive cost, morbidity, and mortality.

NEW Biomea sponsored T1D study planned for 2026*

Long term dosing of icovamenib in T1D to show continuous C-peptide increase



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