biomea FUSION™

Corporate Presentation 4Q 2024

Disclaimer

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A Long History of Developing Successful Drugs - Together

Thomas Butler
Chairman & CEO

biomea FUSION

Co-Founder

The FUSION™ SYSTEM
icovamenib*
Co-Inventor

imbruvica® (ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

Veklury® remdesivir 100 MG FOR INJECTION
Co-Inventor

Ramses Erdtmann
President & COO

biomea FUSION

Co-Founder

imbruvica® (ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

Juan Frías, M.D.
Chief Medical Officer

once weekly mounjaro® (tirzepatide) injection 0.5 mL
2.5 mg | 5 mg | 7.5

farxiga® (dapagliflozin) 5mg & 10mg tablets
Jardiance® (empagliflozin) tablets 10 mg/25 mg
once weekly trulicity® (dulaglutide) injection 0.5 mL
0.75 mg | 1.5 mg | 3.0 mg | 4.5 mg
ONCE-WEEKLY wegovy® semaglutide injection 2.4 mg

Byetta® (exenatide) injection
Invokana® (canagliflozin) tablets

OZEMPIC® semaglutide injection 0.5mg, 1mg, 2mg
anuvia® sitagliptin

Naomi Cretcher
Chief of People

imbruvica® (ibrutinib)
560. 420. 280, 140 mg tablets | 140, 70 mg capsules

Heow Tan
Chief Technical & Quality Officer

ZADAXIN

imbruvica® (ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES (II)

PLENAXIS

HylatopicPlus Cream

Steve Morris, M.D.
Chief Development Officer

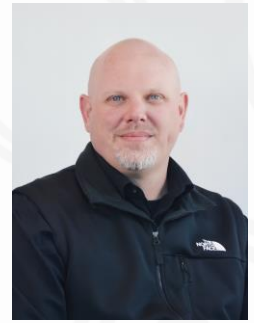
XALKORI® CRIZOTINIB

ZYKADIA® ceritinib 150 mg tablets

LORBRENA® LORLATINIB | 100 mg tablets

ALECENSA® alectinib 150 mg capsules

ALUNBRIG™ BRIGATINIB 30mg TABLETS



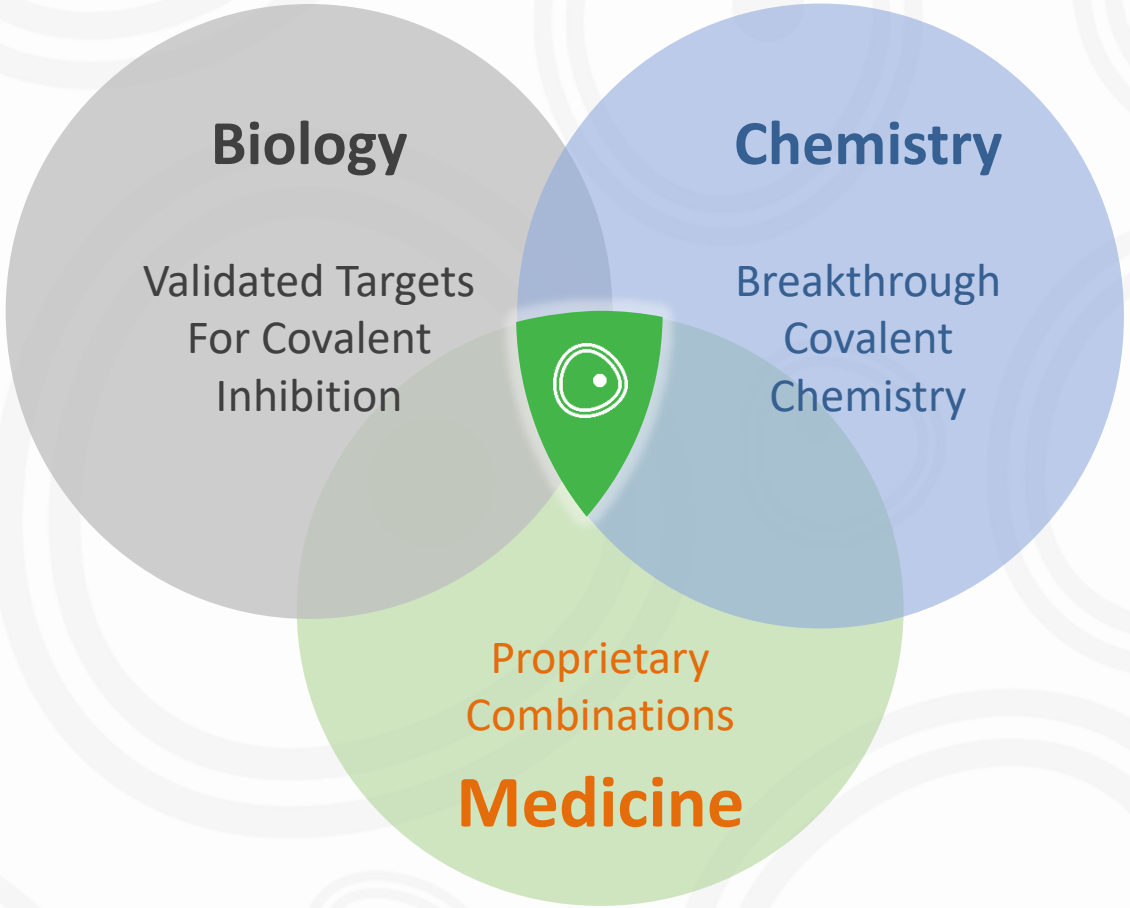
Franco Valle
Chief Financial Officer

imbruvica® (ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

AMTAGVI™ (lifileucel) Suspension for IV infusion

*Note: icovamenib is an investigational new drug

"We Aim to Cure" by Addressing Validated Targets with Breakthrough Covalent Chemistry in Proprietary Combinations



Validated Targets

Drugs pursuing **Validated Disease Targets** have a ~2x higher likelihood of approval than molecules pursuing a new mechanism of action

Sources: Nelson et al. (2015) Nat Genet.; Thomas et al. (2016) BIO; In a Landscape of 'Me Too' Drug Development, What Spurs Radical Innovation? HBS Weekly Review (Jun 2018)

Covalent Inhibitors

Covalent Small Molecule Inhibitors provide deep target inactivation and a wider therapeutic window, allowing for longer duration on therapy

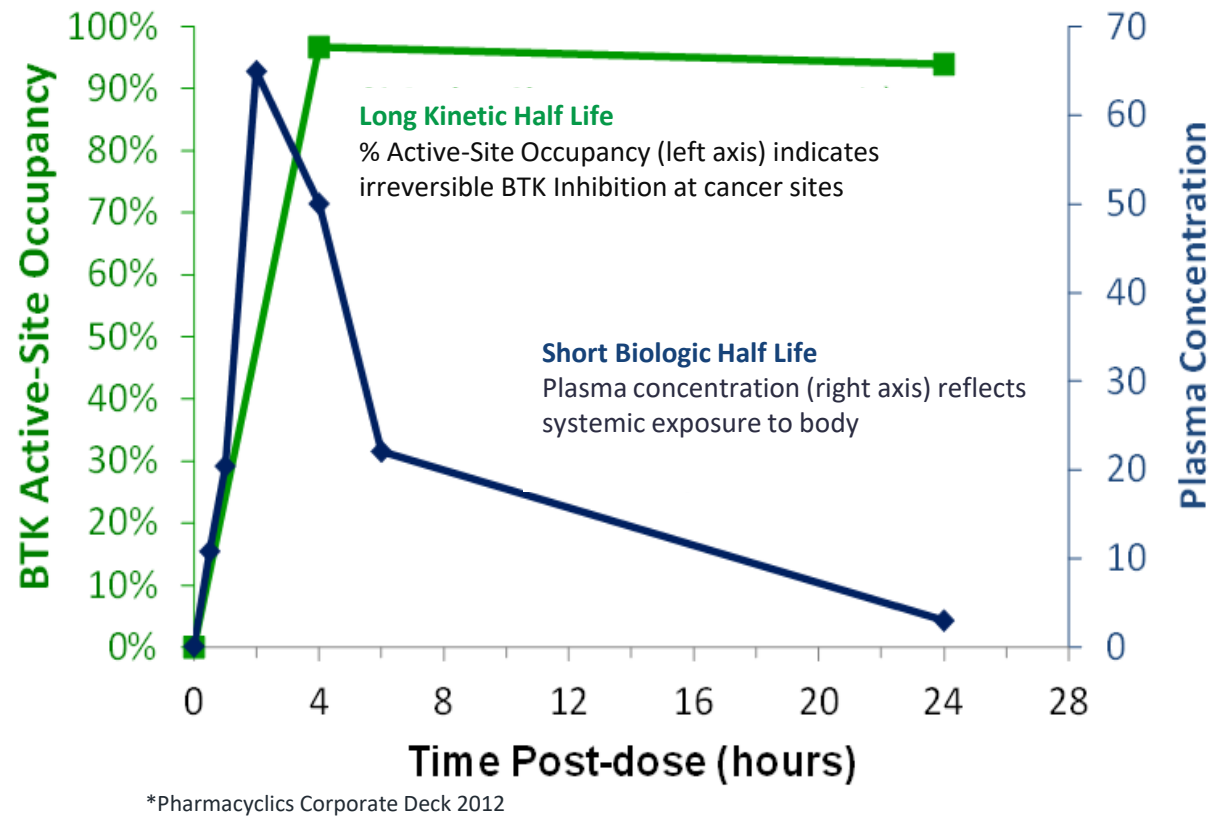
Sources: Singh et al. (2011) Nature Reviews Drug Discovery; Cheng et al. (2020) Journal of Hematology & Oncology; Strelow (2017) SLAS Discovery; Kalgutkar & Dalvie (2012) Expert Opin. Drug Discov.;

Proprietary Combinations

Combination Therapy with non-overlapping resistance mechanisms results in more durable responses and better outcomes

Sources: Palmer et al. (2019) eLife; Mokhtari et al. (2017) Oncotarget

Covalent Inhibitors Have Long Kinetic but Short Biological Half Life



*Pharmacyclics Corporate Deck 2012

High Selectivity

Two-step inhibition: 1) Initial reversible binding followed by 2) covalent interaction, increasing target selectivity

Deep Target Inactivation

Permanent inactivation of bound protein drives target elimination through normal cellular degradation processes

Greater Therapeutic Window

Designed to maintain an effect without sustained systemic exposure, unlike conventional non-covalent inhibitors

BIOMEA FUSION (NASDAQ: BMEA)

Our Mission: Revolutionize Medicine by Creating Therapies that Cure Patients of Their Disease

- First-in-class potential covalent inhibitors enabling broad development plan in metabolic diseases and various cancers

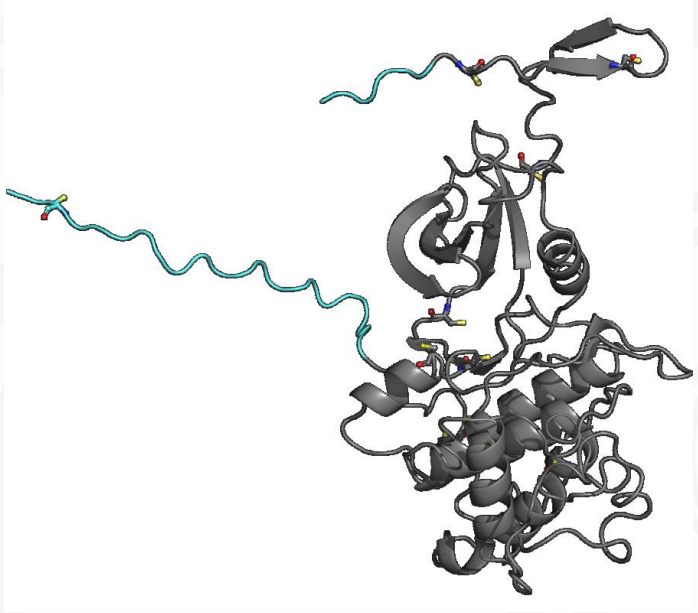
Two clinical stage programs:

- Icovamenib (BMF-219) – Menin Program
- BMF-500 – FLT3 Program

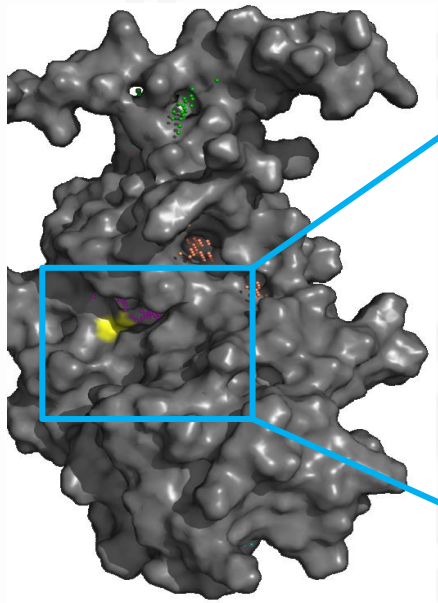
IND enabling studies: BMF-650 – GLP-1 Receptor Agonist

- Covalent inhibitors provide unique PK/PD profiles with maximum pathway disruption and minimum exposure
- Convenient oral route of drug administration
- Type 2 Diabetes: Phase 2b topline Week 26 data readout in 4Q 2024
- Type 1 Diabetes: Phase 2a topline Week 26 data readout in 4Q 2024
- $88.3M cash as of September 30, 2024

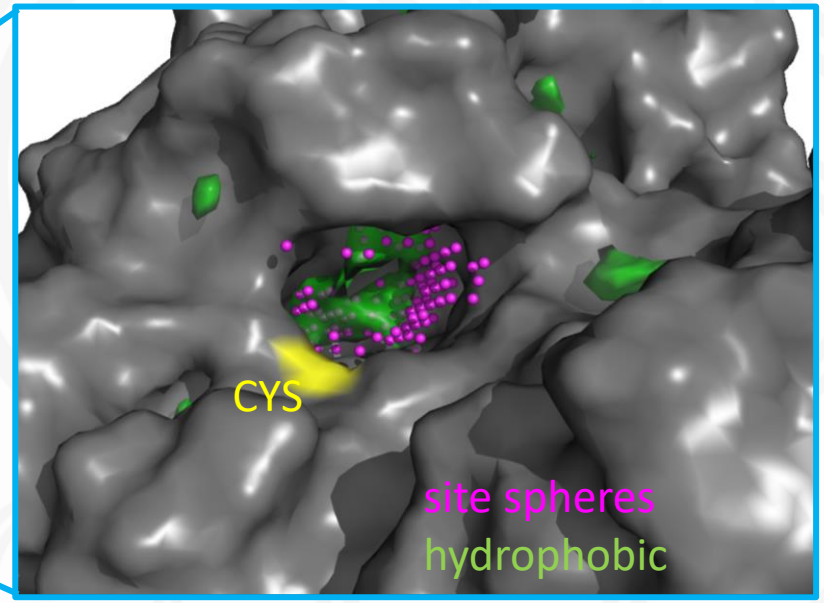
Biomea Fusion System – Discovery and Development of Novel Covalent Inhibitors Against High-Value, Validated Disease Targets



- Predicted structures for ~23,400 human genes; 14,200 novel vs Protein Data Bank
- Analyze individual domains if needed – potential artificial inter-domain pockets
- Manual curation for high interest targets



- AlphaFold 2.0 are apo (without ligand) structures
- Pocket identification using established methods "bindability" ranking



- Top ranking pocket with sufficient hydrophobic character

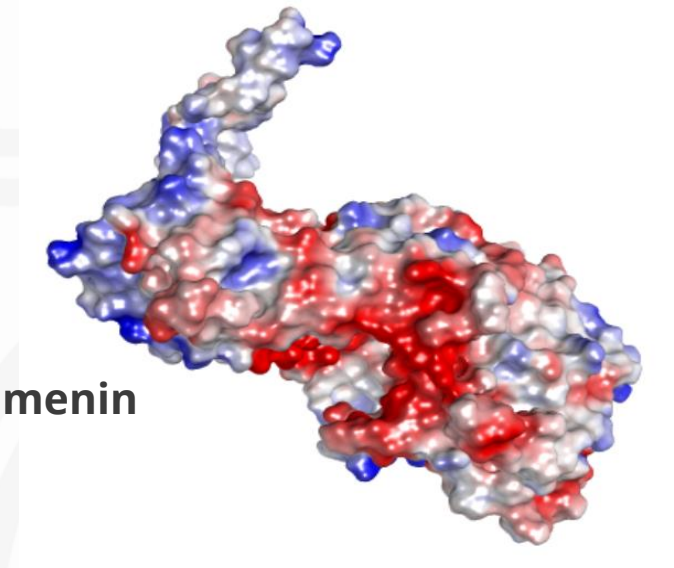
→ Virtual screening for ligands

→ Biomea Linker/Warhead Determination Protocol

→ Lead Molecule(s)

Icovamenib (BMF-219):

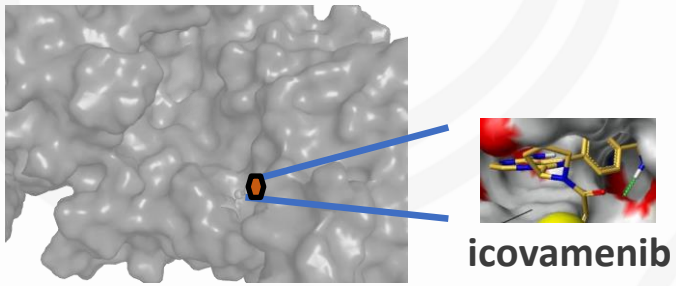
Potential First-in-Class Menin Inhibitor to Stimulate Beta Cell Regeneration



menin

Protein Binding Data

icovamenib K_d (nM) <1.0 x 10^{-12}



icovamenib

Menin has 6 approachable cysteines. icovamenib binds covalently only to the desired cysteine.

Targetable Cysteine	Binding Selectivity
CYS1	100%
CYS2	0%
CYS3	0%
CYS4	0%
CYS5	0%
CYS6	0%

Icovamenib

- First-in-class irreversible covalent menin inhibitor to stimulate beta cell regeneration.
- Convenient oral dosing.
- Robust, wholly owned, internally discovered program.
- Key differentiation: novel PK/PD profile with ability to disrupt multiple binding partners of menin.
- Novel clinical activity with demonstrated clinical efficacy in AML and diabetes (type 1 and type 2).

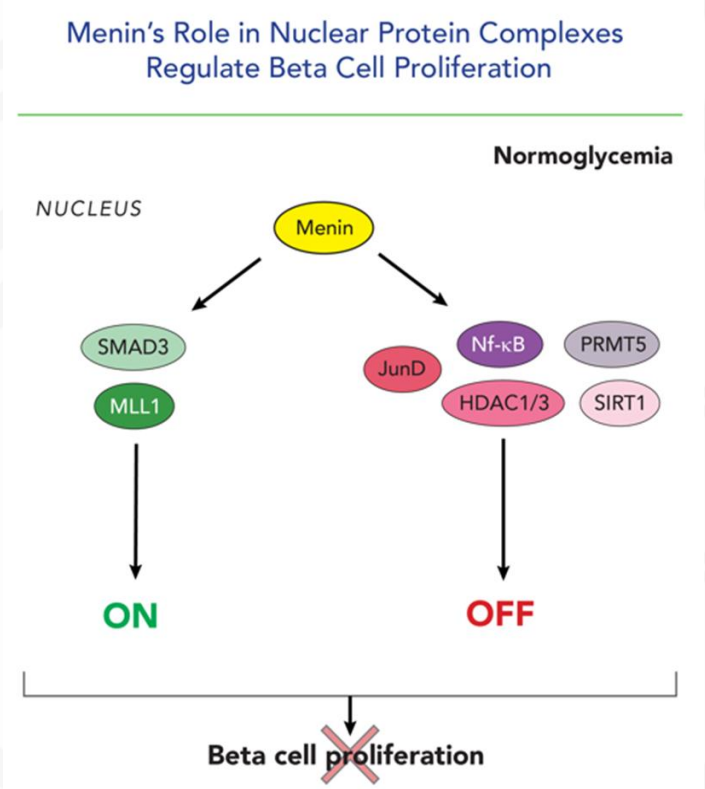
Multiple Upcoming Milestones

	Study	Indications	Milestones
Icovamenib (BMF-219) Menin Program (Potential Best-In-Class)	COVALENT-111	Type 2 Diabetes	**Phase IIb – Topline Week 26 Data Readout (Dec 2024)** *Confirm optimal dosing scheme and define best responding patients*
	COVALENT-112	Type 1 Diabetes	**Phase IIa – Topline Week 26 Data Readout (Dec 2024)** *Initial patients' response with various dosing schedules*
	COVALENT-101	Liquid Tumors	**Phase I - Dose Escalation Completion**
	COVALENT-102	Solid Tumors	**Phase I - Dose Escalation Completion**
BMF-500 FLT3 Program (Potential Best-In-Class)	COVALENT-103	AML/ALL (Acute Leukemia)	**Phase I - Dose Escalation Completion**
BMF-650 GLP-1R Agonist (Potential Best-In-Class)	IND-Enabling Studies	Diabetes/Obesity	**Clearance of IND**

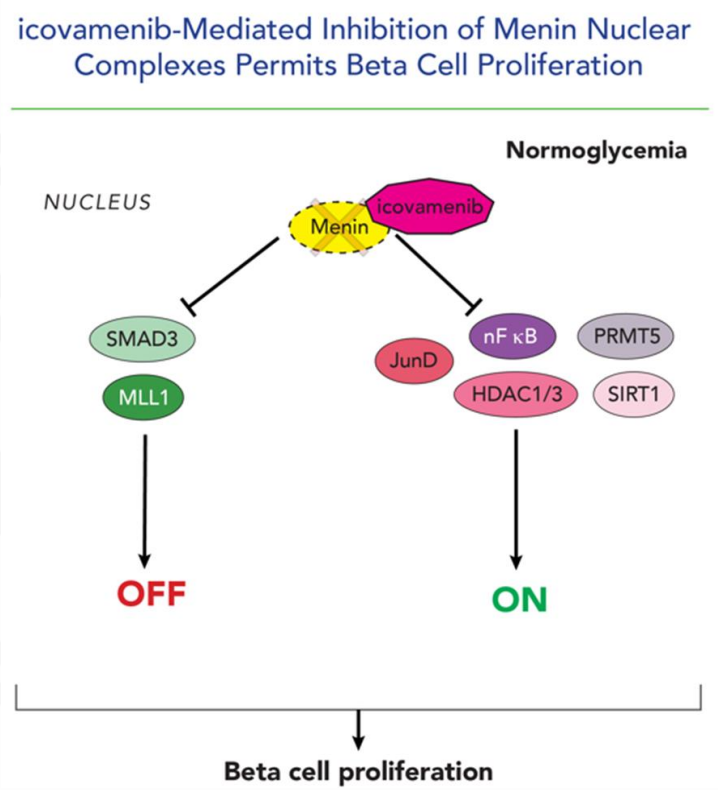
Icovamenib (BMF-219) in Type 2 Diabetes

An oral covalent menin inhibitor in clinical development to investigate its impact on the regeneration of insulin-producing beta cells

Beta-Cell Proliferation and Signaling



Menin-bound protein complexes suppress beta cell replication and function through direct interaction with multiple binding partners that induce transcriptional changes in men in-responsive beta cell growth controlling genes. In complex with SMAD3 or MLL 1, menin transcriptionally activates beta cell growth repressive genes, and in complex with JunD or HDACs, men in represses beta cell growth promoting genes through epigenetic modulation.

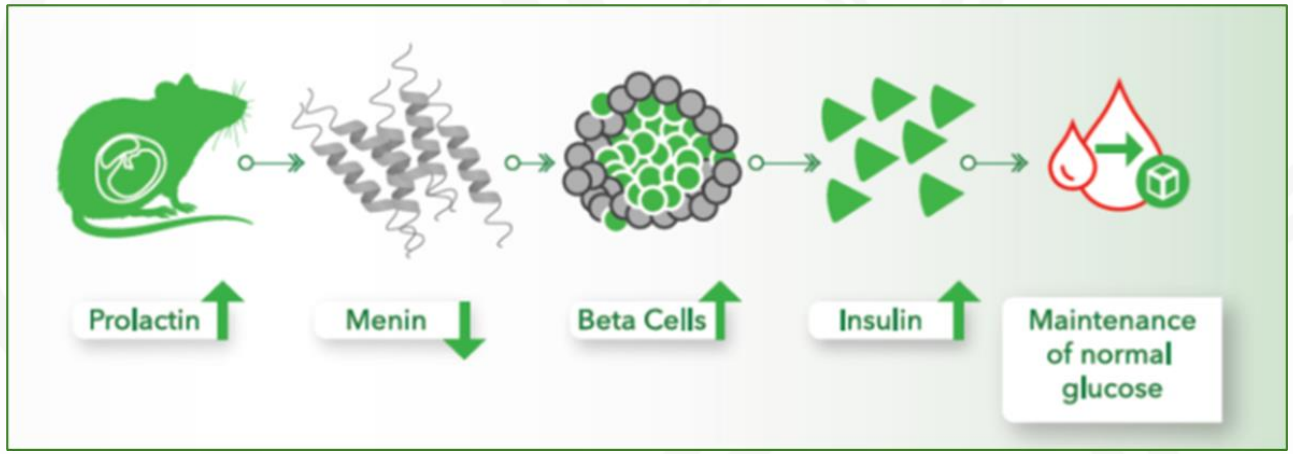


Menin-bound protein complexes suppress beta cell replication and function through direct interaction with multiple binding partners that induce transcriptional changes in menin responsive beta cell growth controlling genes. Icovamenib selectively and covalently binds to menin, disrupting its ability to complex with SMAD3 or MLL1, leading to transcriptional inactivation of beta cell growth repressive genes. Menin inhibition by icovamenib also prevents interaction with JunD or HDACs, permitting beta cell growth promoting gene expression through epigenetic modulation, and overall promoting beta cell proliferation.

Physiologic states associated with beta cell regeneration

Menin is downregulated by prolactin during pregnancy allowing for beta cell replication and prevention of gestational diabetes

- In 2007, Stanford University researchers found that menin regulated adaptive islet growth in pregnant mice
- Prolactin, a hormonal regulator of pregnancy, repressed beta cell menin levels and stimulated beta cell proliferation



Science
AAAS

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

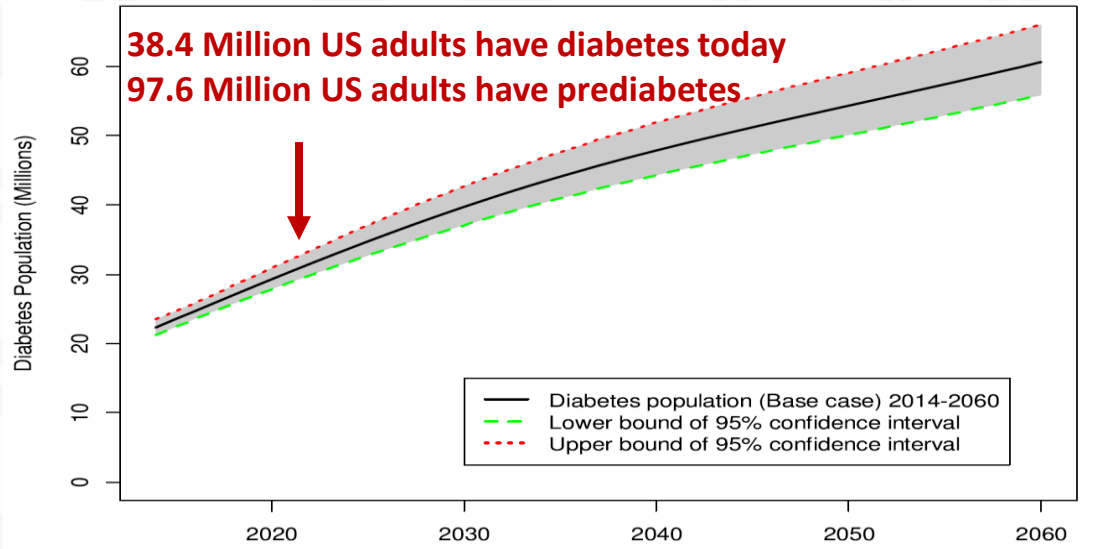
Satyajit K. Karnik,[1] Hainan Chen,[1*] Graeme W. McLean,[1*] Jeremy J. Heit,[1*] Xueying Gu,[1] Andrew Y. Zhang,[1] Magali Fontaine,[2] Michael H. Yen,[1,3] Seung K. Kim[1,3]†

During pregnancy, maternal pancreatic islets grow to match dynamic physiological demands, but the mechanisms regulating adaptive islet growth in this setting are poorly understood. Here we show that menin, a protein previously characterized as an endocrine tumor suppressor and transcriptional regulator, controls islet growth in pregnant mice. Pregnancy stimulated proliferation of maternal pancreatic islet β-cells that was accompanied by reduced islet levels of menin and its targets. Transgenic expression of menin in maternal β-cells prevented islet expansion and led to hyperglycemia and impaired glucose tolerance, hallmark features of gestational diabetes. Prolactin, a hormonal regulator of pregnancy, repressed islet menin levels and stimulated β-cell proliferation. These results expand our understanding of mechanisms underlying diabetes pathogenesis and reveal potential targets for therapy in diabetes.

Karnik SK, et al. Science. 2007;318(5851):806-9.

2 in 5 Americans will Develop Diabetes during Their Lifetime

- In the U.S. **80% of people with diabetes will die from this disease**. Premature mortality caused by diabetes results in an estimated **12-14 years of life lost**.
- Diabetes creates one of the largest economic burdens on the U.S. health care system. **$1 out of every $4 in US health care** costs is being spent on caring for people with diabetes.
- Diabetes **remains unresolved for almost 50% of patients on current standard of care.**



- There are over 60+ approved type 2 diabetes agents, but **none of them address the root cause of the disease**.

FDA

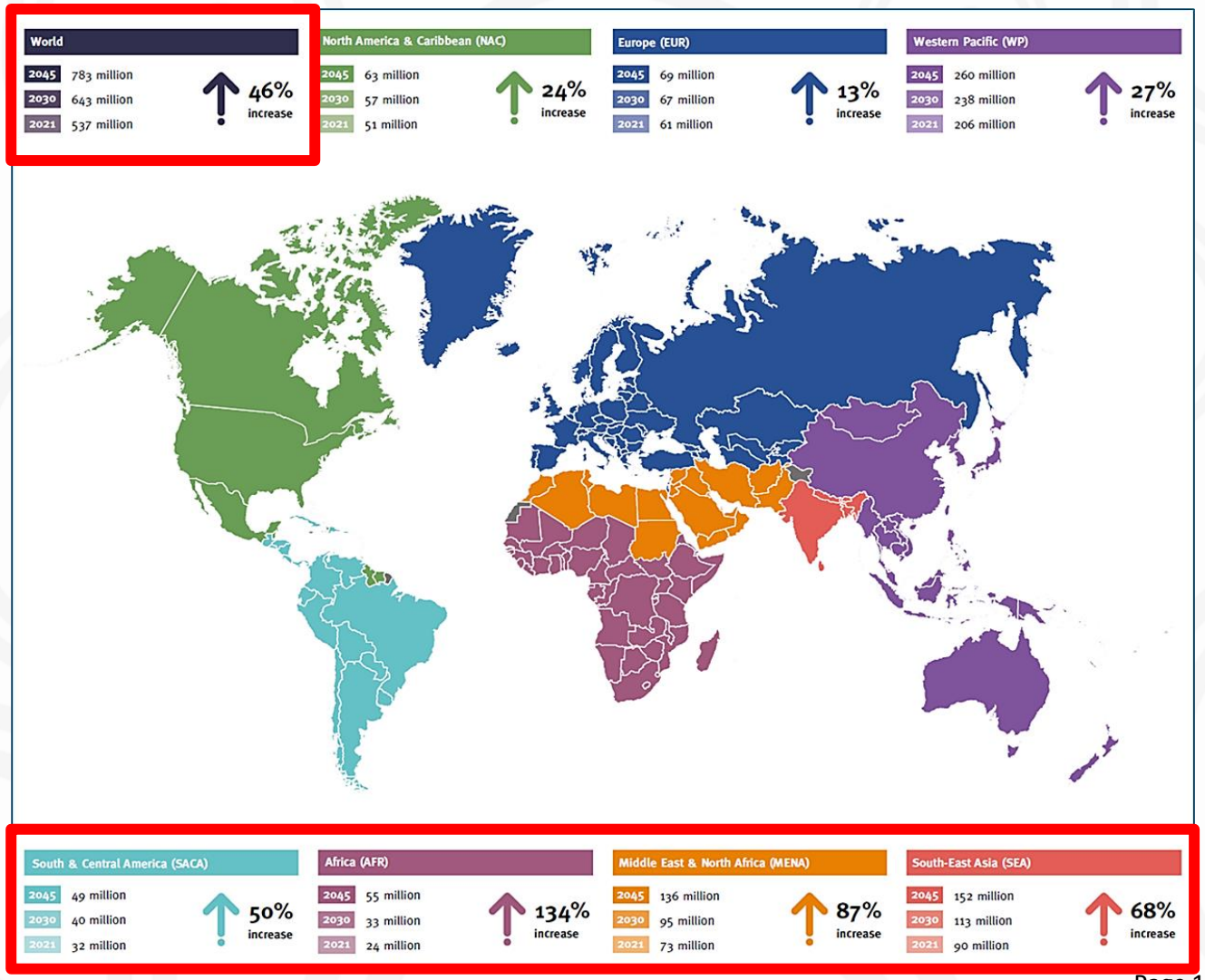
"Diabetes is a common disease that affects nearly 40 million people in the U.S. and is projected to affect more in the coming years. **The need for more antidiabetic treatment options is clear**," said Lisa Yanoff, M.D., deputy director of the FDA's Center for Drug Evaluation and Research, alongside FDA's updated draft guidance for industry titled, "Diabetes Mellitus: Efficacy Endpoints for Clinical Trials Investigating Antidiabetic Drugs and Biological Products Guidance for Industry" published on **May 25, 2023**.

Source: National library of Medicine 1(2); 2007 Jul PMC3068646; Clin Diabetes. 2020 Jul;
National Diabetes Statistics Report published in 2024 by CDC;
Real-world trends in GLP-1 treatment persistence and prescribing for weight management (BHI Report)

Ever-Increasing Global Prevalence of Diabetes

- ↑ Complications
- ↓ Life Expectancy
- ↓ Quality of Life
- ↑ Healthcare Costs

- A significant unmet need exists for developing therapeutics that address the root cause of diabetes (beta cell dysfunction) and that are potentially disease modifying.
- We, at Biomea Fusion, are at the forefront of this effort!



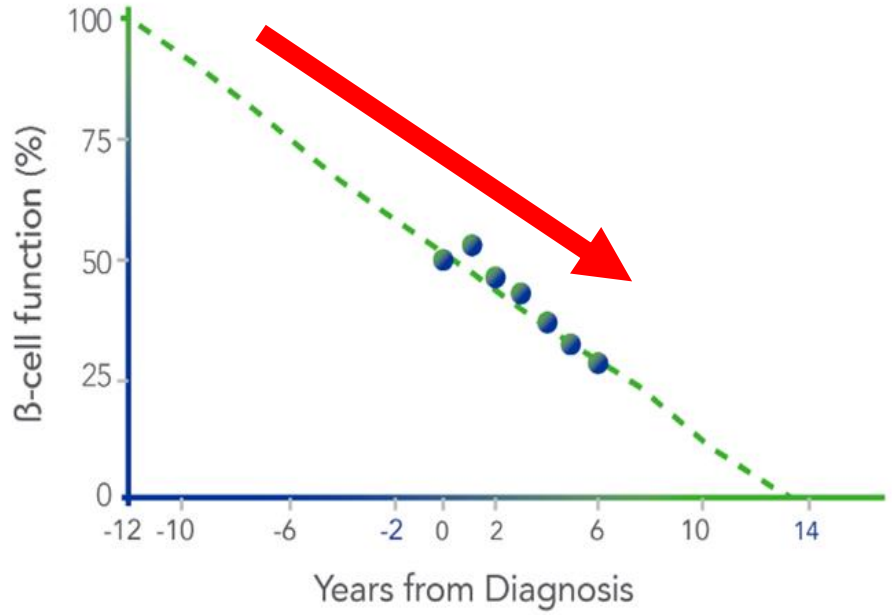
IDF Diabetes Atlas, 10th edition

None of Today's Type 2 Diabetes Agents Address the Root Cause of Diabetes

– The Progressive Decline in Beta-Cell Mass and Function

Loss of Beta Cell Function

The Root Cause of Diabetes

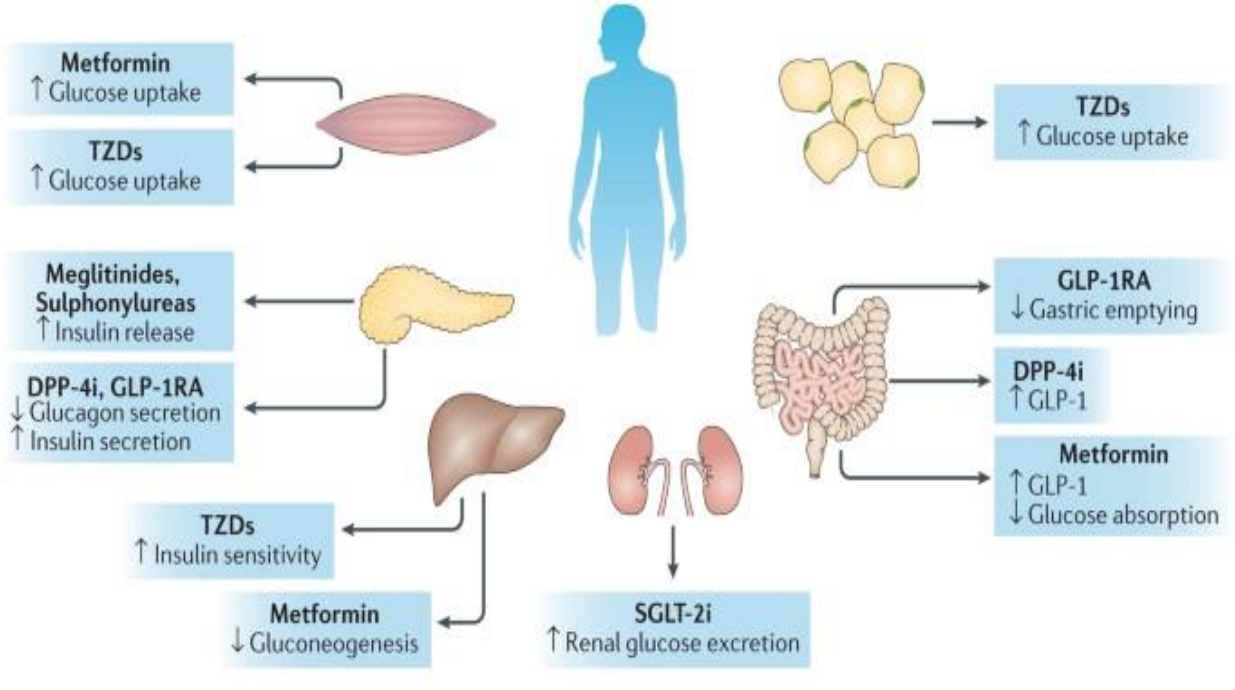


Adapted from DeFronzo RA. *Diabetes.* 2009;58(4):773-795.

Currently Approved Therapies

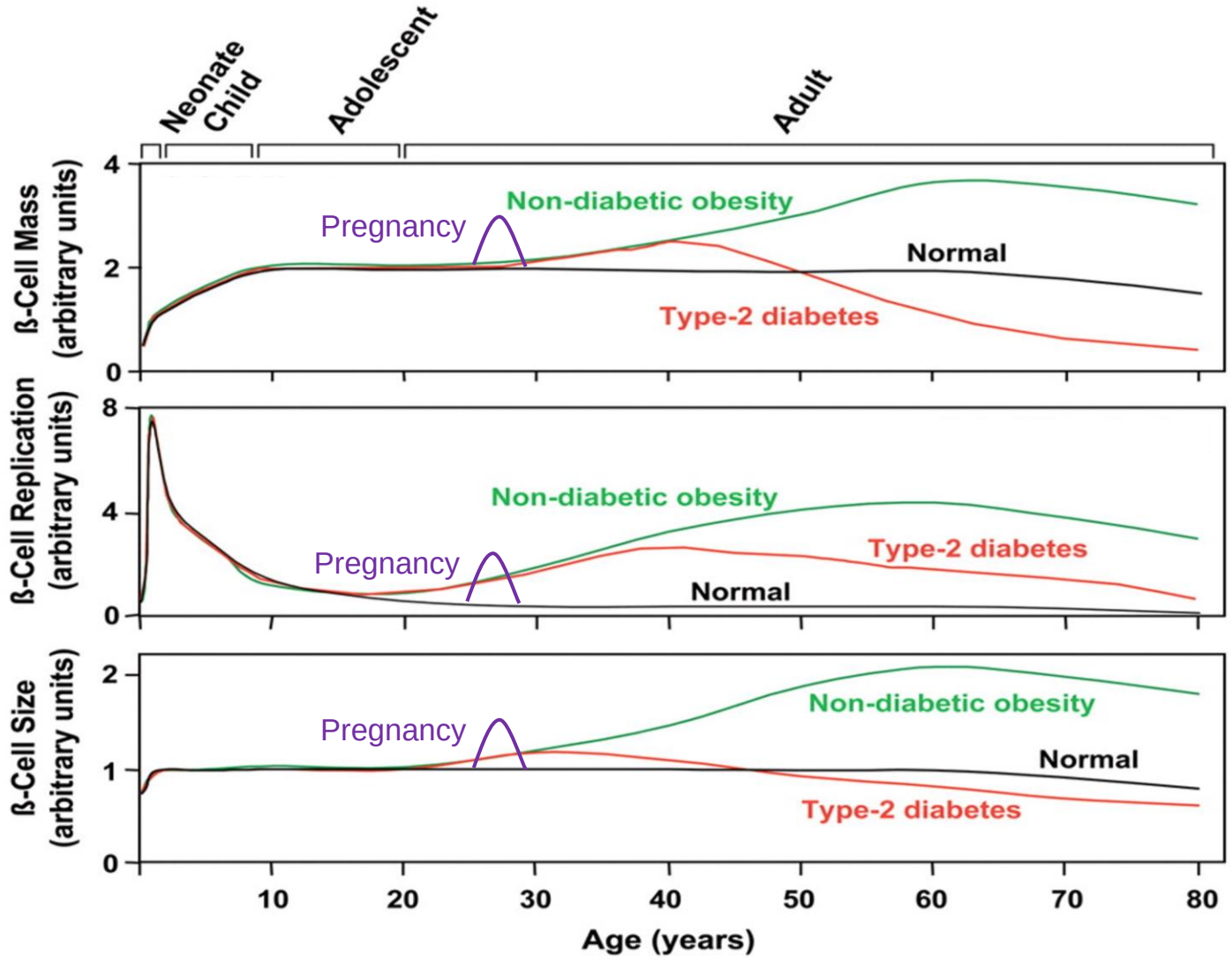
Targeting the Symptoms of Type 2 Diabetes

HYPERGLYCEMIA



Nat Rev Endocrinol 12, 337–346 (2016). https://doi.org/10.1038/nrendo.2016.51

Beta Cells Compensate Physiological and Pathophysiological States



β-Cell Mass

In obesity, the beta cell mass, replication and size expands.

β-Cell Replication

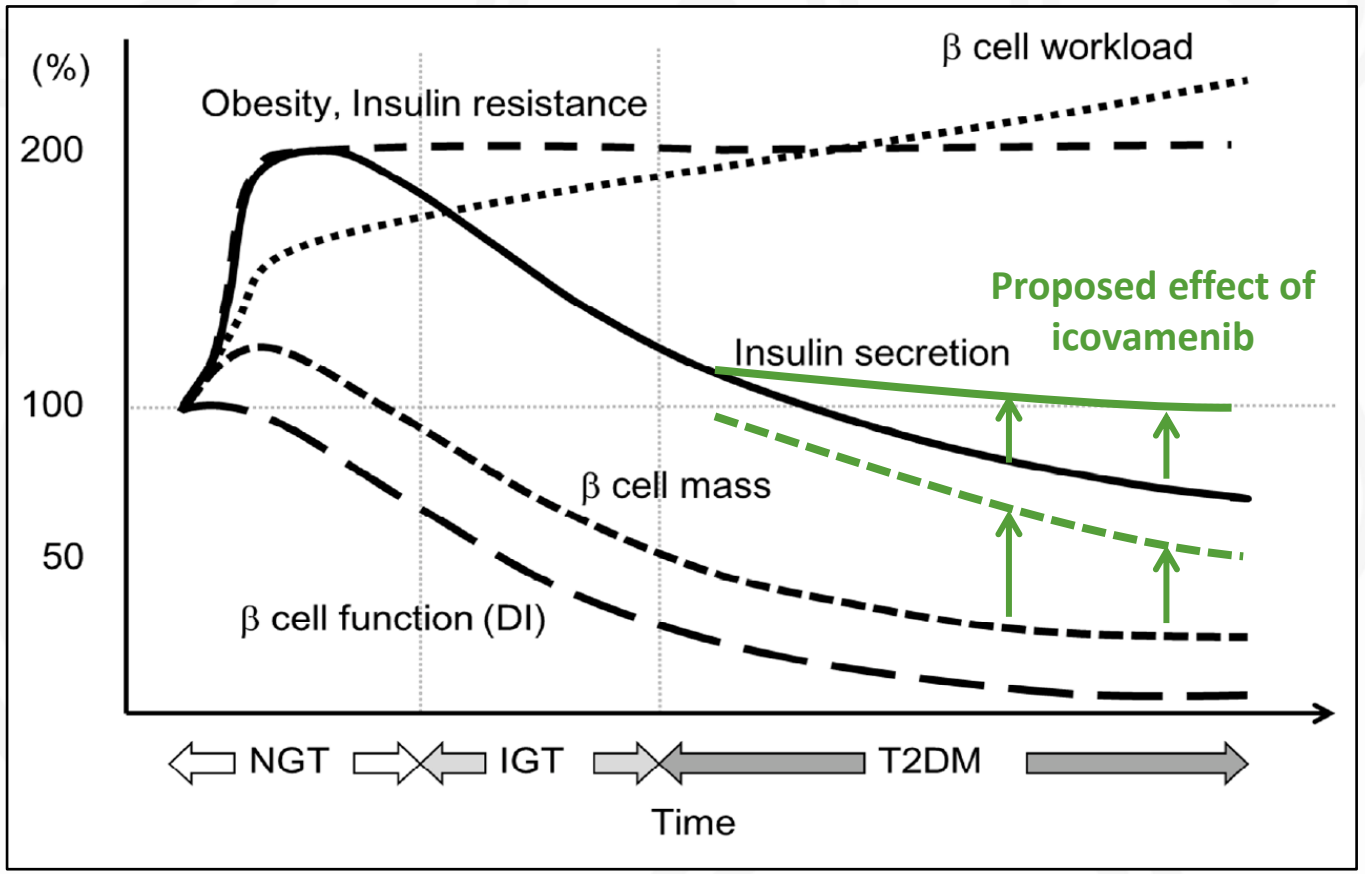
In diabetes the beta cell mass, replication and size at first increases and then gradually declines.

β-Cell Size

In pregnancy as well, the beta cell mass, replication and size expands.

Adapted from Science 2005

A 50% Loss of Beta-Cell Mass leads to Type 2 Diabetes; Icovamenib Has Shown to Regenerate the Beta-Cell Mass and Increases Natural Insulin Production



icovamenib is aimed to increase beta cell mass and function, thereby increase insulin production in order to achieve glycemic control - without the need of continuous medication.

*Normal Glucose Tolerance **(NGT)** followed by Impaired Glucose Tolerance **(IGT)** followed by Type 2 Diabetes Mellitus **(T2DM)**. Insulin Resistance leads to an increase in Beta Cell Workload which ultimately leads to Beta Cell Failure and Death and the Progression of Type 2 Diabetes.

Source: Int. J. Mol. Sci. 2016, 17, 744; doi:10.3390/ijms17050744

Most Effective Type 2 Diabetes Agents Achieve HbA1c Reductions of 0.7% - 1.7%

Currently Approved Type 2 Diabetes Agents w/Chronic Dosing			
Drug (Mechanism of Action)	**Medication Route**	**Observation Period**	**Mean HbA1c Reduction (placebo adj., %)**
Ozempic (GLP 1 Agonist), Chronic Dosing	Injectable	Week 30	-1.2 (0.5mg), -1.5 (1mg)
Mounjaro (GLP-1/GIP Agonist), Chronic Dosing	Injectable	Week 40	-1.7 (5mg), -1.6 (15mg)
Jardiance (SGLT2 Inhibitor), Chronic Dosing	Oral	Week 24	-0.7 (10mg), -0.9 (25mg)
Januvia (DPP4 Inhibitor), Chronic Dosing	Oral	Week 24	-0.8 (100mg)
Summary	-	-	**0.7% ~ 1.7%**

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

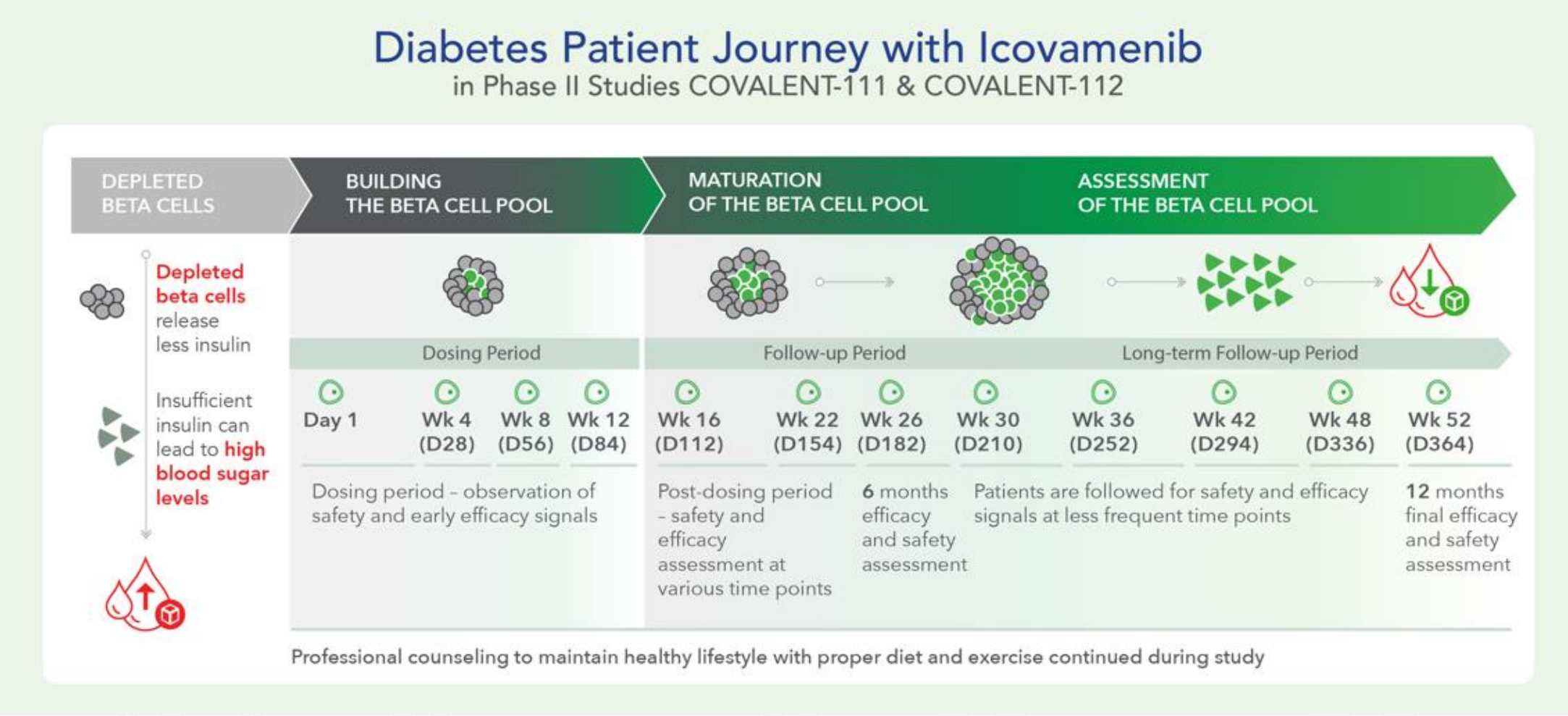
Oral Agents – Efficacy Benchmarks for Chronic Treatments

HbA1c Reduction by 0.5% - 1.67% at Week 26

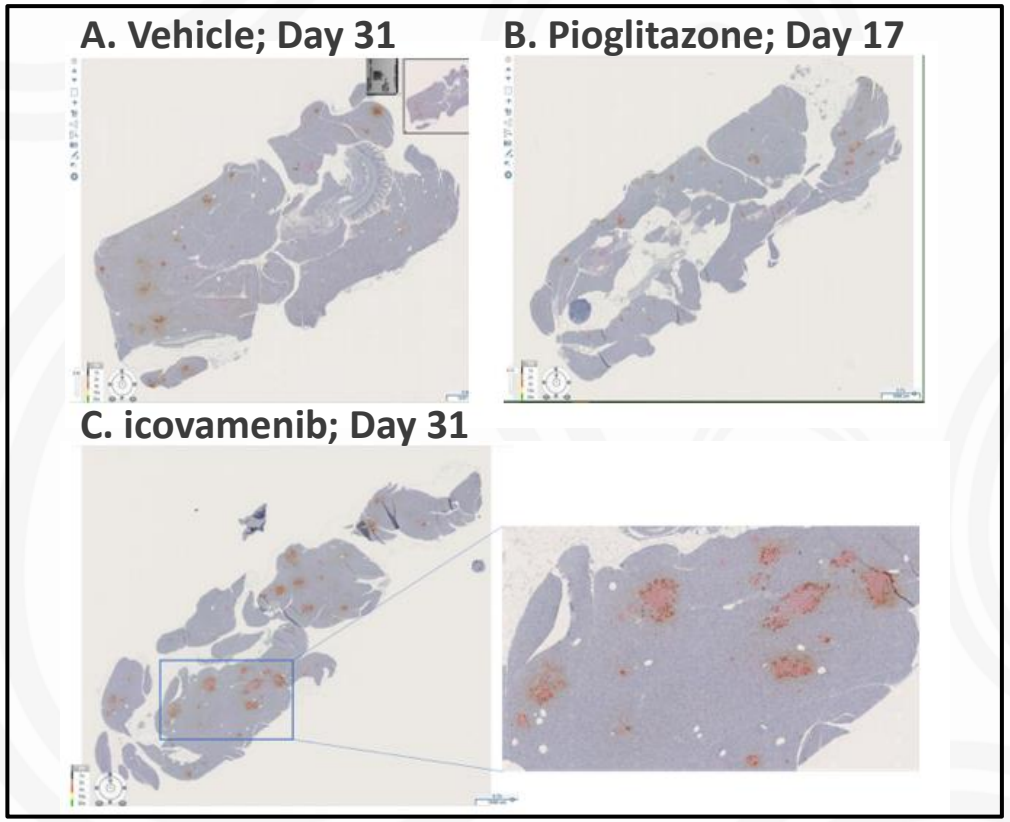
Drug	Development Status	MOA	Mean Reduction HbA1c (Wk 26, placebo adj.)
Rybelsus (Oral semaglutide)	Approved	GLP-1	0.9% (7mg); 1.1% (14mg)
Structure Therapeutics	Clinical Development	GLP-1	1.02% (Week 12)
Orforglipron	Clinical Development	GLP-1	1.67%
Jardiance (empagliflozin)	Approved	SGLT-2	0.7% (10mg); 0.9% (25mg)
Farxiga (dapaglifozin)	Approved	SGLT-2	0.5% (5mg); 0.7% (10mg)
Invokana (canagliflozin)	Approved	SGLT-2	0.91% (100mg); 1.16% (300mg)
Metformin	Approved	MET	1.0%

Rybelsus FDA label; Structure Therapeutics Provides Comprehensive GSBR-1290 Program Update Including Clinically Meaningful Proof-of-Concept Data From Phase 2a Clinical Study; Frias et al. 2023 Aug 5;402(10400):472-483 ; Jardiance FDA label; Farxiga FDA label; Invokana FDA label; MET FDA label.

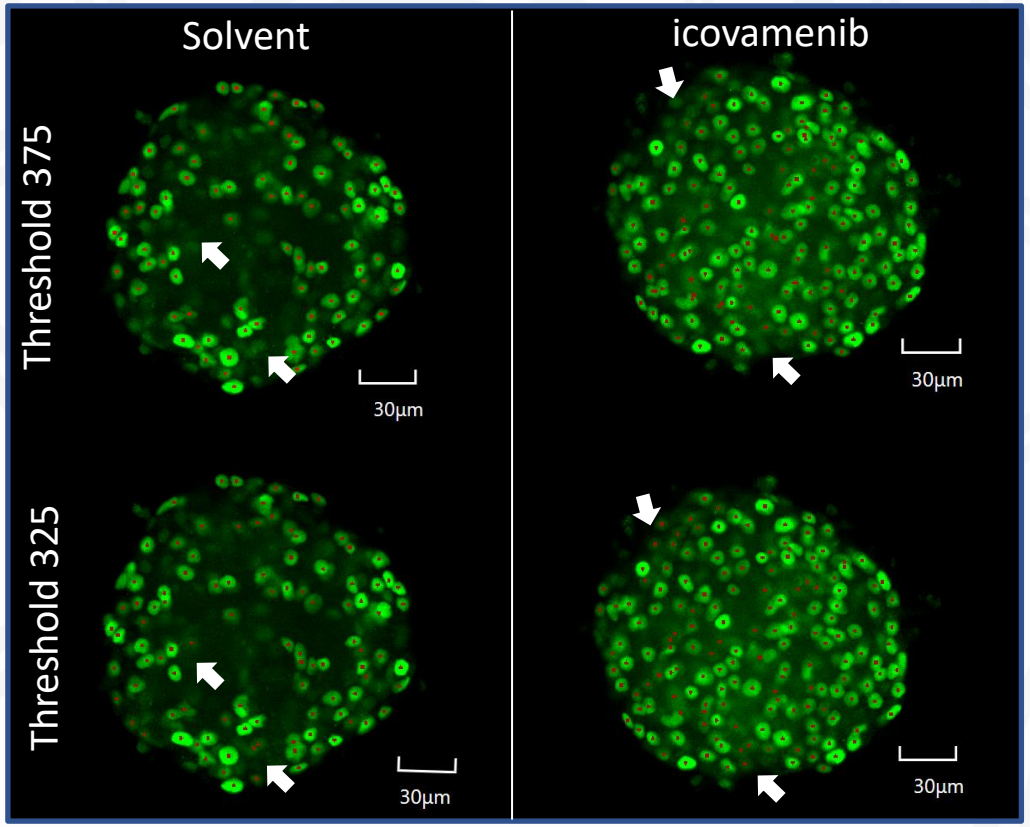
Icovamenib Aims to Proliferate Beta Cells with Short Term Dosing to Achieve Durable Glycemic Control



Icovamenib Increases Beta-Cell Mass in Both in Vivo Rodent Models and ex Vivo Human Islets



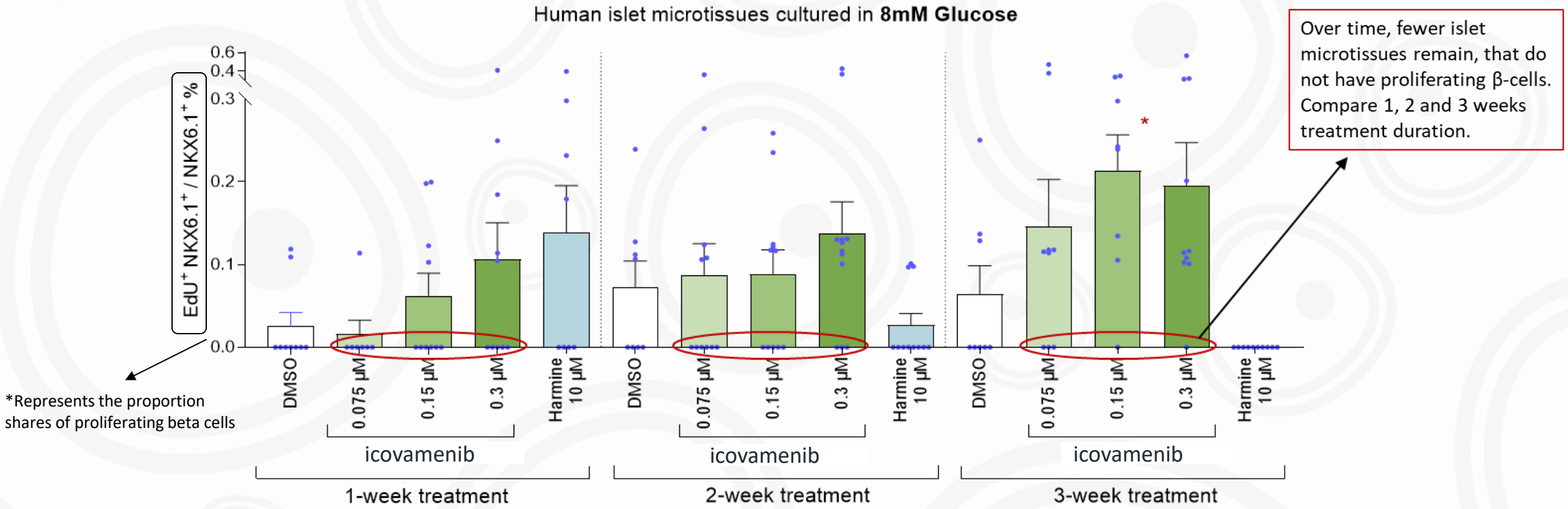
ZDF Diabetic Model: A) Vehicle-treated animal, Day 31. Beta islets display low congregation and growth, while alpha cells dominate. B) Pioglitzaone-treated animal, Day 17. Beta islets display congregation and growth. C) icovamenib treated animal, Day 31. Beta islets display high congregation and continue to increase and mature. Red is insulin-beta islets, brown is glucagon-alpha cells.



Human Donor Islets (Ex Vivo): icovamenib led to a statistically significant increase in the number of beta cells re-entering the cell cycle

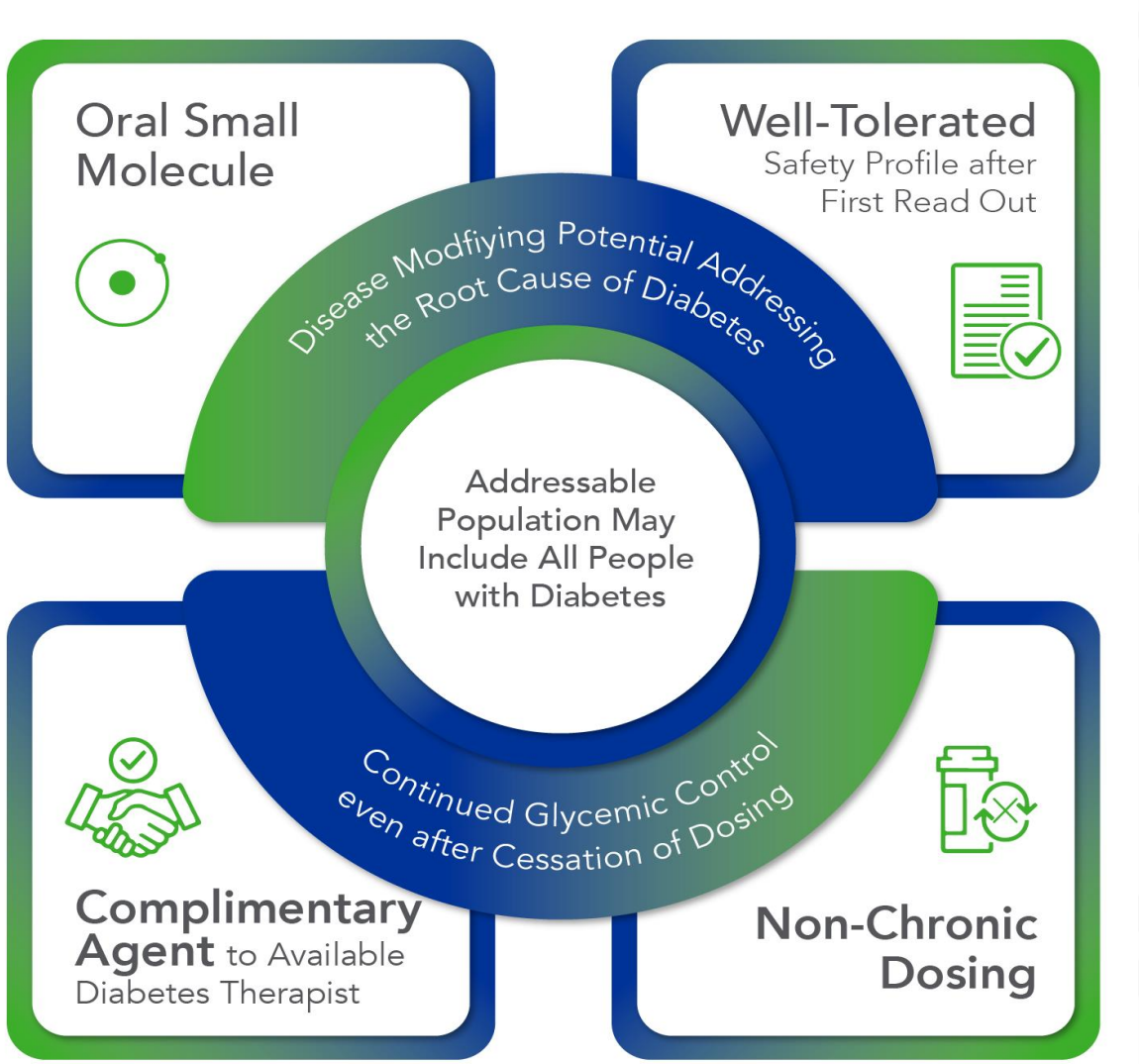
Longer Dosing is Predicted to Generate an Increase in Responder Rates Based on Human Donor Islet Experiments

Proliferating beta cells plotted as fraction of total beta cells



Data represent mean ±SEM of 1 donor with n = 9-12 technical replicates.
One-way ANOVA with Dunnett's post hoc test rel. to DMSO control. *p < 0.05, **p < 0.01, ***p < 0.001

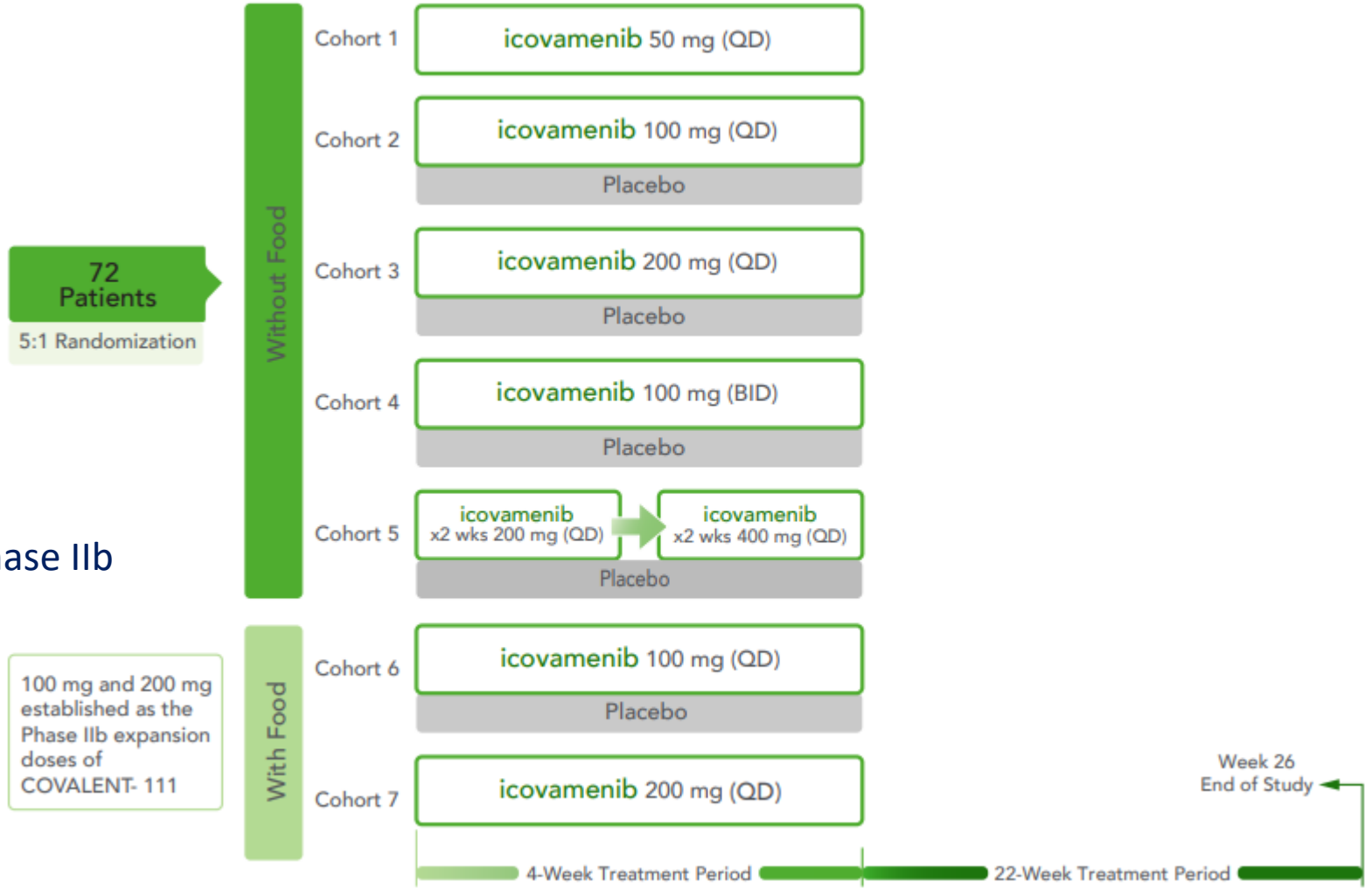
Investigational icovamenib - A Unique Value Proposition for Beta-Cell Regeneration



COVALENT-111 Study Design (Type 2 Diabetes Patients Failing Standard of Care)

Phase 2a Double-Blinded, Randomized Placebo-Controlled Study in T2D - Completed

Dose Escalation Port



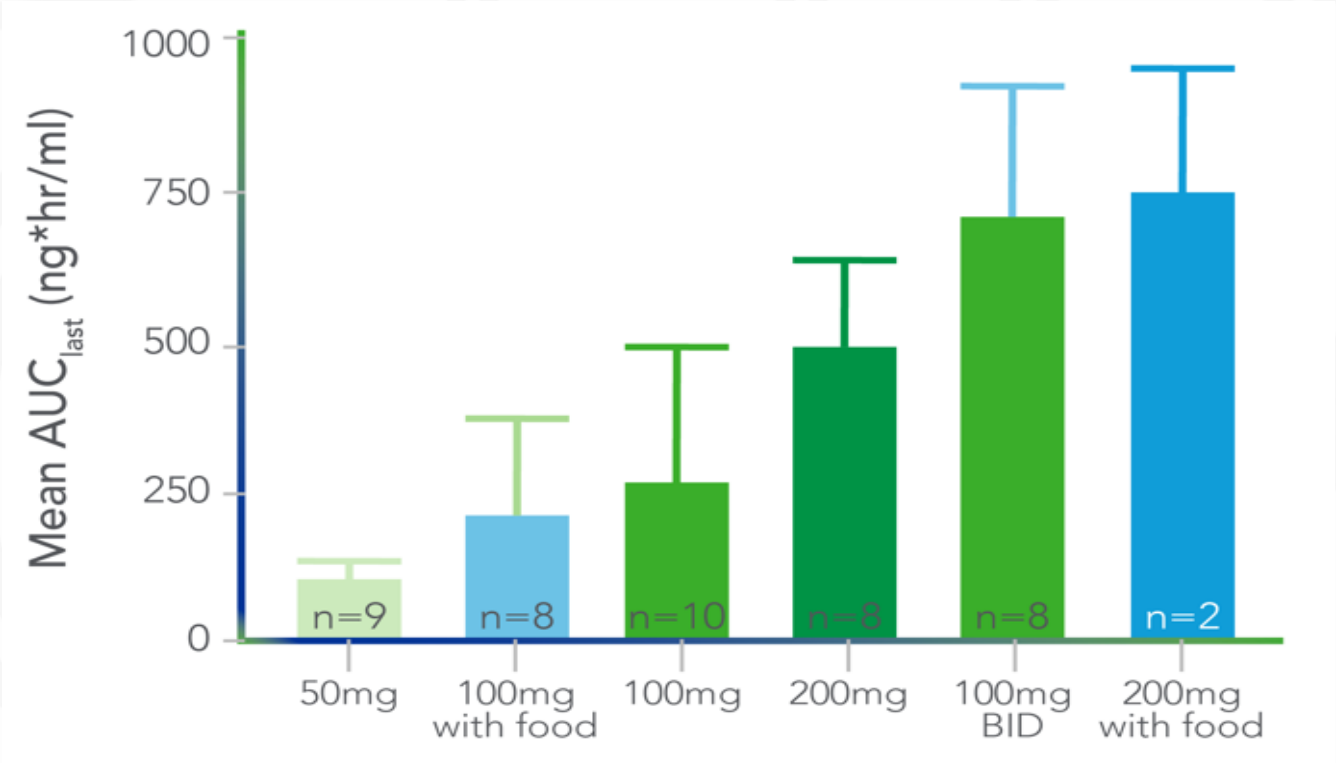
100 mg and 200 mg established as the Phase IIb expansion doses of COVALENT- 111

100 mg and 200 mg established as the Phase IIb expansion doses of COVALENT- 111

biomea FUSION™ We Aim to Cure™

Dose-Dependent PK Response Demonstrated

PK Response Across Cohorts (Week 4)



(Abitbol et al. ATTD 2024)

- Dose-dependent PK response is demonstrated across different dose cohorts.
- Increase in AUC is shown in higher dose cohort (200mg QD).

Lasting HbA1c Reduction at Week 26 (4 Weeks On Therapy, 22 Weeks Off Therapy)

Change in HbA_{1c} at Week 26 Across Various Cohorts (Placebo unadjusted)

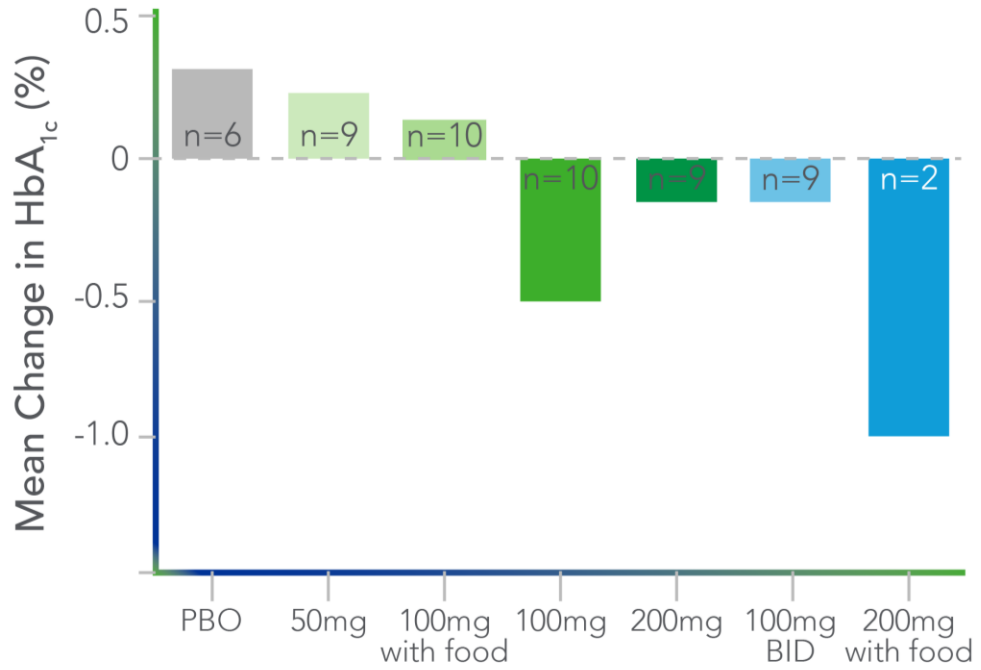


Fig. PK at Week 4 and Corresponding HbA_{1c} Response at Week 26 (Abitbol et al. ATTD 2024)

Response Rate (≥ 1% HbA_{1c} Reduction at Week 26)

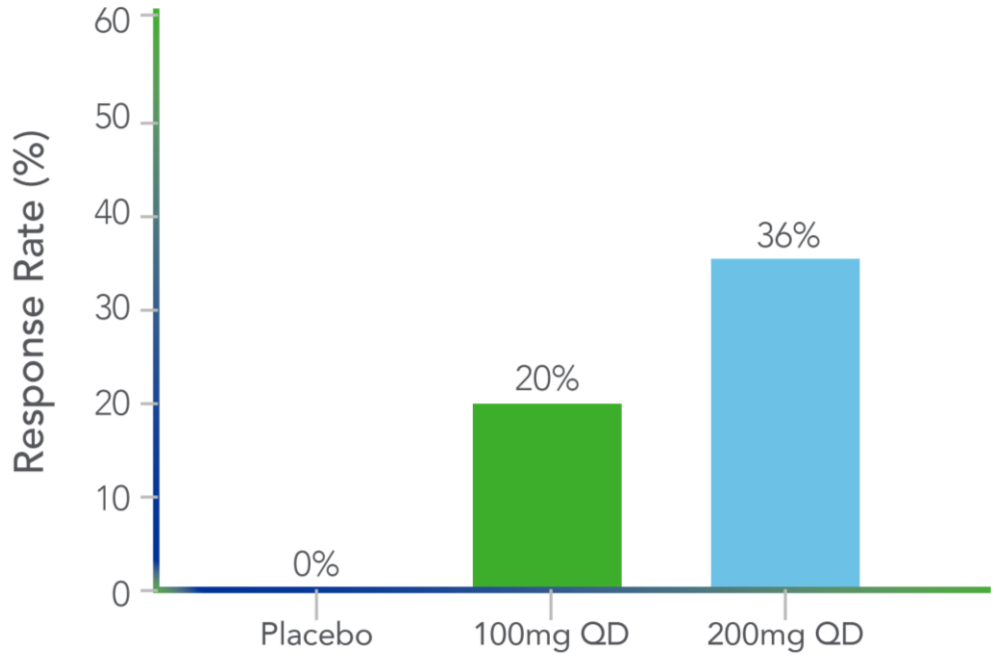
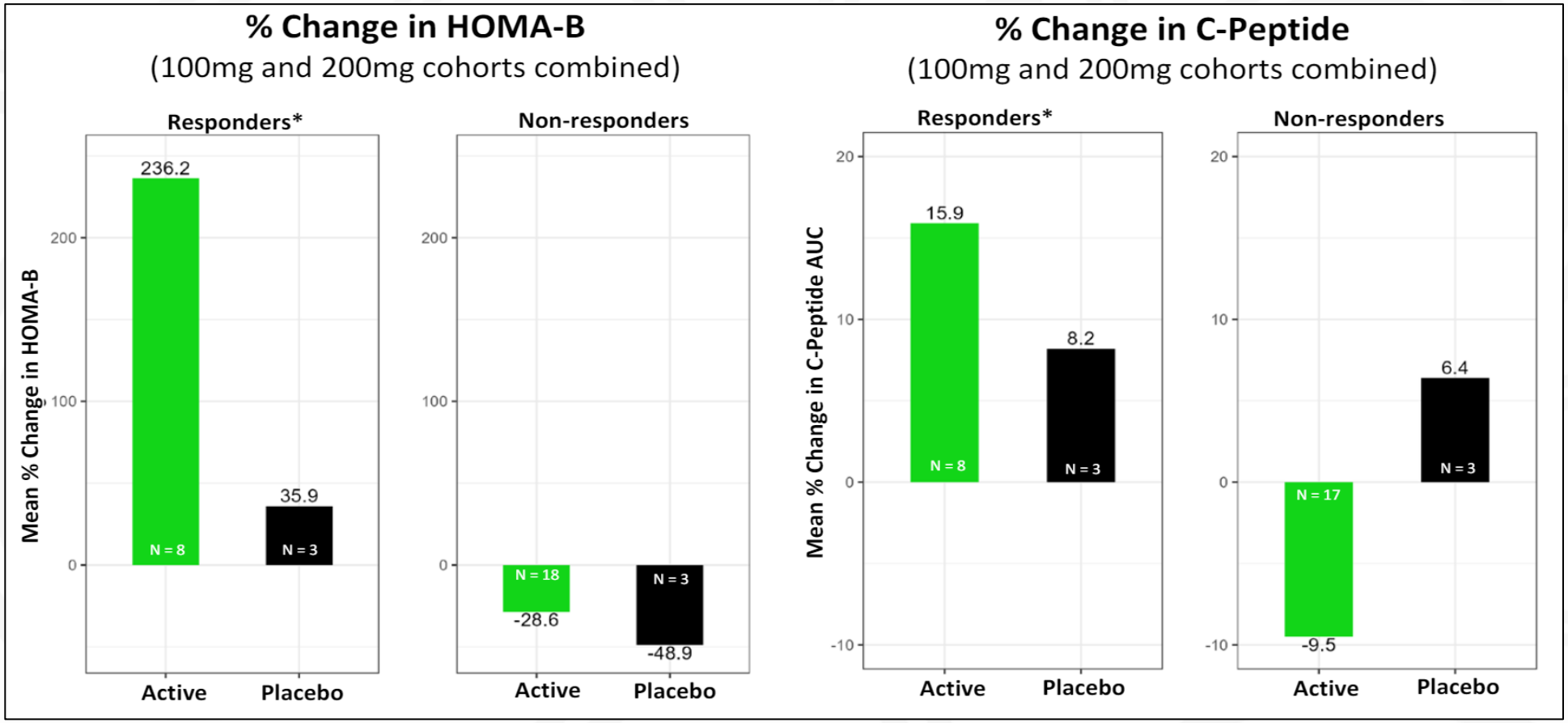


Fig. A Durable Glycemic Response Was Seen in 20% and 36% of Patients in Once Daily 100 mg and 200 mg Cohorts, Respectively (Abitbol et al. ATTD 2024)

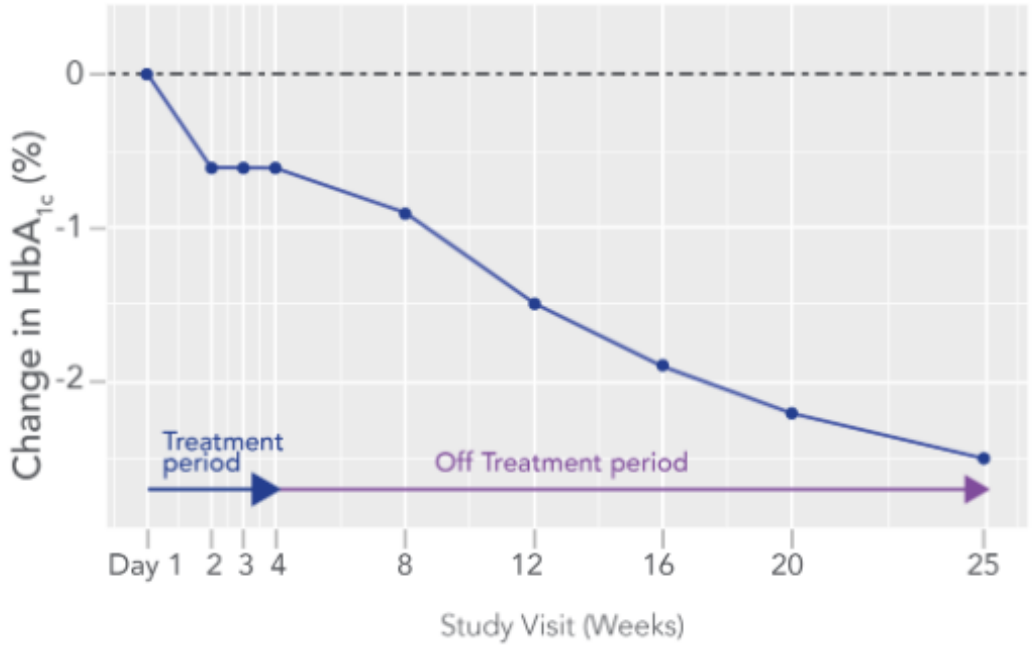
Beta-Cell Proliferation Supported by Increase in Homa-B and C-Peptide at Week 26



* Responders have baseline HOMA-B < 200 and have achieved at least 0.5% decrease in HbA1c at Week 26

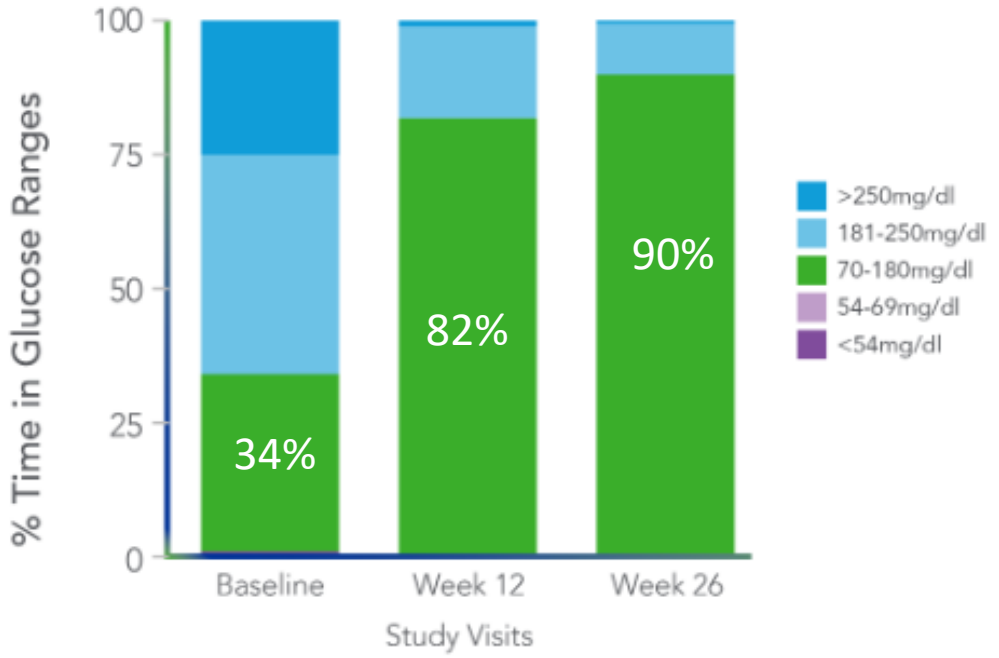
Case Study: 29-Year-Old Man with 4-Year History of Type 2 Diabetes

Change in HbA_{1c} (%)



- 29-year-old man with 4-year history of T2D
- Metformin and empagliflozin
- HbA_{1c} 9.5%; FPG 146 mg/dL; BMI 25.6 kg/m²

Continuous Glucose Monitoring



- icovamenib 200 mg once daily without food for 4 weeks
- CGM at Week 21 with ~90% $TIR_{70\text{-}180\ mg/dL}$
- No tolerability issues or related adverse events

Case Study: 29-Year-Old Man with 4-Year History of Type 2 Diabetes

- 29-year-old man with 4-year history of T2D
- Metformin and empagliflozin
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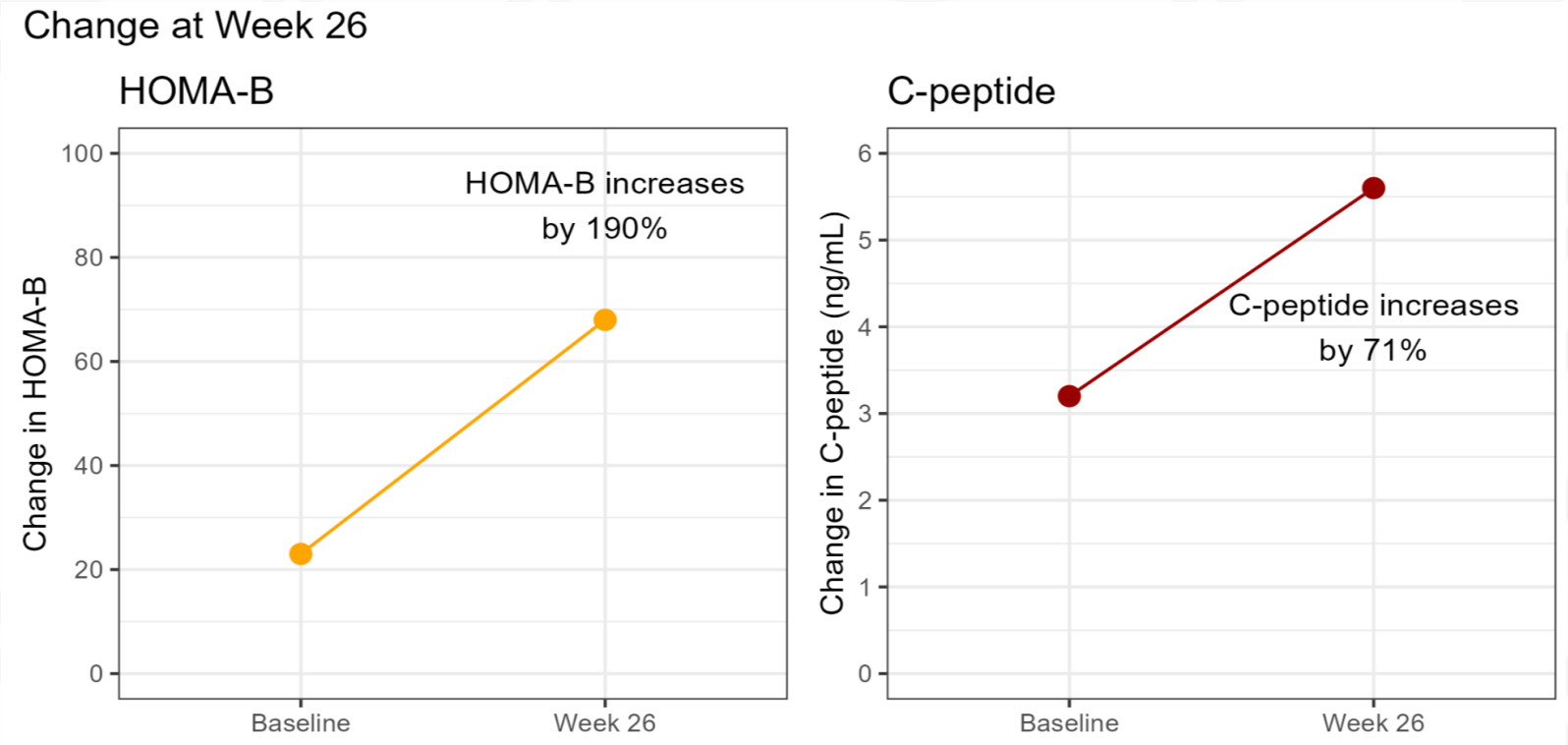
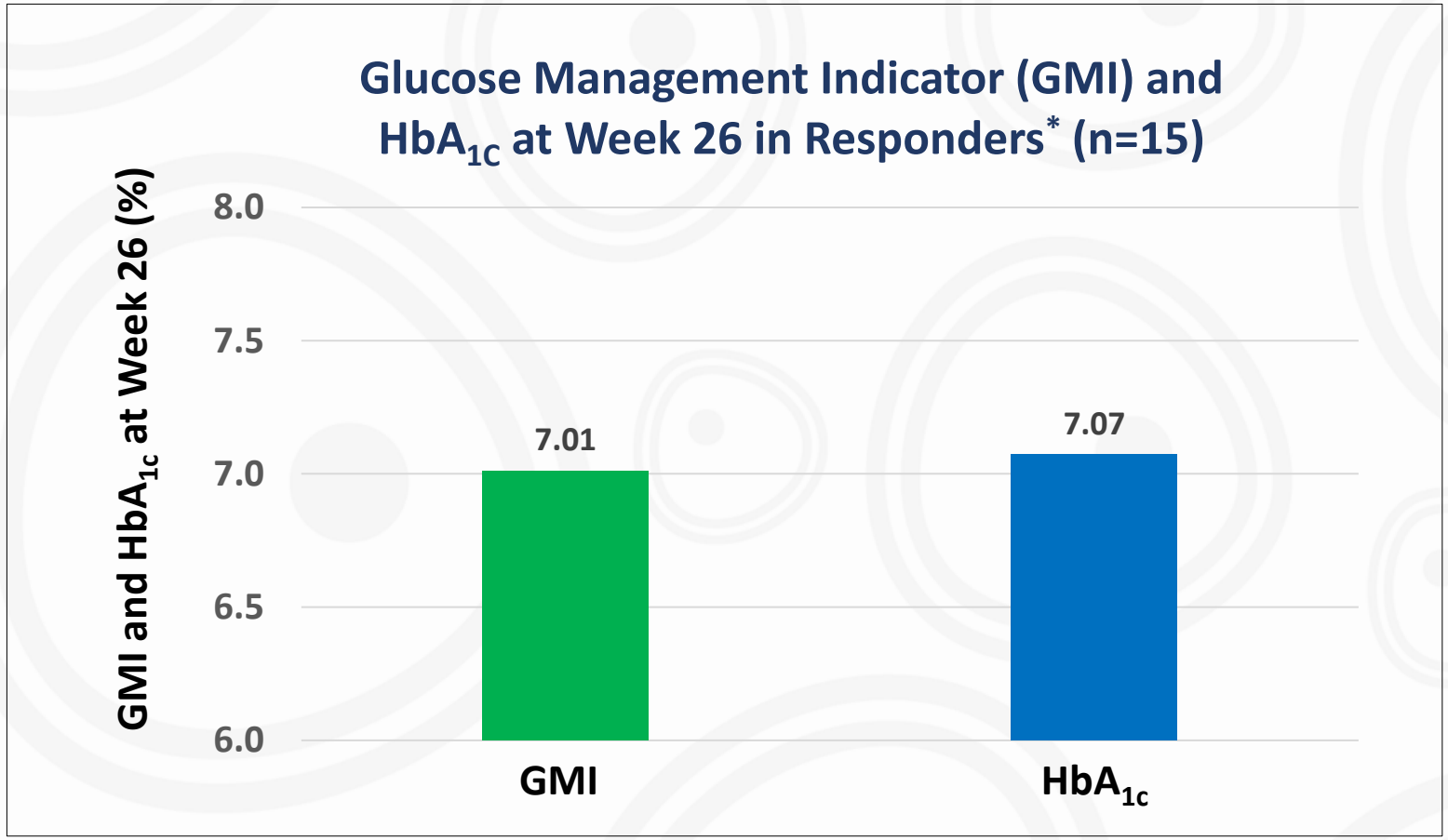


COVALENT-111 (Type 2 Diabetes)

Clinical Evidence Showing Change in HbA_{1C} is a Function of the Change in Glucose Level



GMI values came from the glucose monitoring device, confirming that HbA_{1C} is a function of the change in glucose, experienced after the use of icovamenib.

*Responder defined as study participants with HbA1c reduction from baseline of 0.5% or greater at Week 26
COVALENT-111 Escalation Cohorts 2-7, n=15 responders
Glucose Management Indicator (GMI) is from CGM session closest to the Week 26 study visit

Summary of icovamenib Clinical Results in Type 2 Diabetes

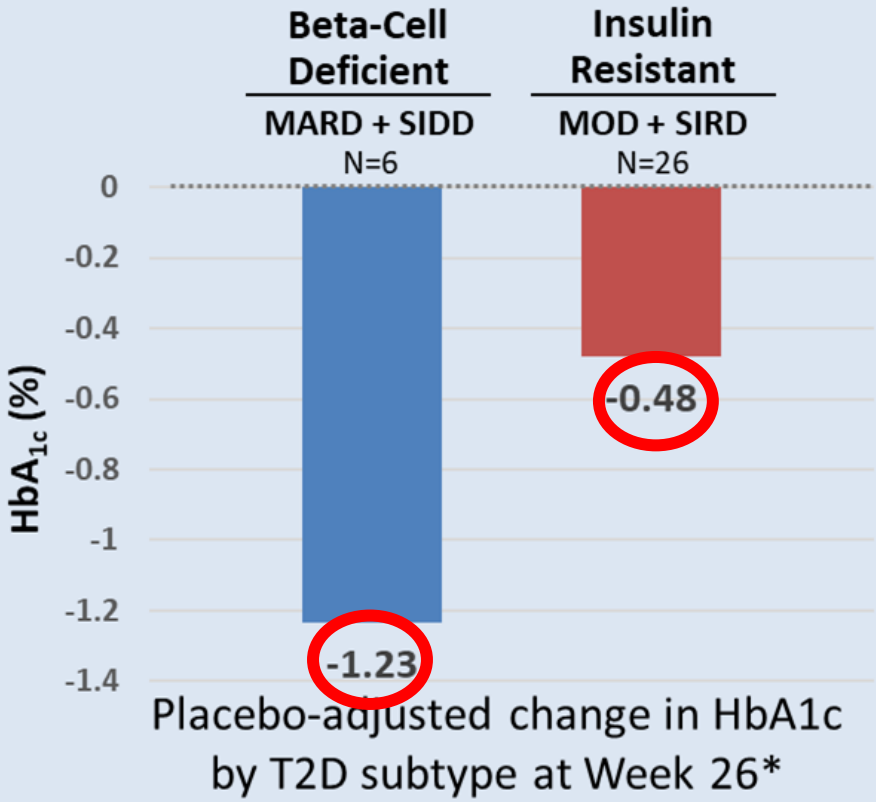
- Icovamenib was generally well tolerated with no serious adverse events and no adverse event-related study discontinuations, and no symptomatic or clinically significant hypoglycemia.
- Patients in COVALENT-111 are displaying improved glycemic control while off therapy beyond Week 26 following the 28-day treatment with icovamenib, supporting enhanced beta-cell function as the mechanism of action.
- The Escalation Portion of COVALENT-111 demonstrated dose dependent PK responses in patients; Improvement of key markers of beta cell growth and function (C-peptide, Homa B) were shown; Durable glycemic response (≥1.0% HbA1C reduction) was improved from 20% (100 mg QD cohorts) to 36% (200 mg QD cohorts) portion of patients.
- Both dose levels (100mg and 200 mg) have been selected for the Expansion Phase, where patients will be dosed up to 12 weeks (compared to 4 weeks in the Escalation Phase) with extended follow-up to Week 52.

Next Steps:

- Topline Week 26 data readout of COVALENT-111 Phase 2b with approximately 200 patients expected for 4Q 2024 to confirm optimal dosing scheme and define the patients who respond best to icovamenib

COVALENT-111 MAD:

HbA1c change at Week 26 by T2D subtype



Placebo-adjusted change in HbA1c by T2D subtype at Week 26*

*includes Cohorts 2,3,4 & 7 (100mg QD/BID and 200mg QD, cohorts representative of exposure expected in expansion phase, Arms A-C)

MARD, mild age-related diabetes
SIDD, severe insulin-deficient diabetes
MOD, mild obesity-related diabetes
SIRD, severe insulin-resistant diabetes

ATTD Advanced Technologies & Treatments for Diabetes ATTD-ASIA 18-20 NOVEMBER 2024 SINGAPORE

Frías JP, et al. (ATTD-Asia 2024, November 19, 2024)
Subtyping per Ahlqvist E, et al. Lancet Diabetes Endocrinol. 2018;6:361-369

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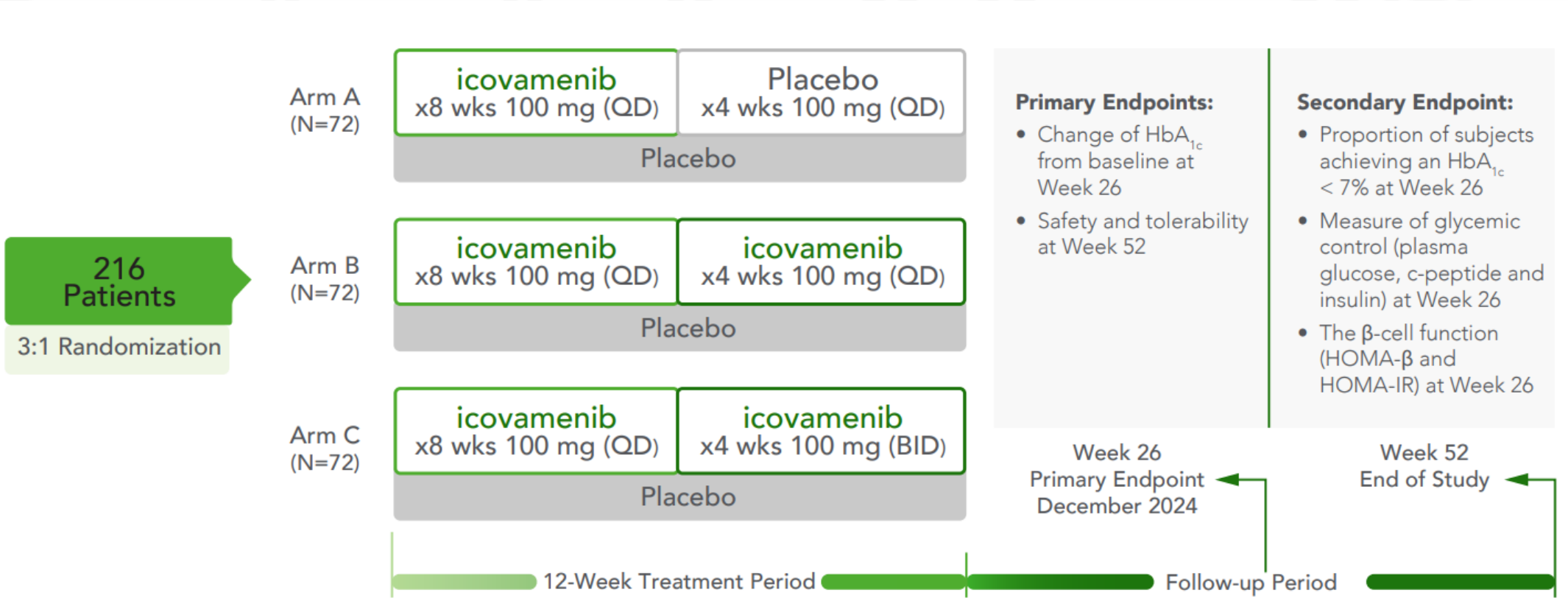
COVALENT-111 Study Design (Type 2 Diabetes Patients Failing Standard of Care)

Phase 2b Double-Blinded, Randomized Placebo Controlled Study in Type 2 Diabetes

Enrolling Patients Failing Standard of Care (up to 3 Anti-Diabetic Medications)

Dose Expansion Portion



New Treatment Potential in Diabetes and for Obesity

Combining icovamenib with GLP-1 Based Therapy

Potential benefits of using *icovamenib together with approved GLP-1 based therapeutics:*

- Lower dosing requirements of existing GLP-1 based therapy
- Improved tolerability
- Improved adherence
- Improved therapeutic window
- Improved initial responsiveness
- Greater patient persistence and treatment results with GLP-1 based therapeutics

Next steps in Biomea clinical development:

- COVALENT-211 (icovamenib in combination with GLP-1 based therapeutics)

Menin Suppresses GLP-1 Receptor Transcript Levels

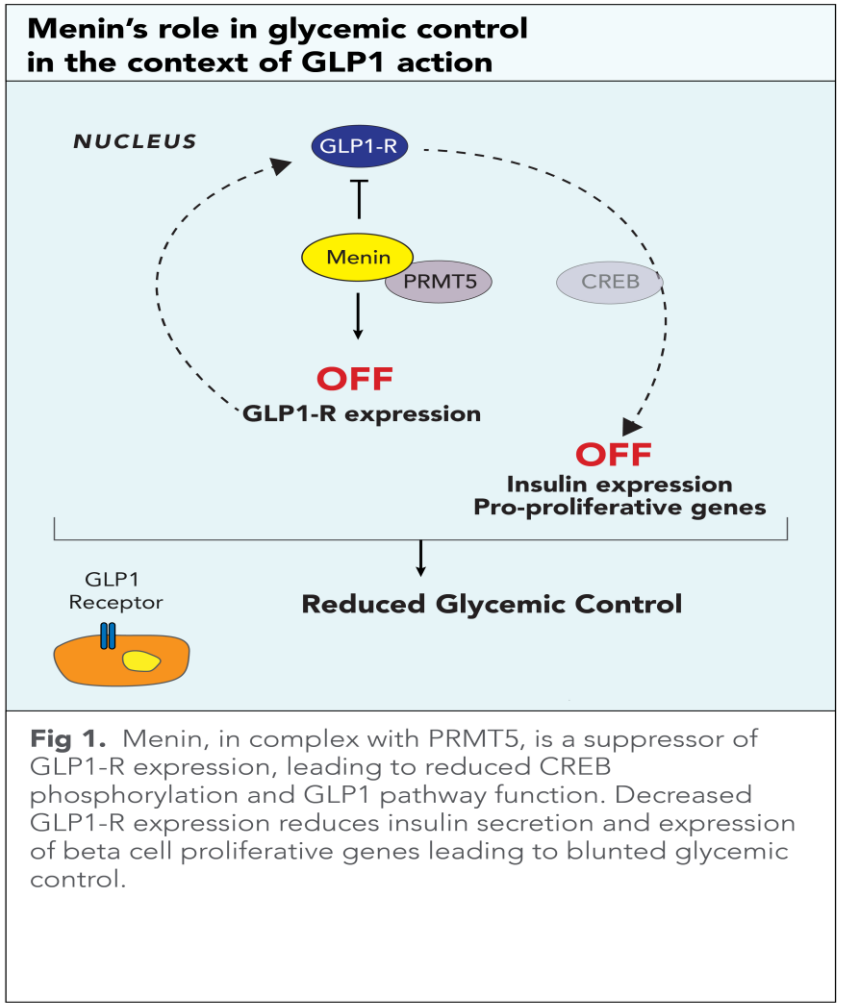


Fig 1. Menin, in complex with PRMT5, is a suppressor of GLP1-R expression, leading to reduced CREB phosphorylation and GLP1 pathway function. Decreased GLP1-R expression reduces insulin secretion and expression of beta cell proliferative genes leading to blunted glycemic control.

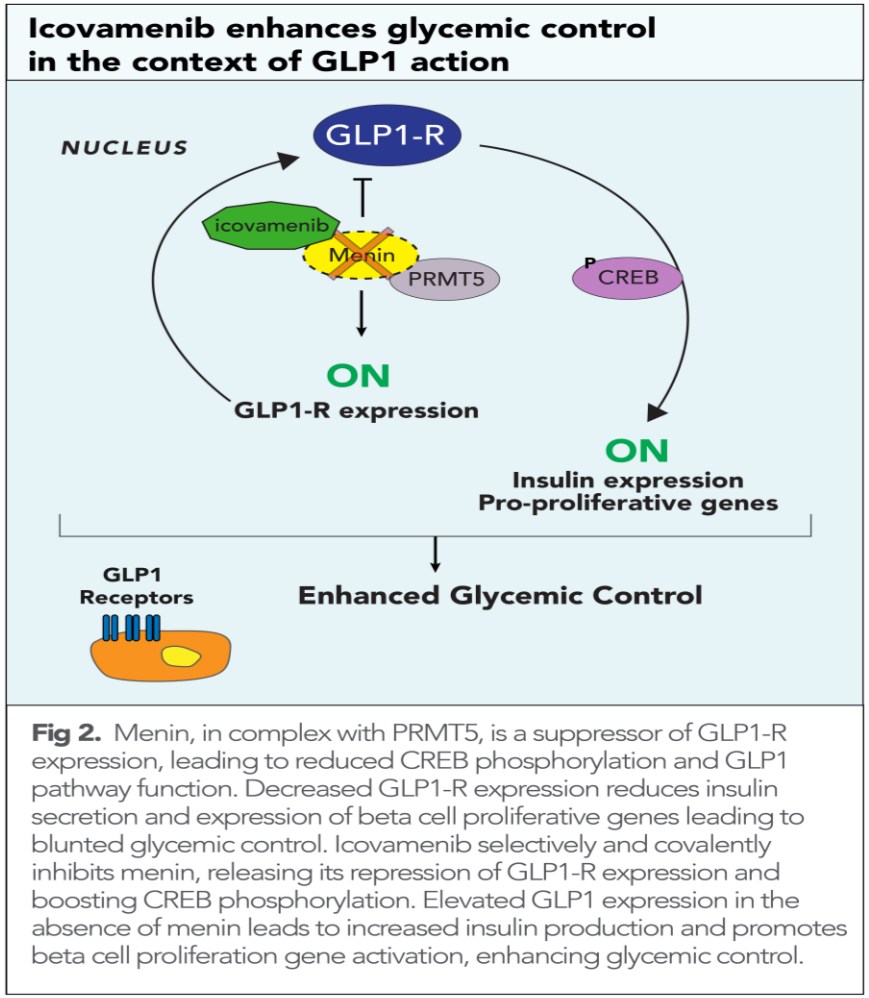
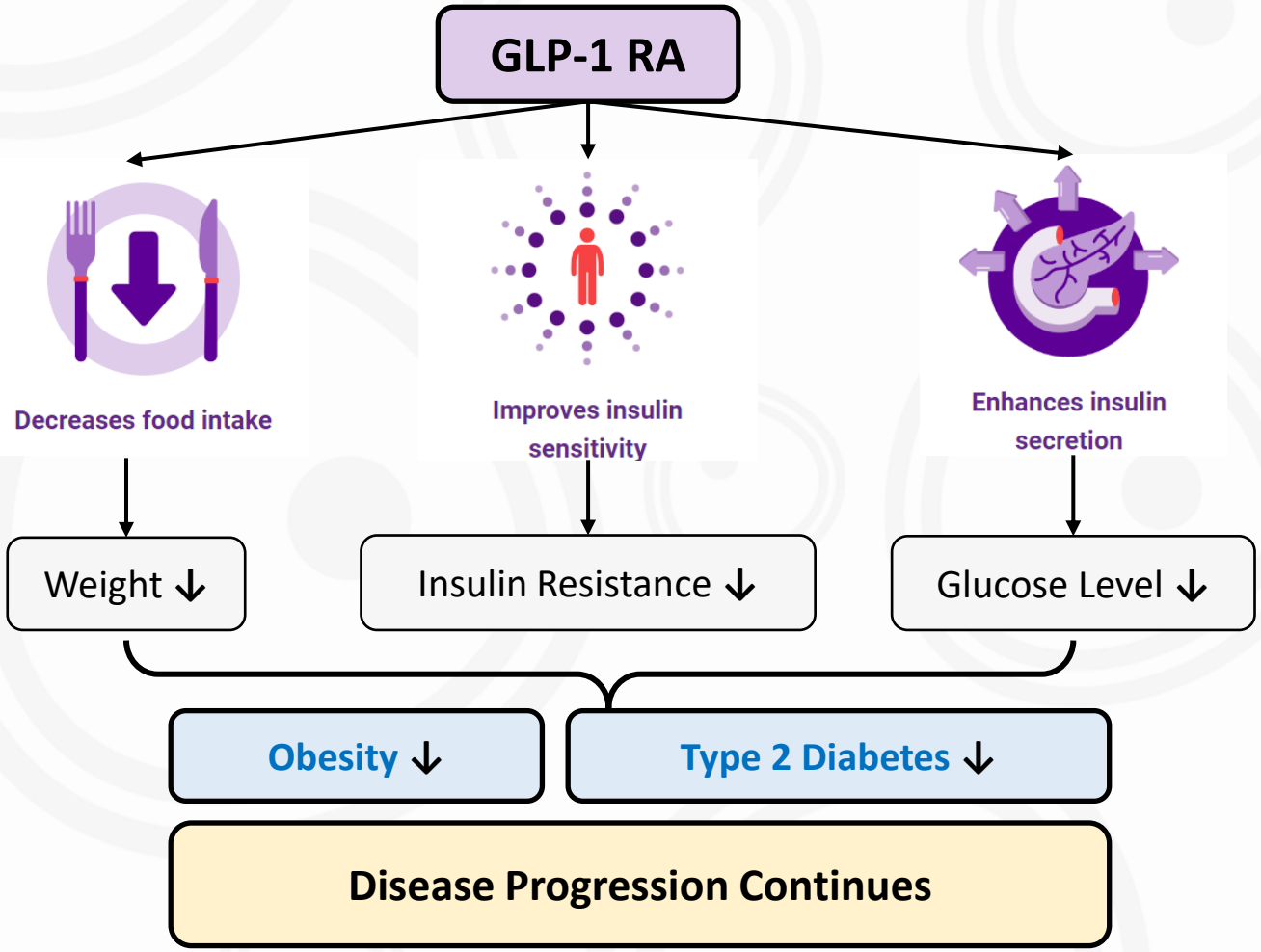
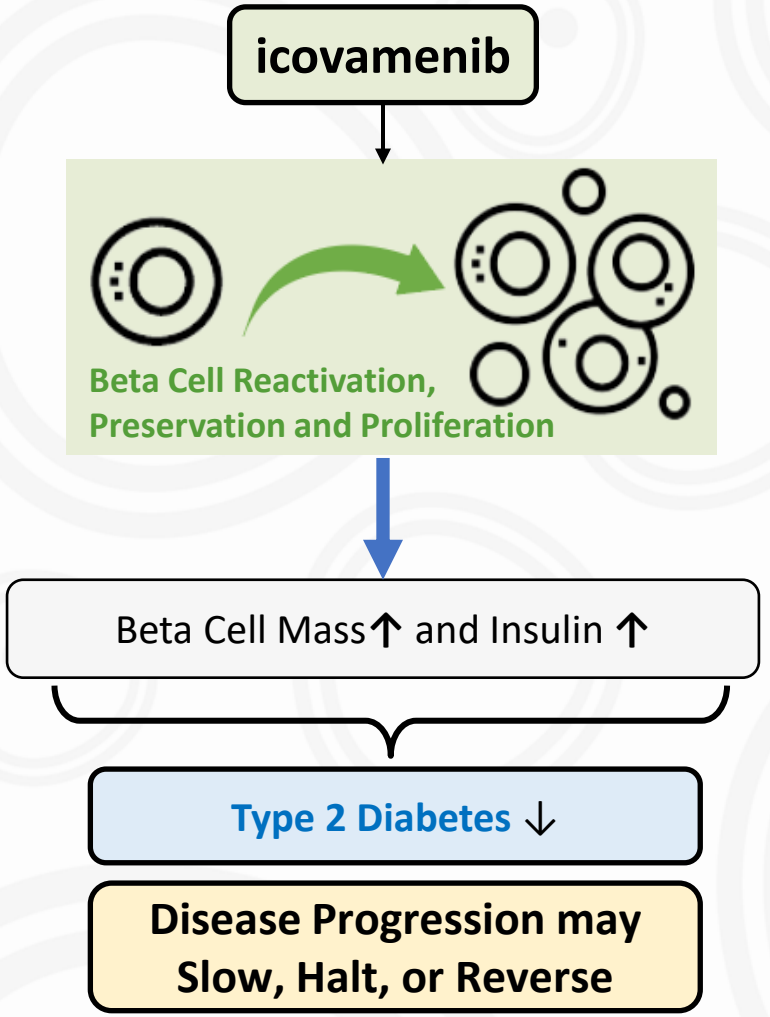


Fig 2. Menin, in complex with PRMT5, is a suppressor of GLP1-R expression, leading to reduced CREB phosphorylation and GLP1 pathway function. Decreased GLP1-R expression reduces insulin secretion and expression of beta cell proliferative genes leading to blunted glycemic control. Icovamenib selectively and covalently inhibits menin, releasing its repression of GLP1-R expression and boosting CREB phosphorylation. Elevated GLP1 expression in the absence of menin leads to increased insulin production and promotes beta cell proliferation gene activation, enhancing glycemic control.

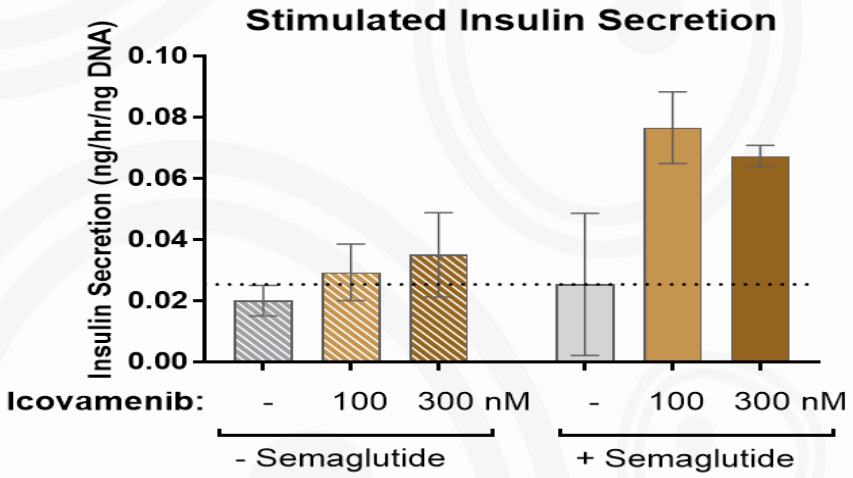
Icovamenib is Potentially Complementary to Existing Antidiabetic Agents

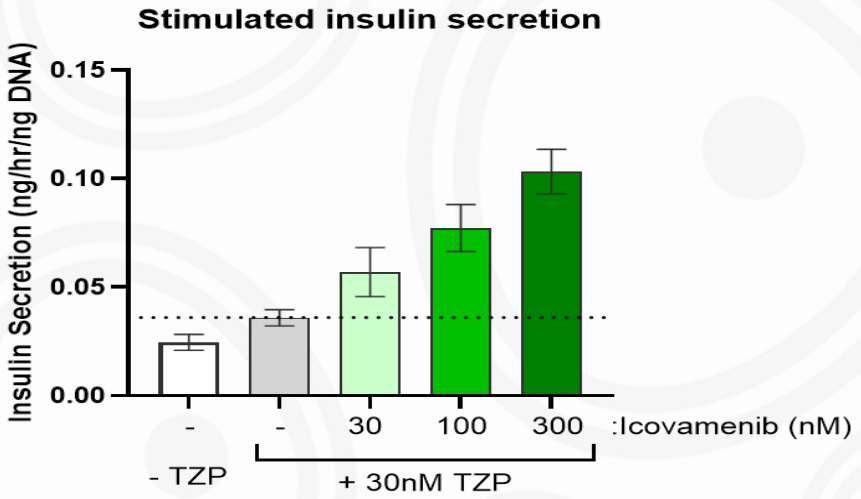


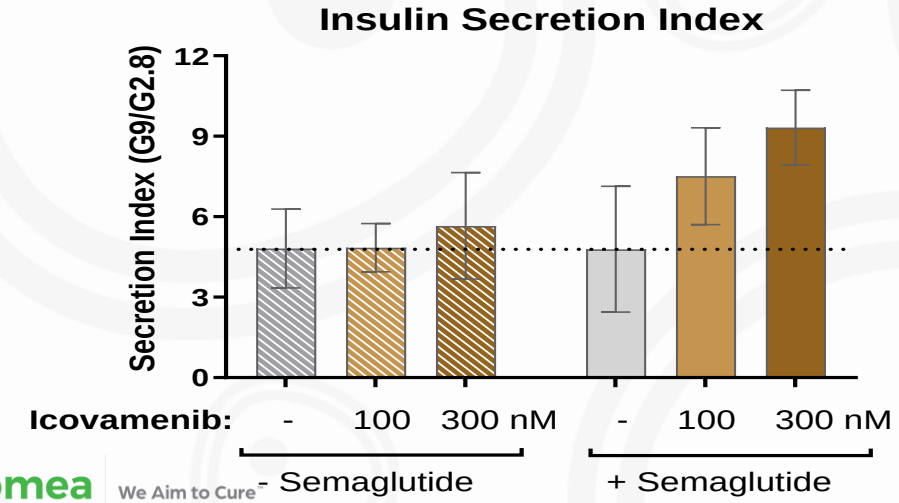


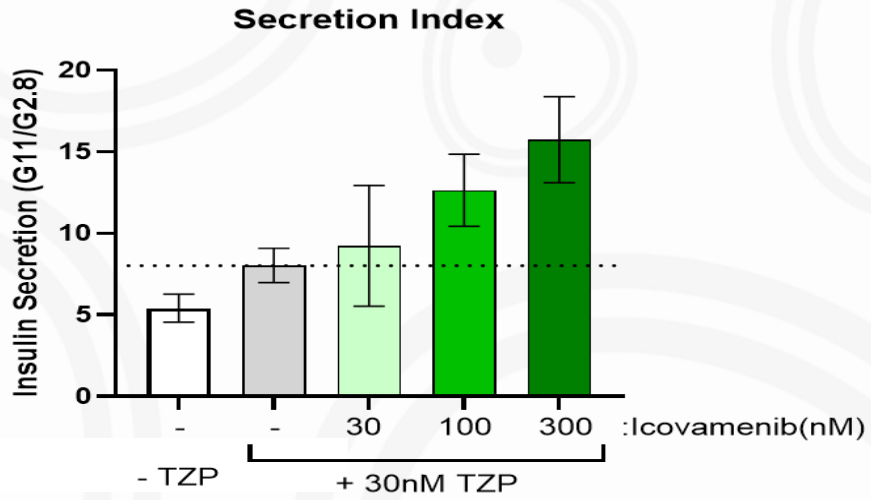
*Mounjaro. Prescribing Information. Lilly USA, LLC.

Combination with icovamenib Enhanced Responsiveness of Human Islets to GLP-1 based Therapies – semaglutide and tirzepatide

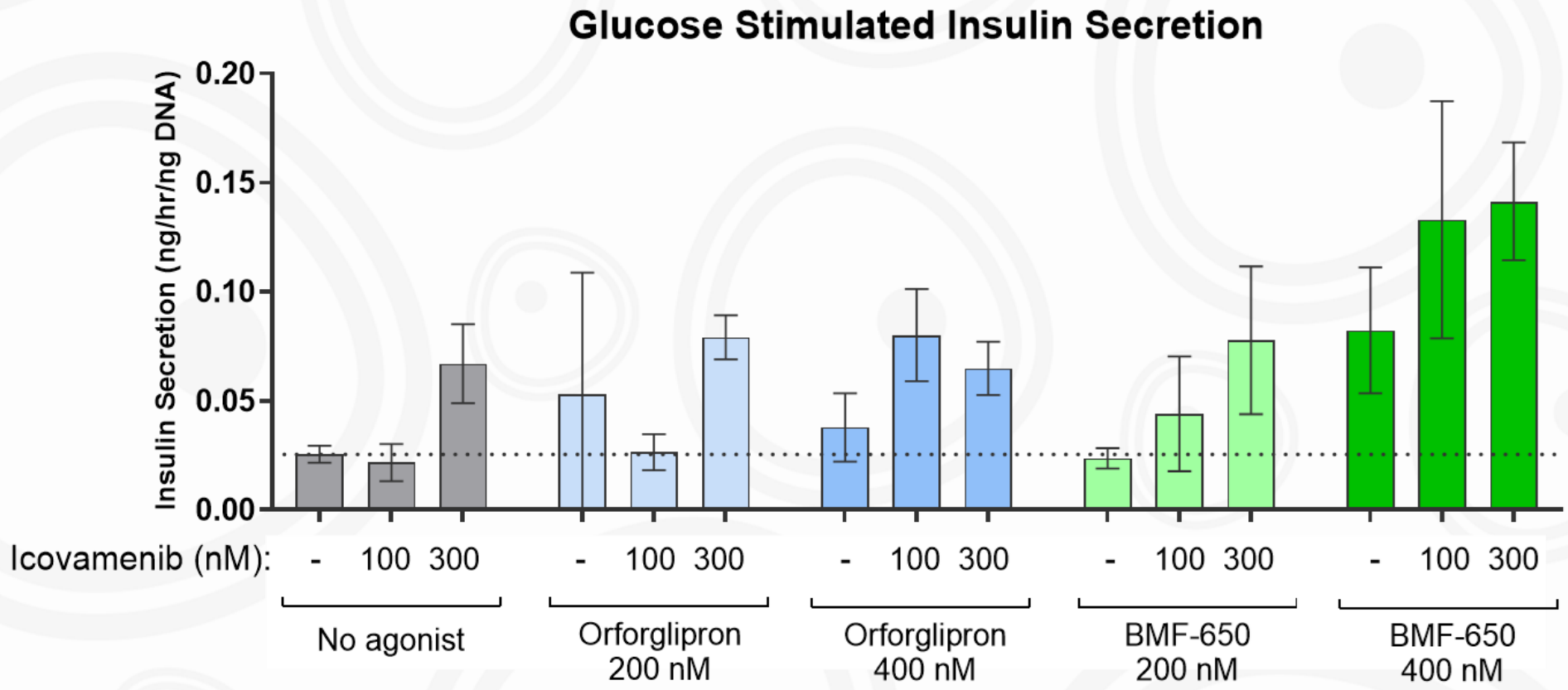








Combination Treatment: icovamenib Enhanced Responsiveness of Islets to Small Molecule GLP-1 Receptor Agonists - orforglipron and BMF-650



Summary of icovamenib in Combination with GLP-1 Based Therapy

- Menin suppresses the GLP1 receptor pathway function and reduces insulin secretion.
- Icovamenib, covalent inhibition of menin, releases the repression of the GLP1-receptor expression, leading to elevated GLP1 receptor expression and increased insulin production, enhancing glycemic control.
- Pretreatment of icovamenib in combination with a GLP-1 based therapy has shown to enhance insulin secretion; icovamenib more than doubled the insulin secretion versus GLP-1 based therapies alone.
- Potential benefits offered by the combination therapy may include lower dosing requirements for current GLP-1 based therapies; improved tolerability, adherence and therapeutic window; improved initial responsiveness and ultimately, greater patient persistence and treatment results.
- Next Steps: Phase II trial (COVALENT-211) investigate icovamenib in combination with GLP-1 based therapies.

BMF-650 in Type 2 Diabetes & Obesity

An Investigational, Next-Generation, Oral Small Molecule GLP-1 Receptor Agonist

Drive for a Greater "Therapeutic Window" with our Next-Generation Oral GLP-1 Receptor Agonist – BMF-650

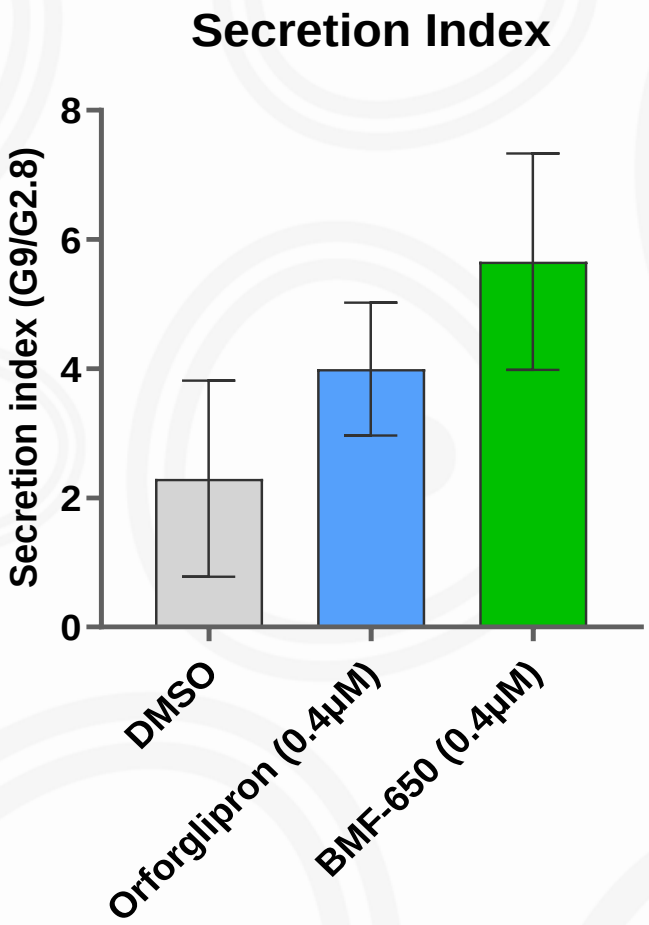
Attributes of Biomea GLP-1 Receptor Agonist Development Candidate:

- Improves intrinsic potency
- Less PK variability
- Greater bioavailability
- Greater protein binding
- Less side effects

Why a greater "Therapeutic Window"?

Only 3 of 10 patients in the real-world setting are staying on a GLP-1 based therapy after 12 months

BMF-650 Showed Improved Glucose-Stimulated Insulin Secretion in Ex Vivo Cultured Healthy Human Islet Experiment



BMF-650 demonstrated improved insulin secretion vs orforglipron

BMF-650 - Investigational, Next Generation Oral Small Molecule GLP-1 Receptor Agonist

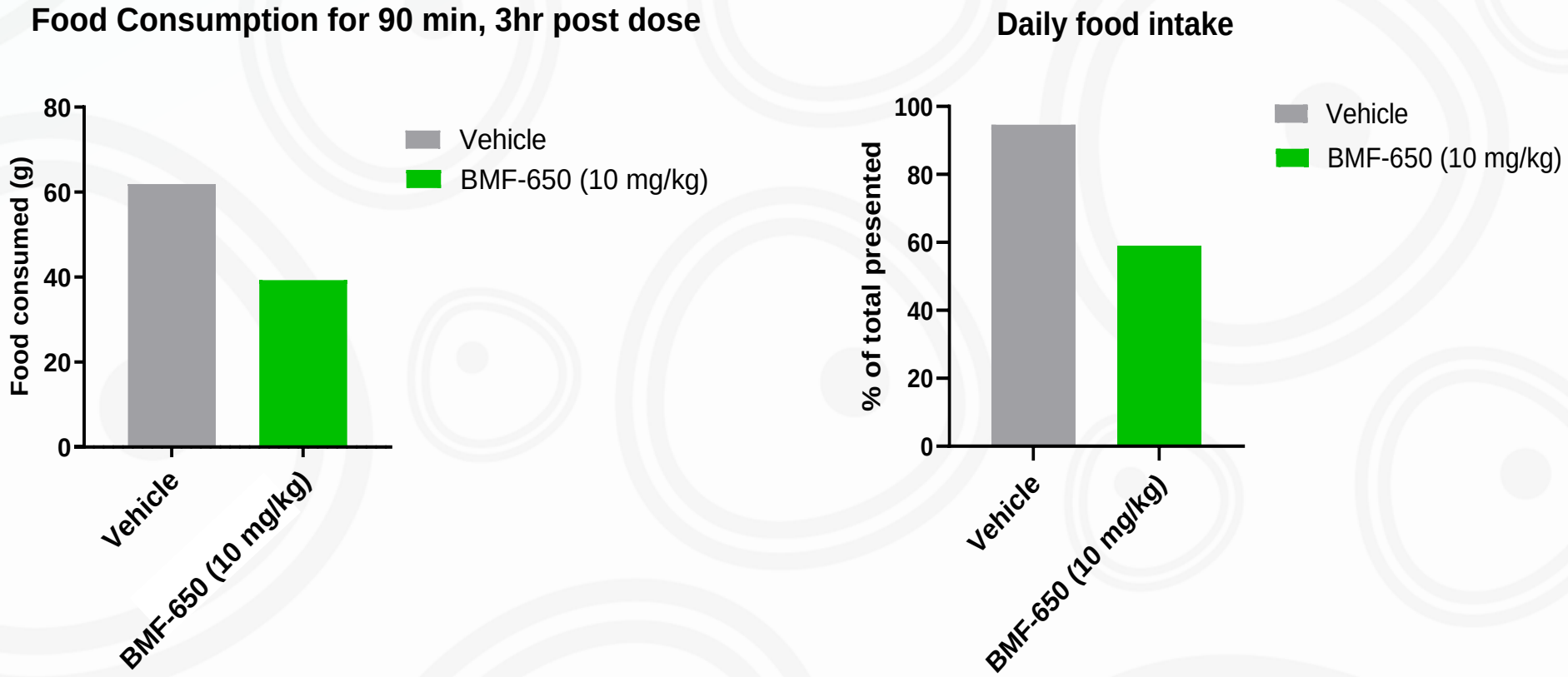
Projected Human Dose for BMF-650 Similar Among the Oral Agents

Dosages Used in Cynomolgus Monkeys are Species Dependent and Specific to Properties of Compounds

	Orforglipron Eli Lilly	BMF-650 Biomea	GSBR-1290 Structure Therapeutics	CT-996 Roche (Carmot)
Doses tested in cynomolgus monkeys to address food intake	HD LD: 0.1 & 0.05 mg/kg	2 and 10 mg/kg	2 to 10 mg/kg	3 to 30 mg/kg
Clinical titration target	45 mg	100 mg (projected)	120 mg	120 mg

BMF-650 Appetite Suppression in Cynomolgus Monkeys

Average of First 90 Minute Window and Average for All Six Days of the Experiment



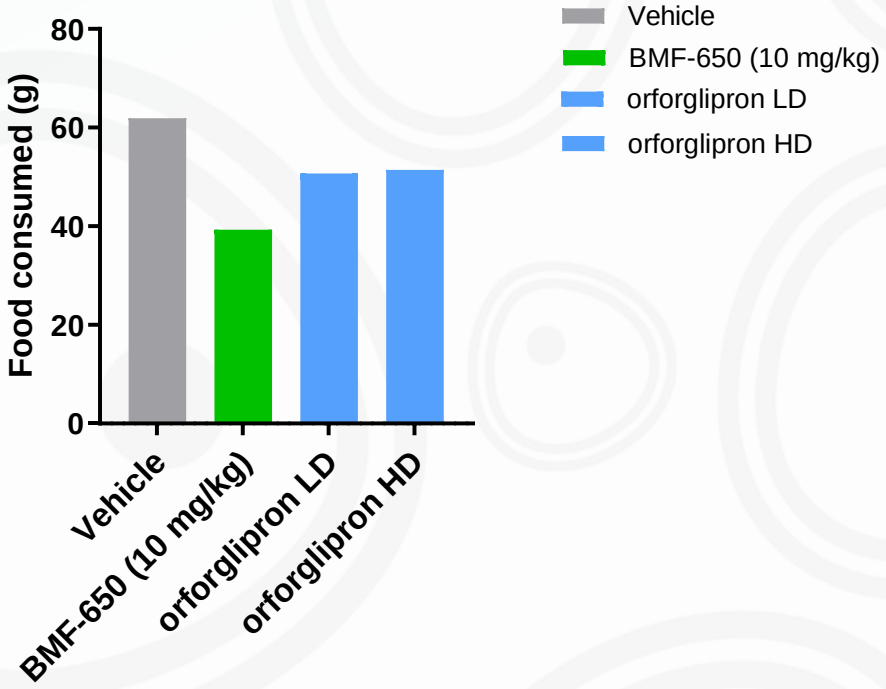
Food consumption tested daily in cynomolgus monkeys (n=4)

BMF-650 demonstrated good appetite suppression over 6 days

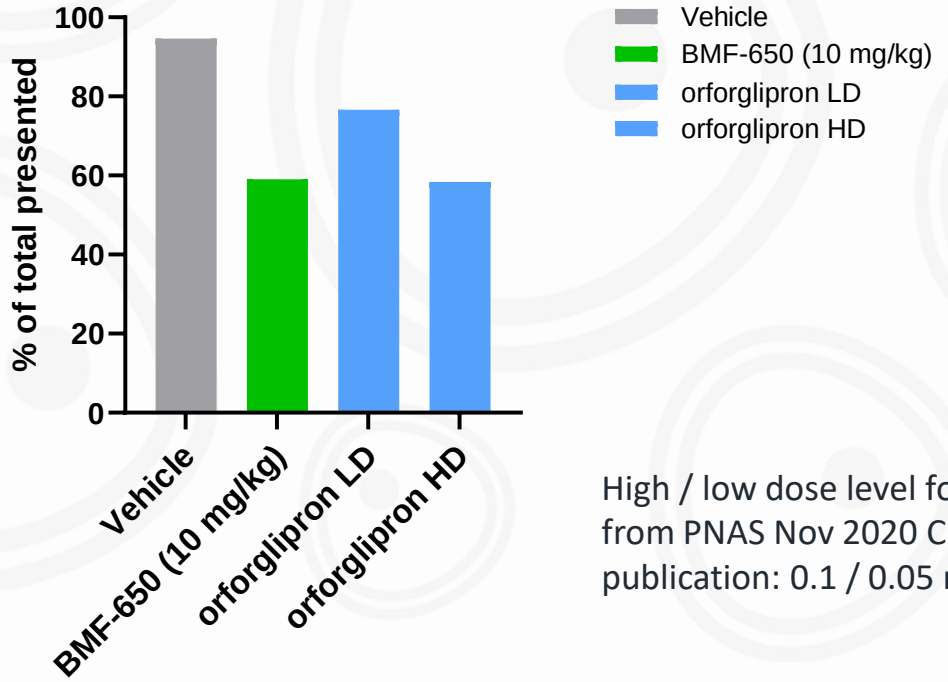
BMF-650 Appetite Suppression in Cynomolgus Monkeys Compares Well to Orforglipron

Average of First 90 Minute Window and Average for All Six Days of the Experiment

Food Consumption for 90 min, 3hr post dose



Daily food intake



High / low dose level for orforglipron from PNAS Nov 2020 Chugai/Lilly publication: 0.1 / 0.05 mg/kg

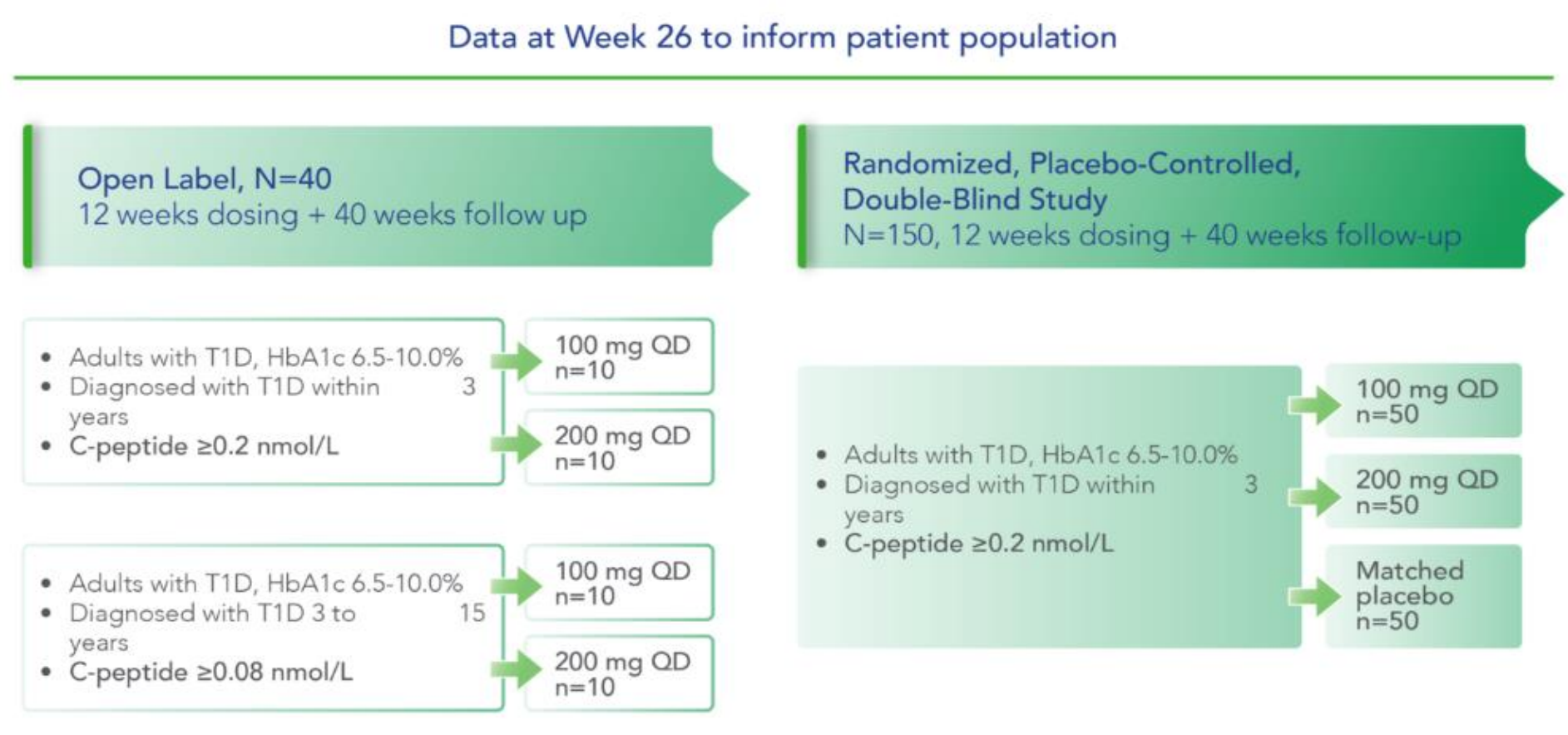
Food consumption tested daily in cynomolgus monkeys (n=4)

BMF-650 demonstrated good appetite suppression over 6 days and compares well to orforglipron

Icovamenib (BMF-219) in Type 1 Diabetes

An Investigational Novel Covalent Menin Inhibitor Developed for Diabetes

COVALENT-112: Open-Label and Randomized, Controlled Trial Assessing Icovamenib in Type 1 Diabetes

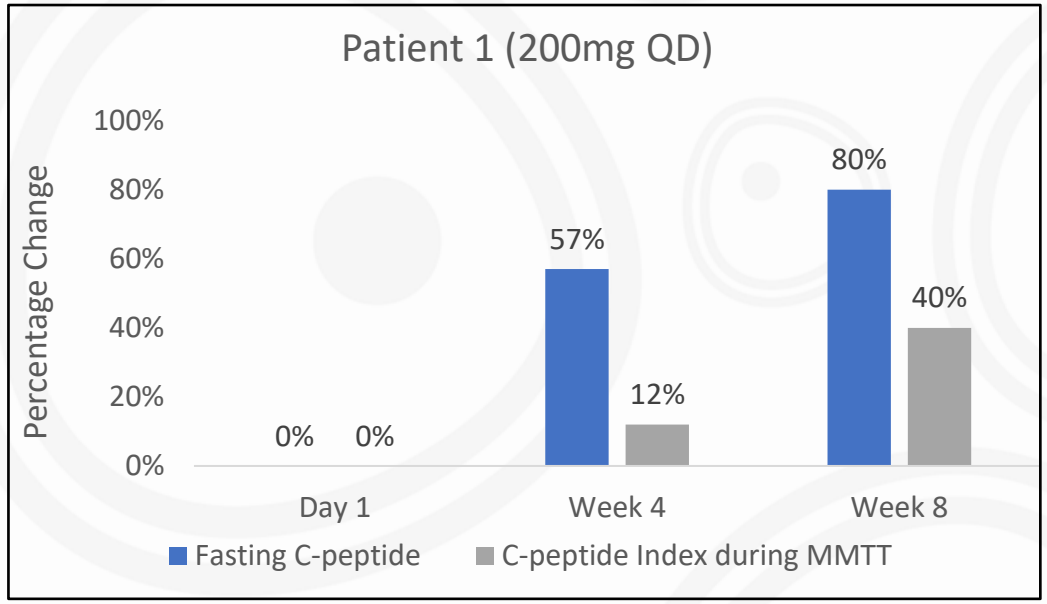


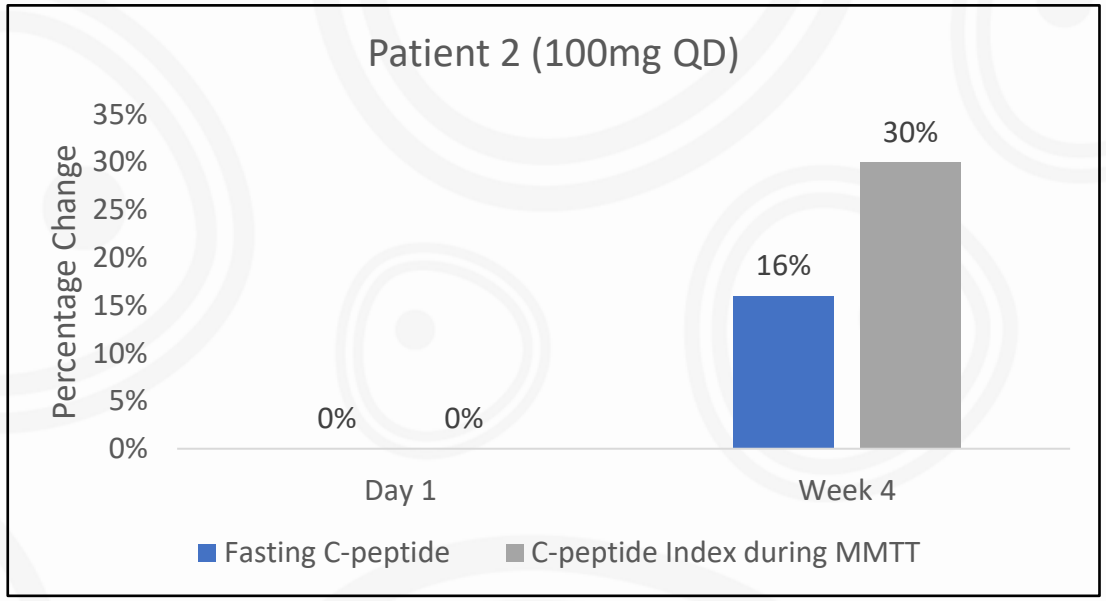
Next Steps: Topline data readout of Phase IIa of COVALENT-112 with approximately 20 patients expected for 4Q 2024

Icovamenib Induces C-Peptide Increase in the First Two Stage 3 Type 1 Diabetes Patients

- 58-year-old
- Diagnosed with type 1 diabetes 3 years ago
- Icovamenib was well tolerated

- 24-year-old; Diagnosed with type 1 diabetes 7 years ago
- Patient had a reduction in daily insulin usage during the first four weeks of the study; icovamenib was well tolerated





*Data cutoff date: March 7, 2024
*The C-peptide index is the ratio of serum C-peptide to plasma glucose levels and is used to evaluate β-cell function

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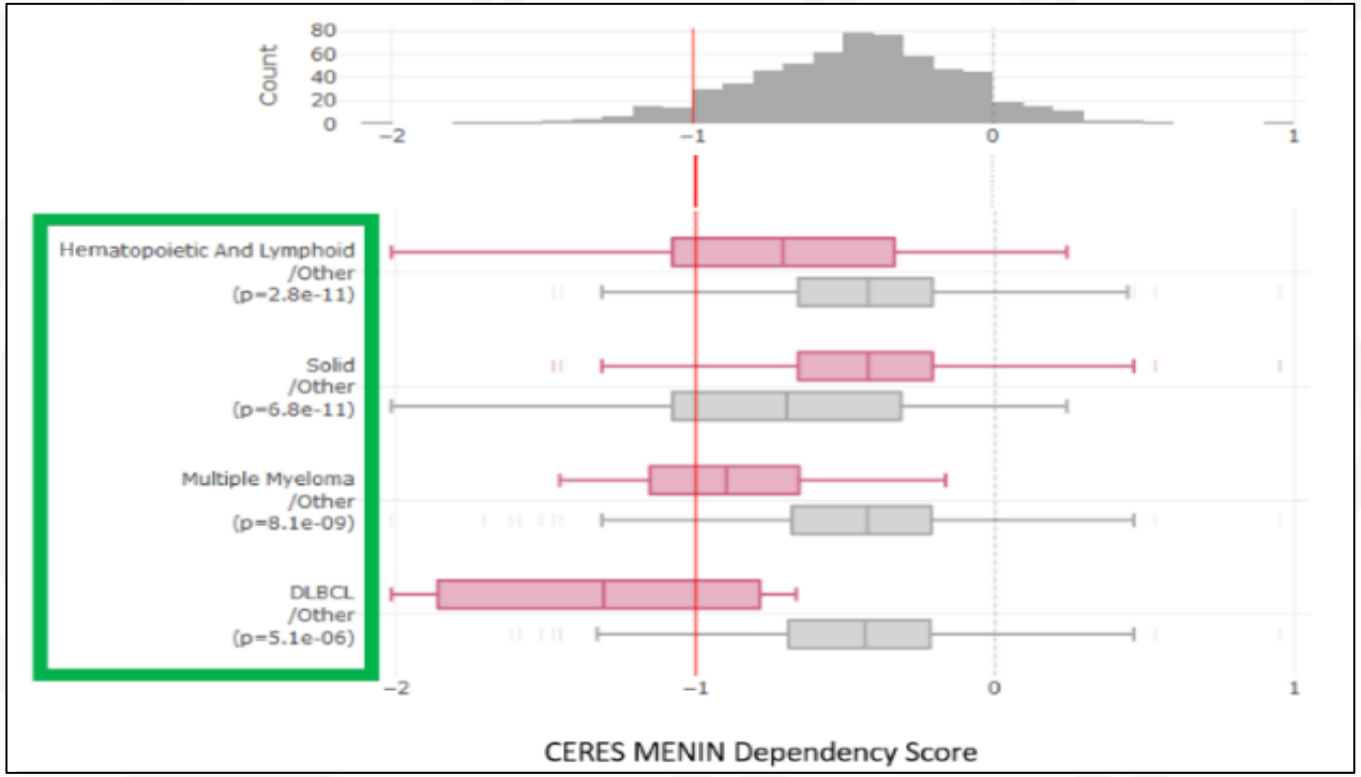
Icovamenib (BMF-219) in Oncology

An Investigational Novel Covalent Menin Inhibitor Developed to Impact Multiple Tumors

Acute Leukemia, DLBCL, MM and Other Tumor Types Have High Menin Dependency Based on Broad Institute DEPMAP Dataset

BROAD Institute Cancer Dependency Map (DEPMAP) for Menin (*MEN1*)



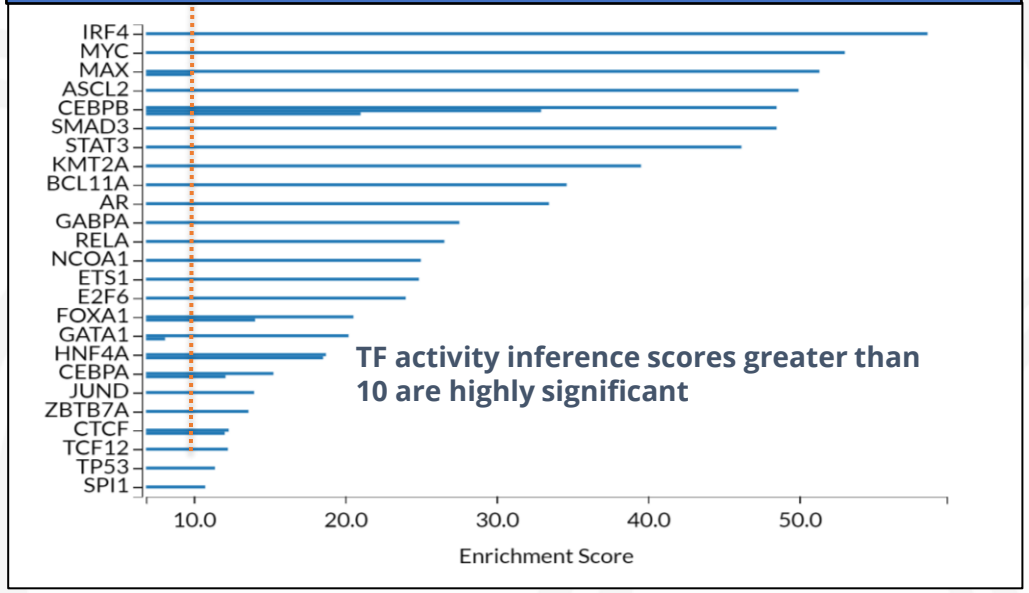
Note: CERES MENIN Dependency scores less than -1 in the various tumor types tested imply that menin is considered essential for cell survival in those tumor types

- Cell viability scores have shown that **menin** plays a key role in **survival of multiple tumors.**
- **High menin dependency in liquid and solid tumors,** beyond acute leukemias, provides rationale for further analysis in dependent tumor types.
- Biomea is exploring the potential for **covalent inhibition of menin in a variety of liquid and solid tumor types.**

Source: Broad Institute DEPMAP Dataset

Icovamenib Disrupts Multiple Binding Partners of Menin, including MYC, MLL, and JUND

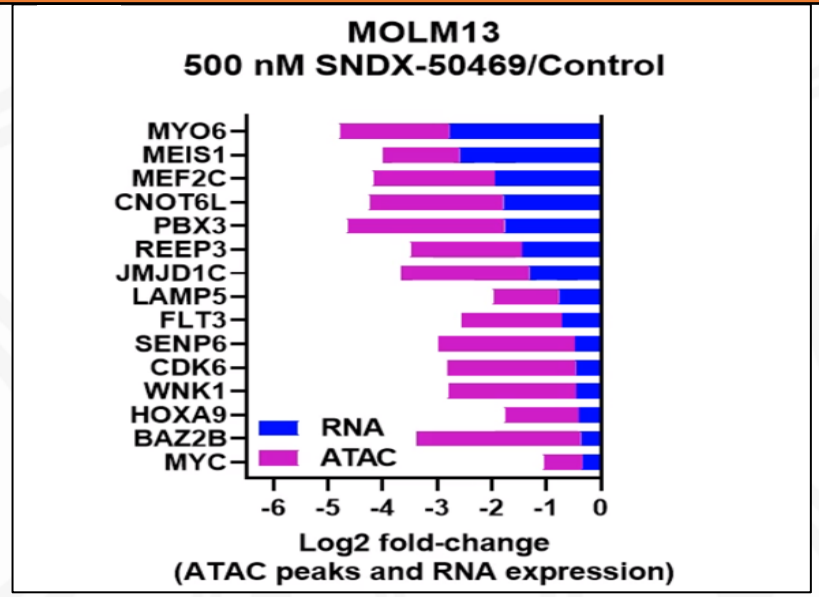
Covalent Menin Inhibitor – icovamenib



TF activity inference using ChIP-seq of differentially expressed genes in MOLM-13 cells incubated with 500nM icovamenib at 24 hours. Each bar represents a study in the GEO repository using the specified TF antibody.

- **In MOLM-13 cells treated with icovamenib, the top transcription factors regulating gene expression are MYC and MAX**
- IRF4, MYC, and MAX are known drivers for some forms of DLBCL, (addicted) multiple myeloma, and multiple additional tumors

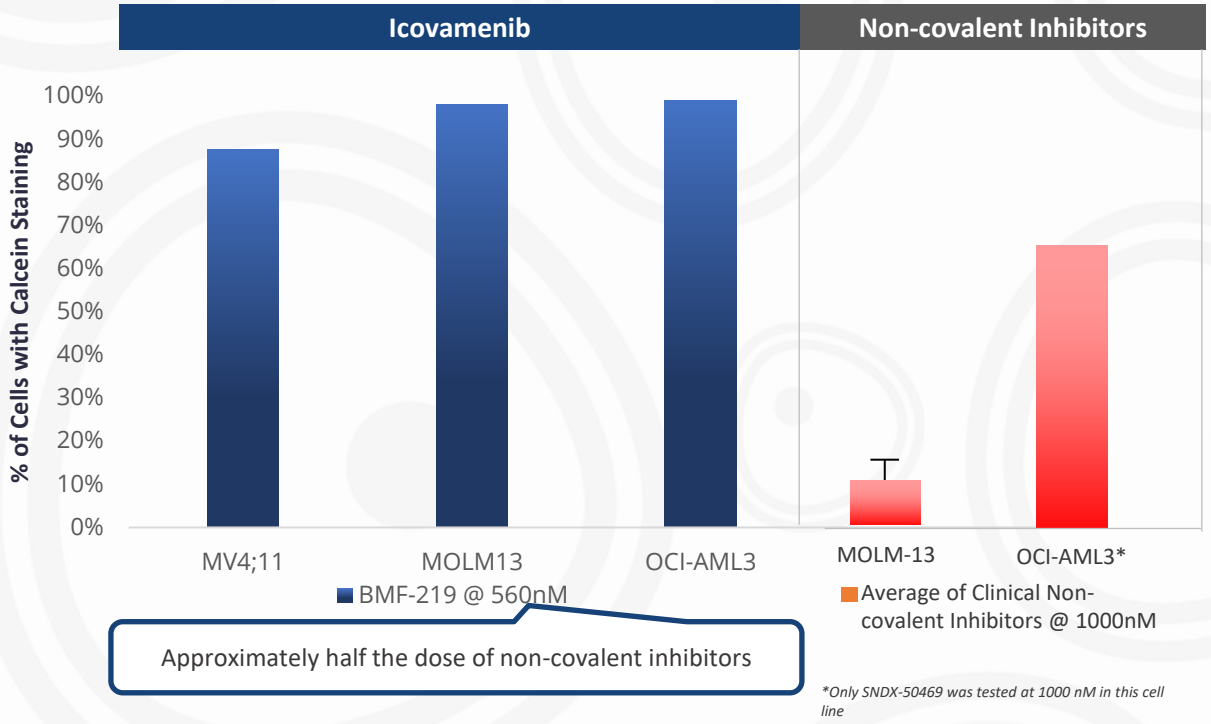
Non-Covalent Menin Inhibitor – SNDX-50469



Blood (2021) 138 (Supplement 1): 3340.

- **Significantly less impact on MYC expression** (2x fold) and genomic function by clinical non-covalent menin inhibitor
- In contrast, **icovamenib treatment led to a ~100-200x reduction in MYC** expression at 24 hours

Icovamenib Superior Cell Killing of the Target AML Cell Lines at Half the Dose vs Reversible Competitive Menin Inhibitors



*Only SNDX-50469 was tested at 1000 nM in this cell line

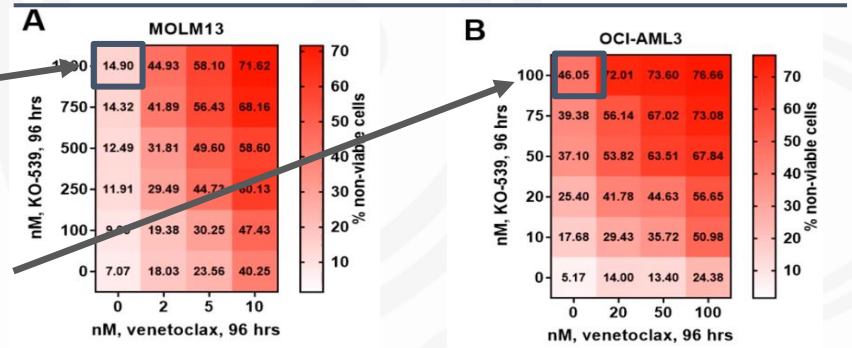
- Icovamenib **killed >90% of AML cells** in MLL-rearranged and NPM1 mutant cell lines at 4 days post-treatment
- Non-covalent menin inhibitors generally report significantly less cell killing of AML cell lines as a single agent

Source Data from ASH 2021 Publications

KO-539 is 15% effective @ 1000nM in MOLM-13 cells and 46% effective @ 1 100nM in OCI-AML3 cells

15% effective @ 1000nM

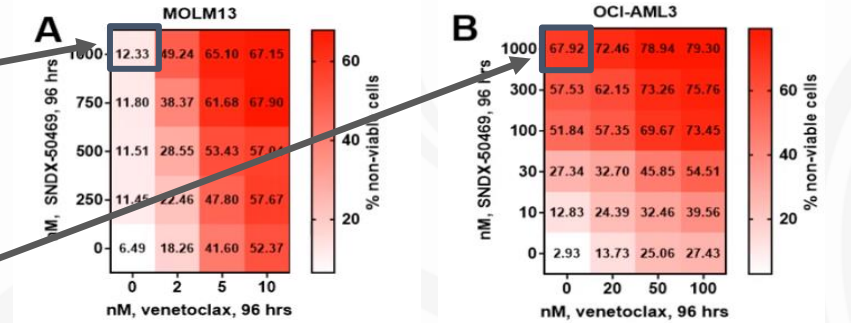
46% effective @ 100nM



SNDX-50469 is 12% effective @ 1000nM in MOLM-13 cells And 68% effective @ 1000nM in OCI-AML3 cells

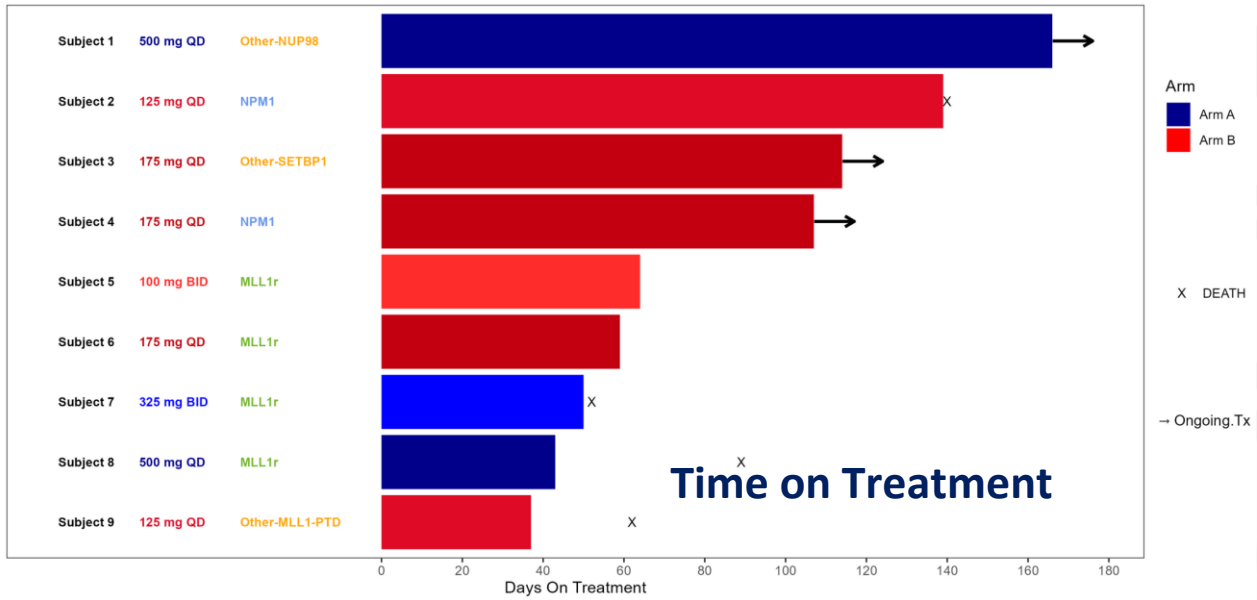
12% effective @ 1000nM

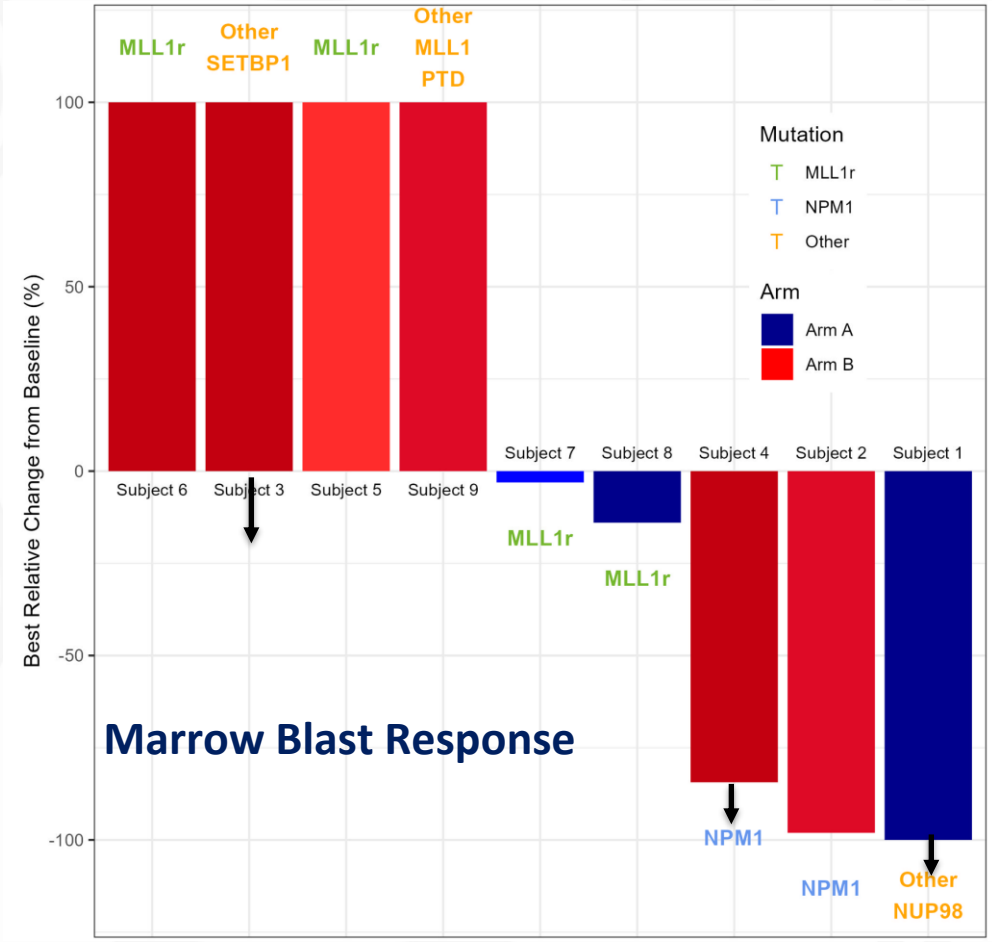
68% effective @ 1000nM



Blood (2021) 138 (Supplement 1): 3340., ASH 2021.

Early Signs of Clinical Efficacy Was Shown in AML Patients Treated with icovamenib





- Efficacy evaluable population is defined as DLT-evaluable patients with AML bearing mutation(s) believed to be menin-inhibitor sensitive who received treatment with icovamenib at ≥500 mg QD (Arm A) or ≥125 mg QD (Arm B)
- Data cutoff included all patients who initiated treatment on or before 06 Sep 2023; responses assessed as per PI using ELN2017 criteria.

- For patients who received at least 2 cycles of therapy: CR/CRi rate = 2/7 (29%); mean time to response = 1.8 months; minimal residual disease negativity achieved in the first CR.
- Duration of treatment (months): mean 2.84 (range: 1.2 - 5.5) ; 3/9 (33%) patients continued treatment as of cutoff date of 31 Oct 2023.
- Icovamenib was generally well-tolerated with no dose-limiting toxicities observed and without treatment discontinuations due to toxicity.

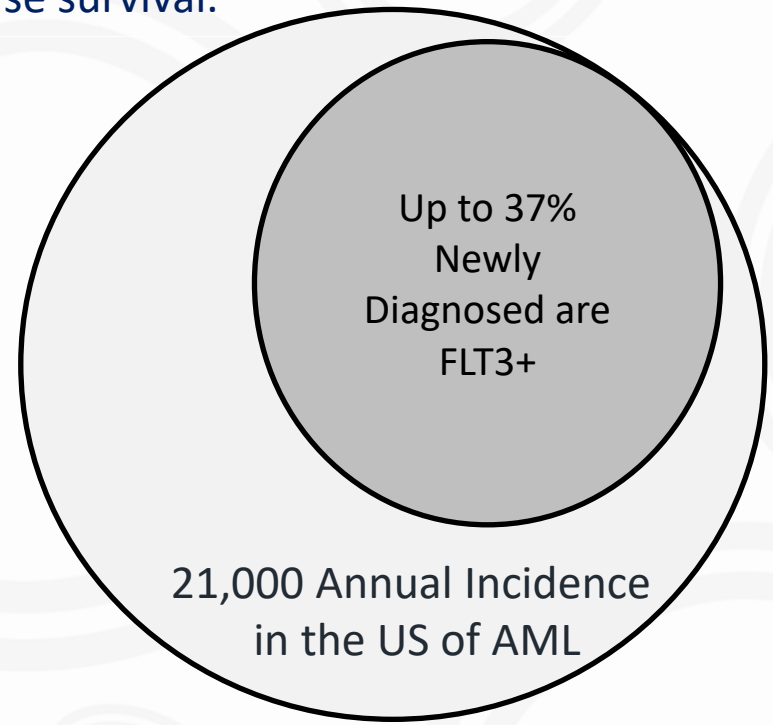
BM blast response for efficacy-evaluable patients (n=9), as described above patients with best relative change from baseline >100% are trimmed

BMF-500 in AML

An Investigational Covalent FLT3 Inhibitor with High Selectivity, Potent and Durable Antileukemic Activity

Relapsed/Refractory FLT3 Mutated AML – A Significant Unmet Need

- FLT3 is the most frequently mutated gene in AML, up to 37% newly diagnosed patients with AML.
- FLT3 Internal Tandem Duplication (ITD) mutation is the most common FLT3 mutation and considered as an aggressive hematologic malignancy with a generally very poor prognosis. FLT3 ITD has been associated with a higher risk of relapse and worse survival.



FLT3 inhibitors 2024 market size forecast: $535M

- VANFLYTA (quizartinib, approved in 2023): in treatment-naïve AML with FLT3 mutation
- XOSPATA (gilteritinib, approved in 2018): in R/R AML with FLT3 mutation; 2023 Revenue: Approx $400M

1.Targeting FLT3 Mutation in Acute Myeloid Leukemia: Current Strategies and Future Directions. Cancers (Basel). 2023 Apr 15;15(8):2312. doi: 10.3390/cancers15082312; Midostaurin FDA label; Quizartinib FDA label; Gilteritinib FDA label.

2. Global FLT3 Inhibitors Market by Type (FLT3-ITD (Internal Tandem Duplication), FLT3-TKD (Tyrosine Kinase Domain)), Product (Gilteritinib, Midostaurin, Quizartinib), Application - Forecast 2024-2030

Approved Agents for FLT3 Mutated AML

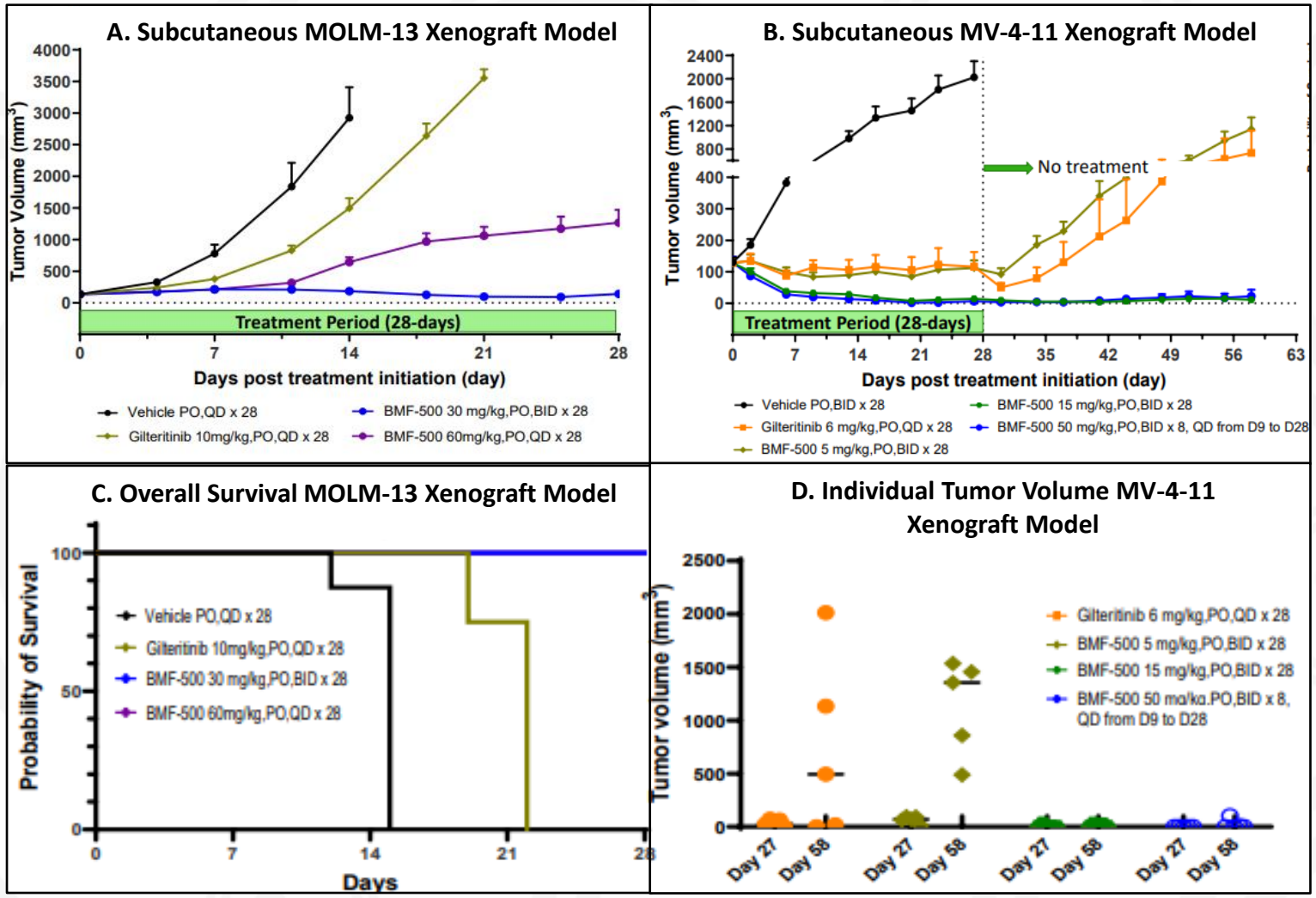
- Significant opportunity for deeper and more durable responses with an improved safety profile over 2nd-generation FLT3 inhibitors, quizartinib and gilteritinib.
- Resistance to FLT3 is a major limitation to long-term survival in AML patients.

Two selective FLT3 inhibitors approved for use in FLT3-mutated AML						
Agent	**Approved Indication**	**Treatment Arm(s)**	**Complete Response (CR)**	**Median Duration of CR**	**Median OS**	**Median Time on Drug**
Quizartinib[1]	Treatment Naïve FLT3	Quizartinib + Chemo	55%	38.6 mo.	HR: 0.78	-
		Placebo + Chemo	55%	12.4 mo.	-	-
Quizartinib[2]	R/R AML with FLT3 (Japan only)	Quizartinib	4.1%	-	6.2 mo.	16 mo.
		Chemo	0.8%	-	4.7 mo.	-
Gilteritinib[3]	R/R AML with FLT3	Gilteritinib	14.2%	14.8 mo.	9.3 mo.	3.5 mo.
		Chemo	10.5%	1.8 mo.	5.6 mo.	-

1. Quizartinib FDA label
2. Quizartinib was only approved for r/r FLT3 AML in Japan; Cortes JE et al. *Lancet Oncol* 2019; 20: 986–99
3. Gilteritinib FDA label

Note: CR defined as an absolute neutrophil count ≥1.0 x 109 /L, platelets ≥100 x 109/L, normal marrow differential with <5% blasts, must have been red blood cells, platelet transfusion independent and no evidence of extramedullary leukemia. CR rates shown are prior to HSCT.

BMF-500 - A Highly Potent and Durable FLT3 Inhibitor in Preclinical Experiments



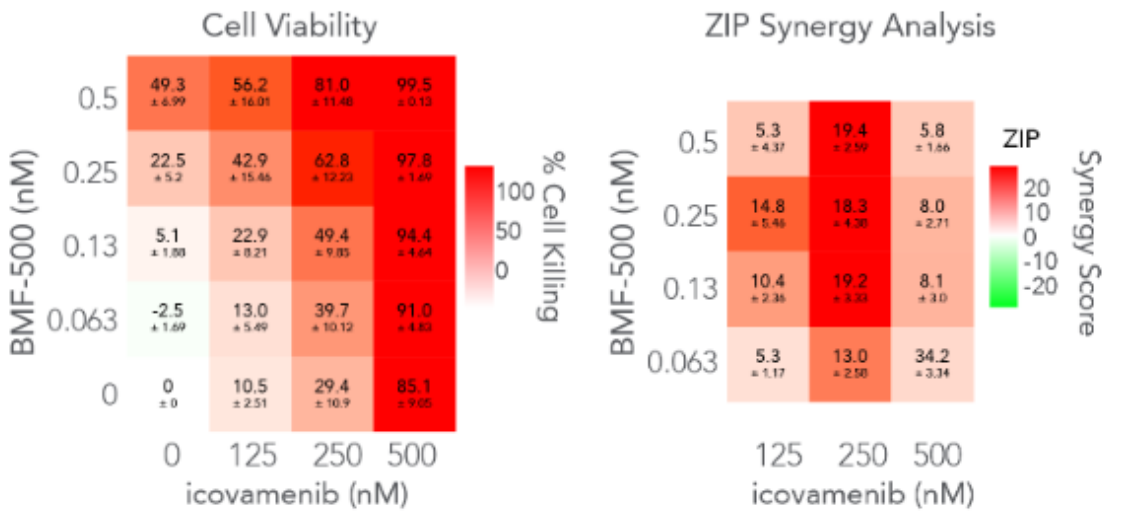
BMF-500 demonstrates antitumor activity with sustained tumor regression at dose levels predicted to be well-tolerated. The overall survival improved significantly with body weight maintenance across treatment groups in two preclinical mouse xenograft models.

biomea FUSION We Aim to Cure™

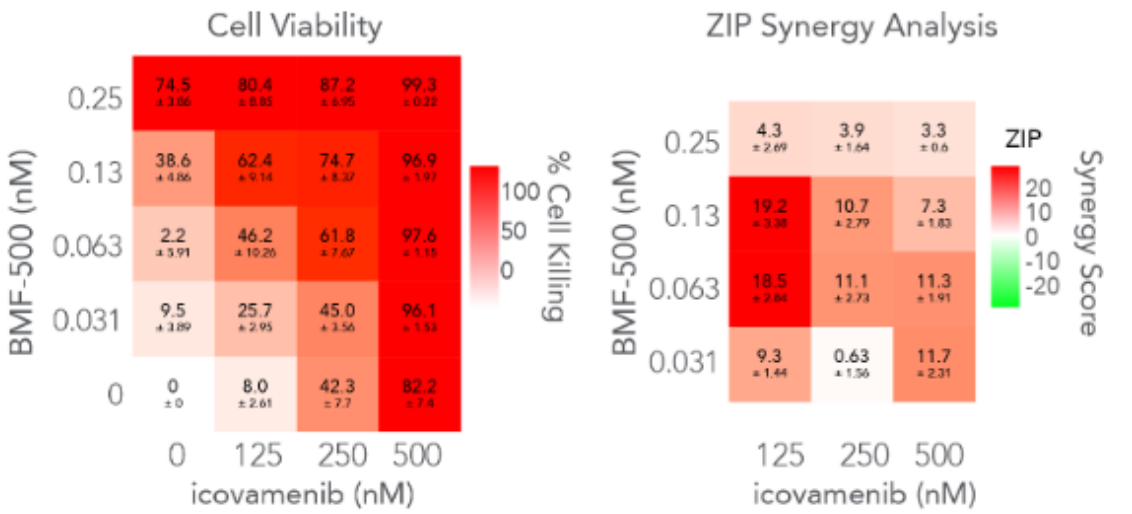
Law et al., ASH 2022 (#2756)

Icovamenib and BMF-500 in Combination Showed Higher Cell Killing at Lower Concentrations

Combination in MOLM-13 (MLL-AF9, FLT3$^{ITD/WT}$) Cell Line



Combination in MV-4-11 (MLL-AF4, FLT$^{ITD/WT}$) Cell Line



Importantly, 50% of all dose levels explored displayed synergistic effects with the combination of icovamenib and BMF-500. All dose combinations showed at least additive effects of these two novel agents.

ZIP Synergy Score:
Below -10 = Antagonistic
-10 to +10 = Additive
Above +10 = Synergistic

Multiple Upcoming Milestones

	Study	Indications	Milestones
Icovamenib (BMF-219) Menin Program (Potential Best-In-Class)	COVALENT-111	Type 2 Diabetes	**Phase IIb – Topline Week 26 Data Readout (Dec 2024)** *Confirm optimal dosing scheme and define best responding patients*
	COVALENT-112	Type 1 Diabetes	**Phase IIa – Topline Week 26 Data Readout (Dec 2024)** *Initial patients' response with various dosing schedules*
	COVALENT-101	Liquid Tumors	**Phase I - Dose Escalation Completion**
	COVALENT-102	Solid Tumors	**Phase I - Dose Escalation Completion**
BMF-500 FLT3 Program (Potential Best-In-Class)	COVALENT-103	AML/ALL (Acute Leukemia)	**Phase I - Dose Escalation Completion**
BMF-650 GLP-1R Agonist (Potential Best-In-Class)	IND-Enabling Studies	Diabetes/Obesity	**Clearance of IND**

As of September 30, 2024

Company Financials (NASDAQ: BMEA)

	Three Months Ended September 30, 2024	Three Months Ended September 30, 2023
Operating expenses:		
R&D	$ 27,244	$ 25,347
G&A	6,795	5,772
Total Operating Expenses	34,039	31,119
Loss from operations	(34,039)	(31,119)
Interest and other income, net	1,252	2,690
Net loss	$ (32,787)	(28,429)
Other comprehensive loss:		
Changes in unrealized gain on short term investments, net	—	—
Comprehensive loss	$ (32,787)	$ (28,429)
Net loss per common share, basic and diluted	$ (0.91)	$ (0.80)
Weighted-average number of common shares used to compute basic and diluted net loss per common share	36,220,736	35,653,988

Q3 Operating Expenses minus Stock Based Comp	**$29.3 M**
Cash, Cash Equivalents, Investments, and Restricted Cash as of 30 September 2024	**$88.3 M**

Contact:
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THANK YOU

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