Backgrounder

Clinical Results of BMF-219 in Diabetes

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Clinical Highlights in Type 2 Diabetes with BMF-219

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

Dose Escalation Portion with 4-Week Dosing of BMF-219 Completed, Dose Expansion Phase with 8-Week and 12-Week Dosing Underway – Data Expected in 2024

Part 1 Dose Escalation,
4 weeks dosing+ 22 weeks follow up

- **Healthy Volunteers** n=16
- **50 mg QD, n=10** x 4 wks
- **100 mg QD, n=20** x 4 wks
- **200 mg QD / 100 mg BID, n=22** x 4 wks
- **200 mg QD,** x 2 wks, **n=10** → **400 mg QD** x 2 wks

Part 2 Dose Expansion, n=216 – 360 incl.
12 weeks dosing + 40 weeks follow-up

Arm A*	**100 mg, n=72** x 8 wks	
Arm B	**100 mg, n=72** x 12 wks	
Arm C	**100 mg, n=72** x 8 wks	→ **200 mg** x 4 wks
Arm D	Dose Selection and Enrollment Pending	
Arm E	Dose Selection and Enrollment Pending	

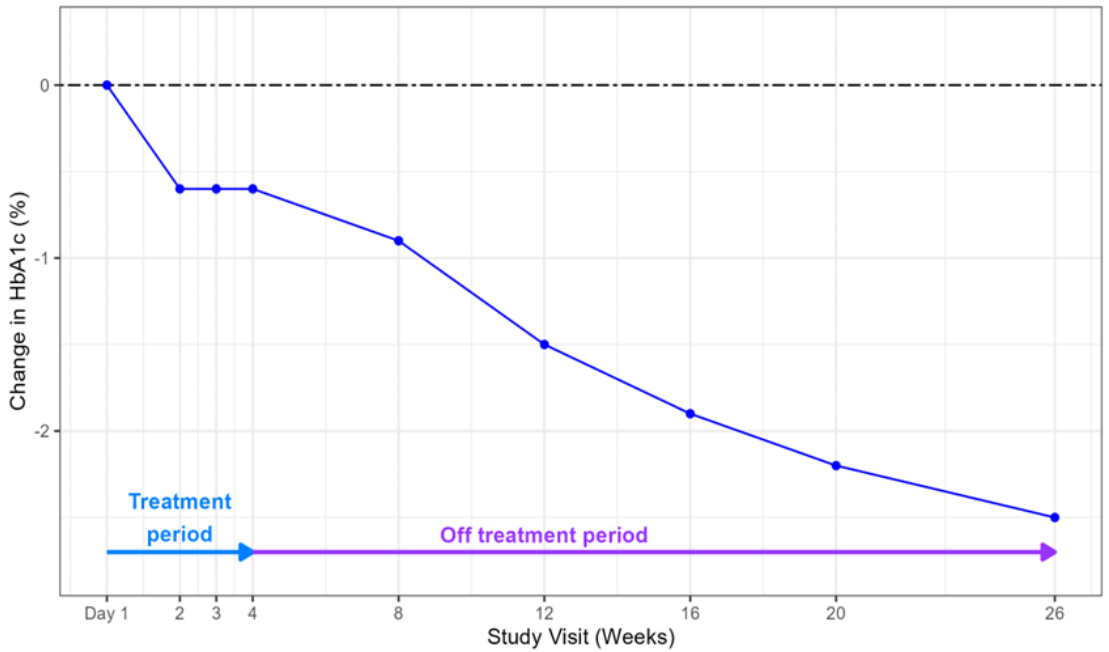
*Redosing if required at Week 22 for an additional 4 weeks.

Case Study: 29-Year-Old Man with 4-Year History of T2D

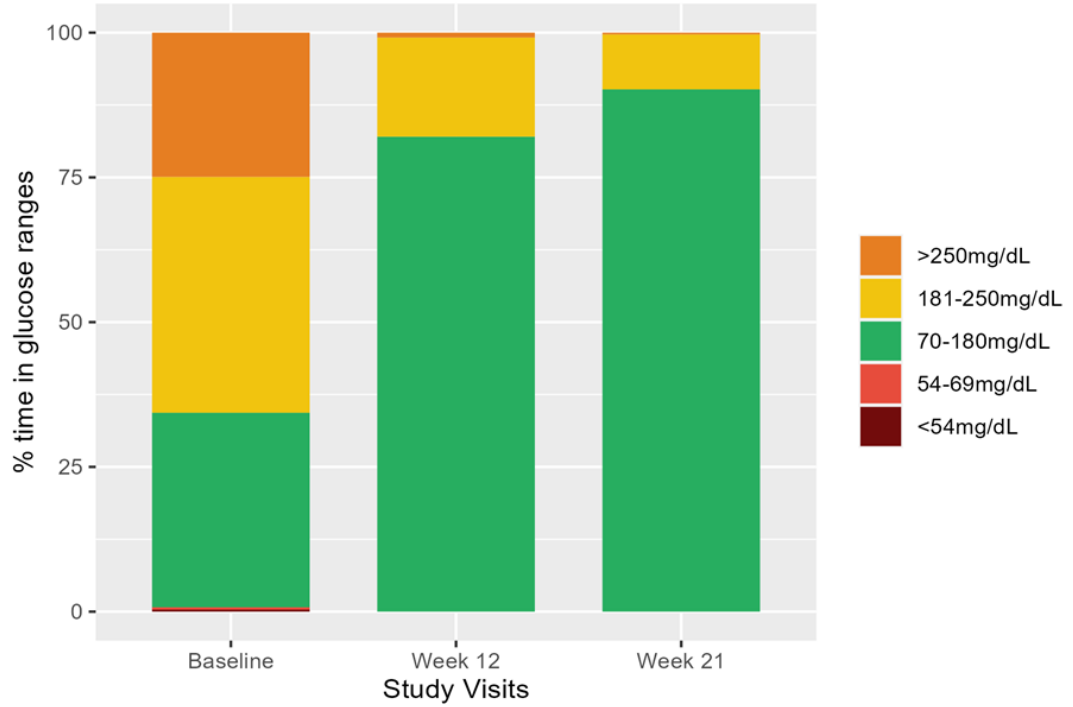
- 29-year-old man with 4-year history of T2D
- Metformin and empagliflozin
- HbA_{1c} 9.5%; FPG 146 mg/dL; BMI 25.6 kg/m^2

- BMF-219 200 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

Change in HbA_{1c} (%)



Continuous Glucose Monitoring



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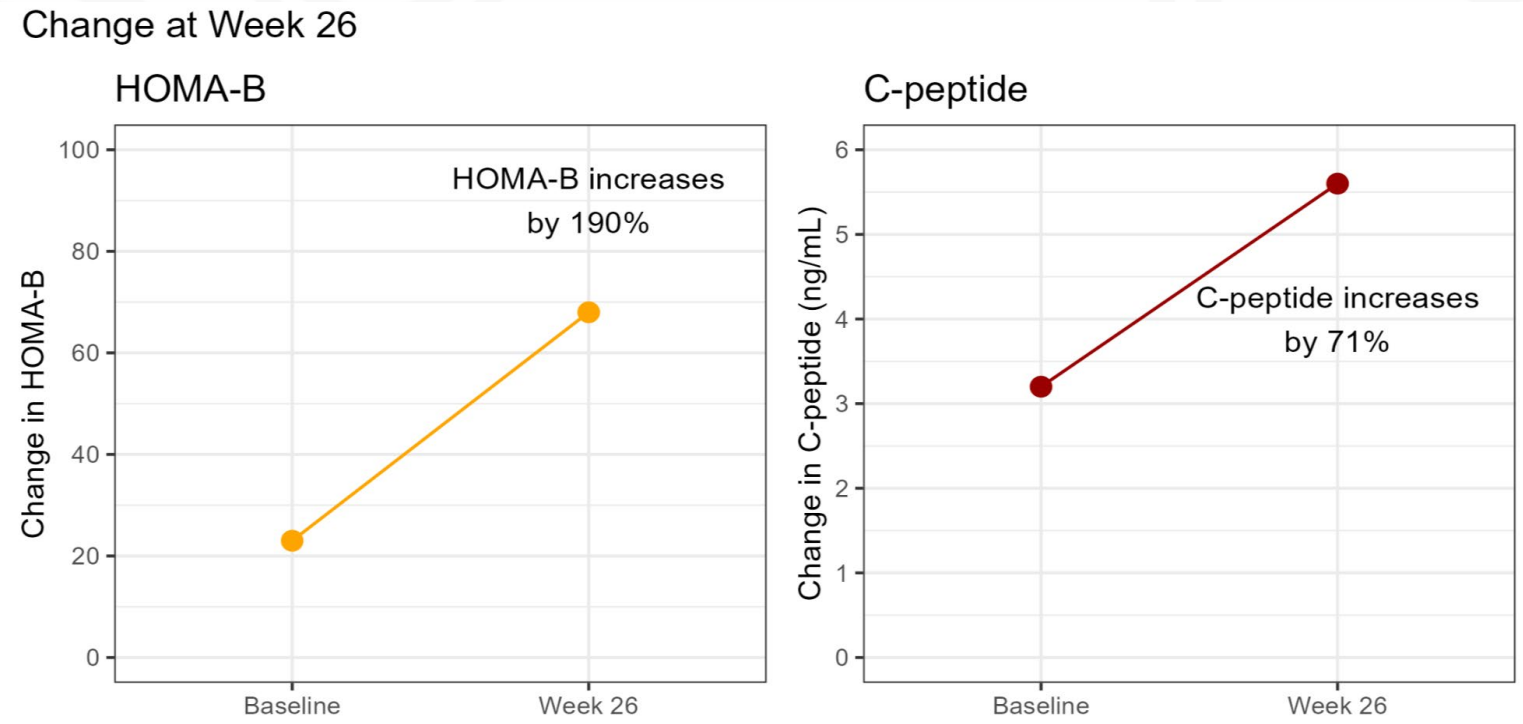
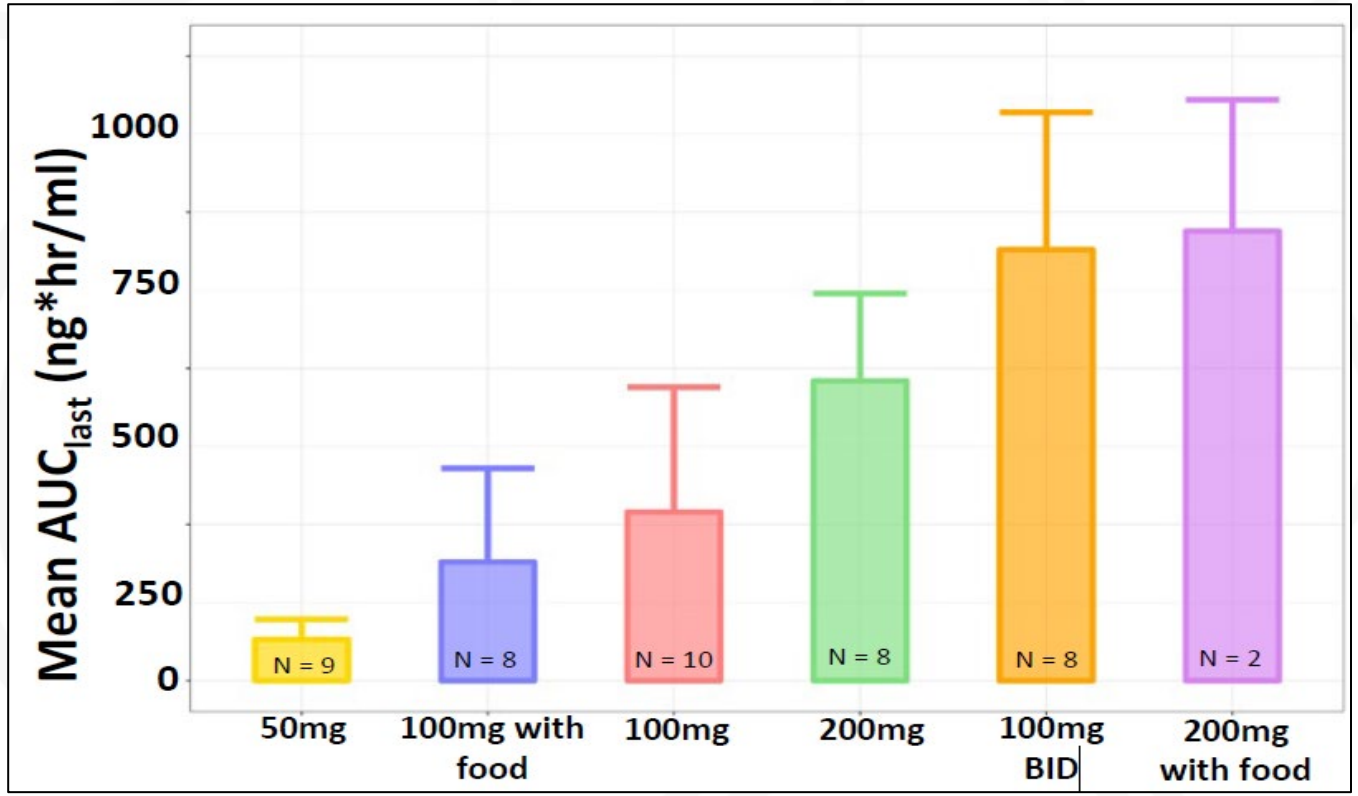


Dose-Dependent PK Response Demonstrated

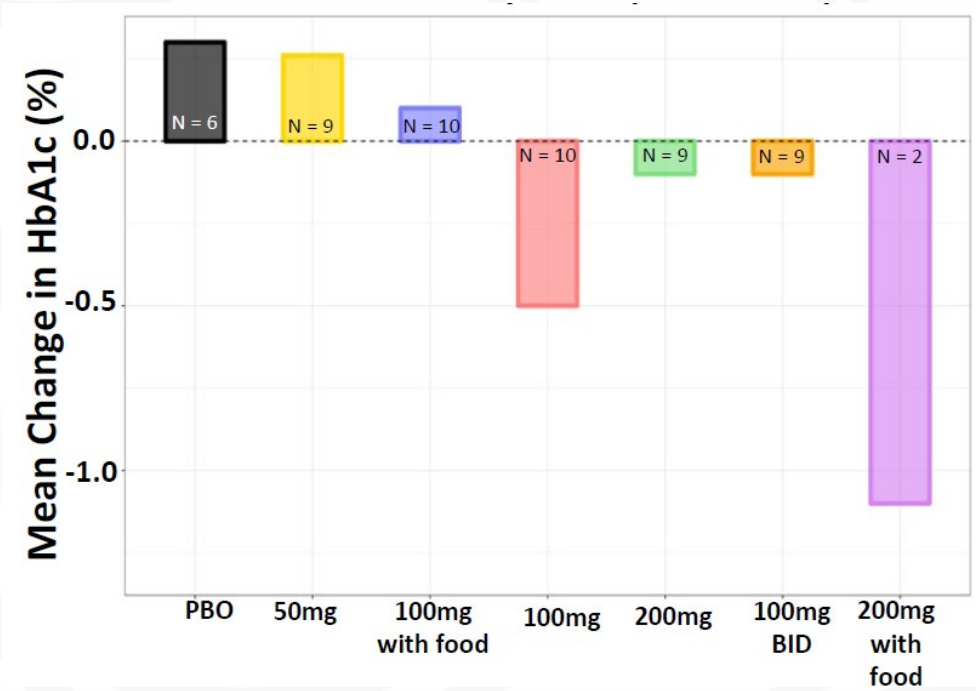
PK Response Across Cohorts (Week 4)



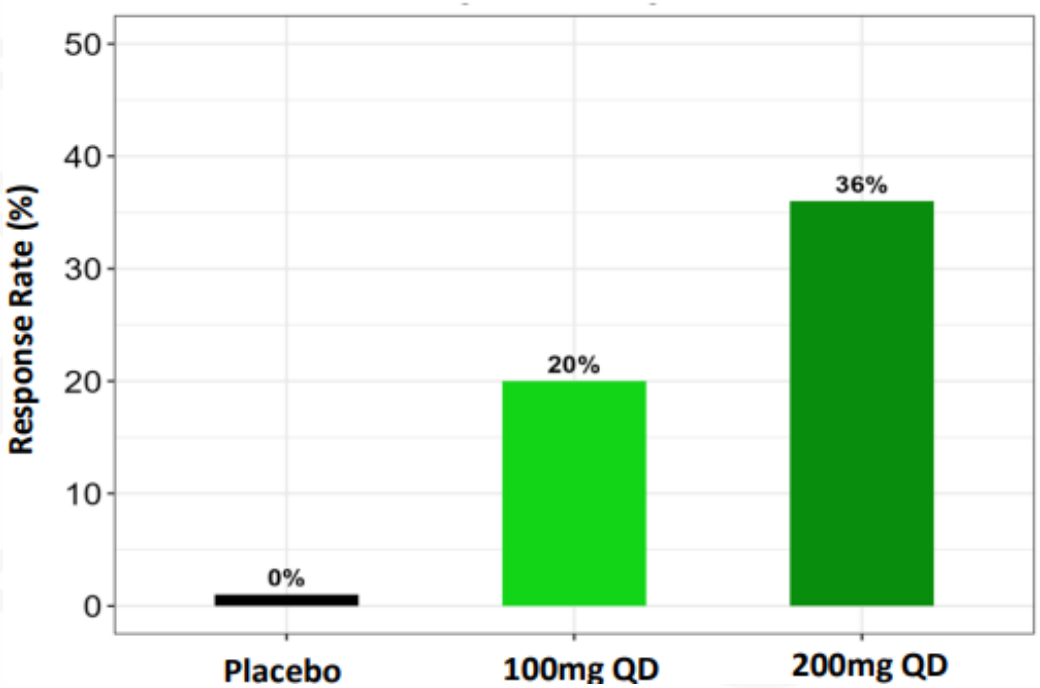
- Dose-dependent PK response is demonstrated across different dose cohorts
- Increase in AUC is shown in higher dose cohort (200mg QD)

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

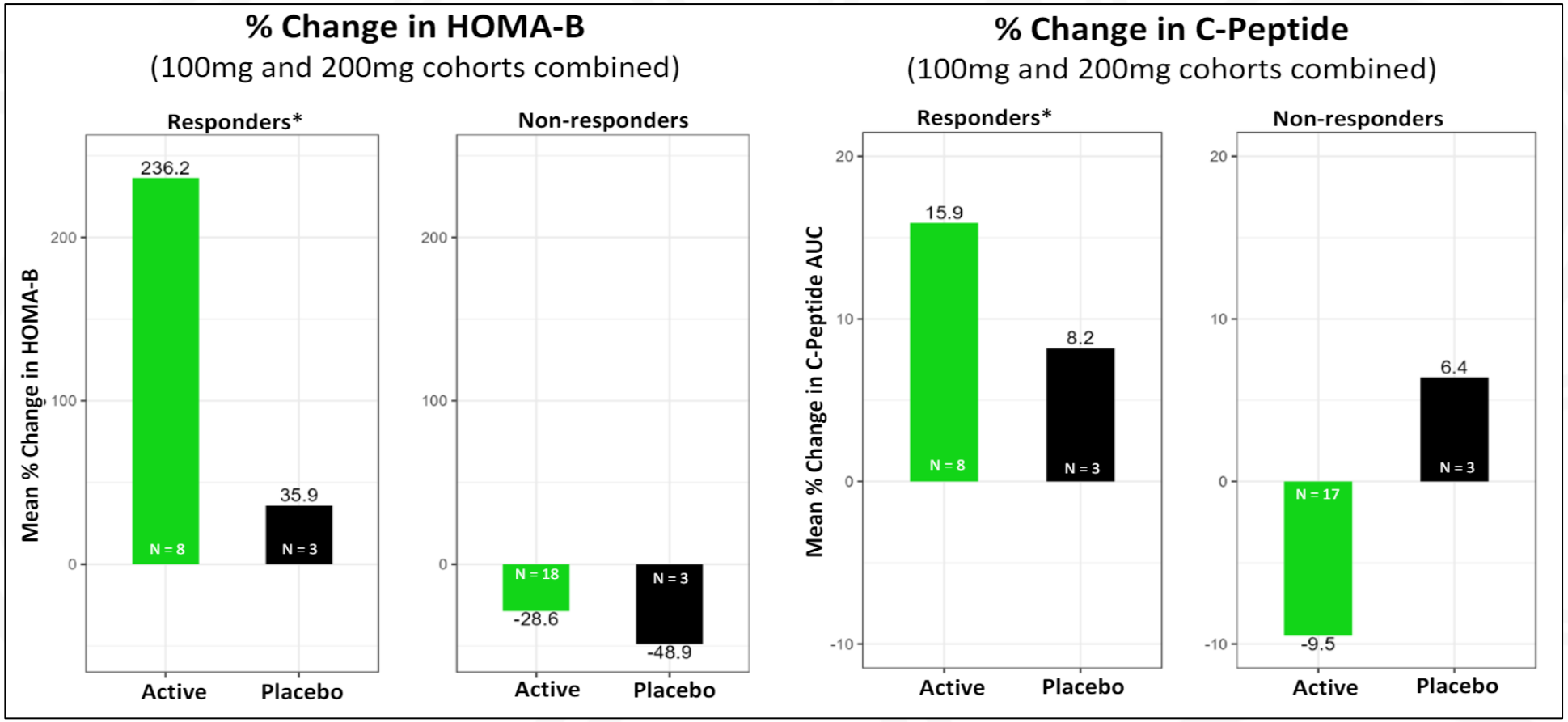
Mean HbA1c Response (Week 26)



Proportion with ≥ 1% HbA1c Reduction (Week 26)



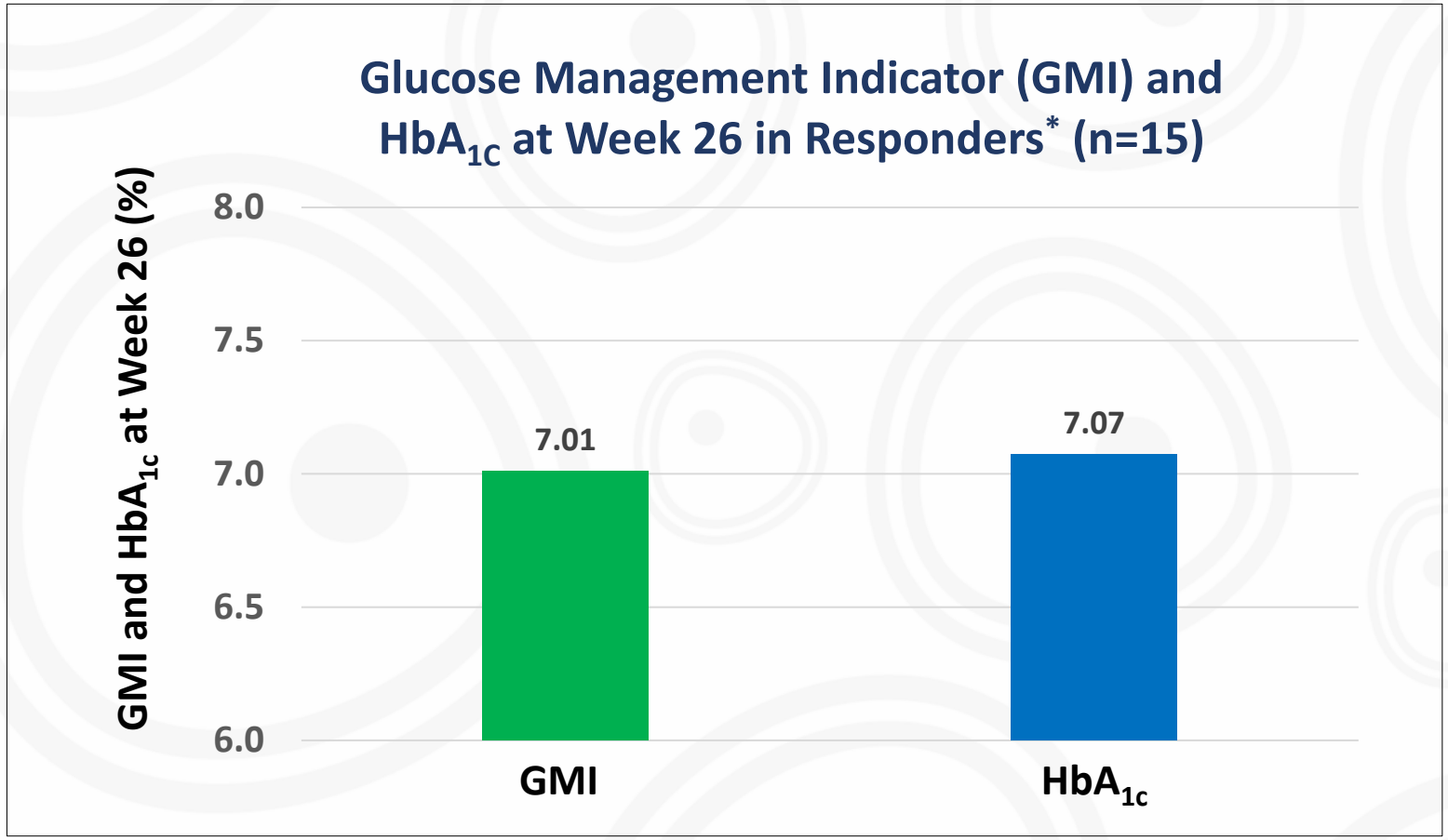
Beta-Cell Proliferation Supported by Increase in Homa-B and C-Peptide at Week 26



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

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 BMF-219.

*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 BMF-219 Clinical Results in Type 2 Diabetes

- BMF-219 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 BMF-219, 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 first 3 Arms of 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:

- Initial 26-week data of the Expansion Phase expected in 4Q24

Clinical Highlights in Type 1 Diabetes with BMF-219

COVALENT-112 (Type 1 Diabetes) Study Design

COVALENT-112: Open-Label and Randomized, Controlled Trial Assessing BMF-219 in Type 1 Diabetes

Open Label, N=40
12 weeks dosing+ 40 weeks follow up

- Adults with T1D, HbA1c 6.5-10.0%
- Diagnosed with T1D within 3 years
- **C-peptide ≥0.2 nmol/L**

→ **100 mg QD, n=10**
→ **200 mg QD, n=10**

- Adults with T1D, HbA1c 6.5-10.0%
- Diagnosed with T1D 3 to 15 years
- **C-peptide ≥0.08 nmol/L**

→ **100 mg QD, n=10**
→ **200 mg QD, n=10**

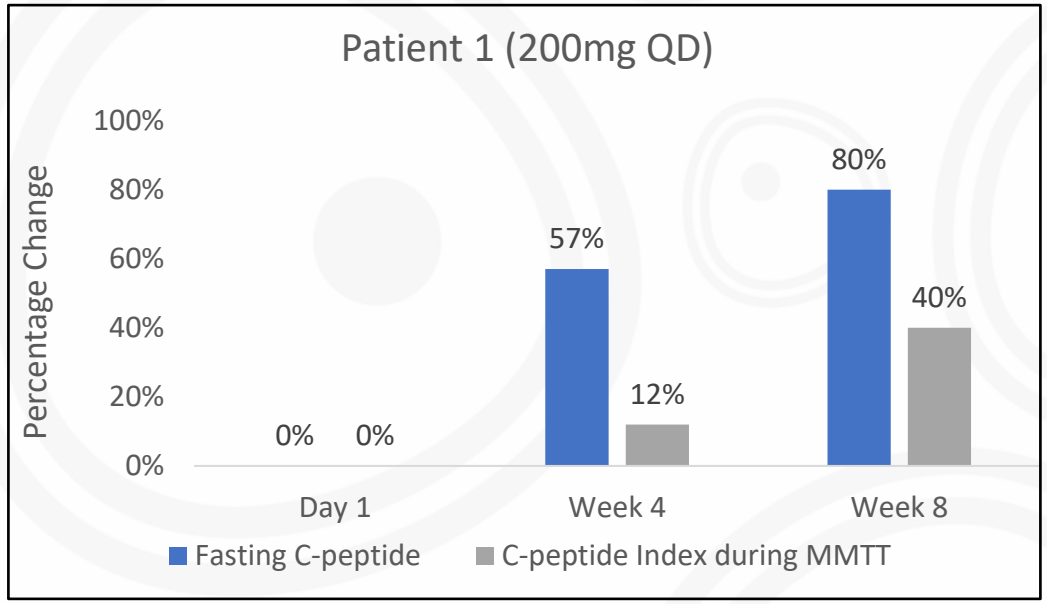
Main Study (Randomized, placebo-controlled, double-blind)
N=150, 12 weeks dosing + 40 weeks follow-up

- Adults with T1D, HbA1c 6.5-10.0%
- Diagnosed with T1D within 3 years
- C-peptide ≥0.2 nmol/L

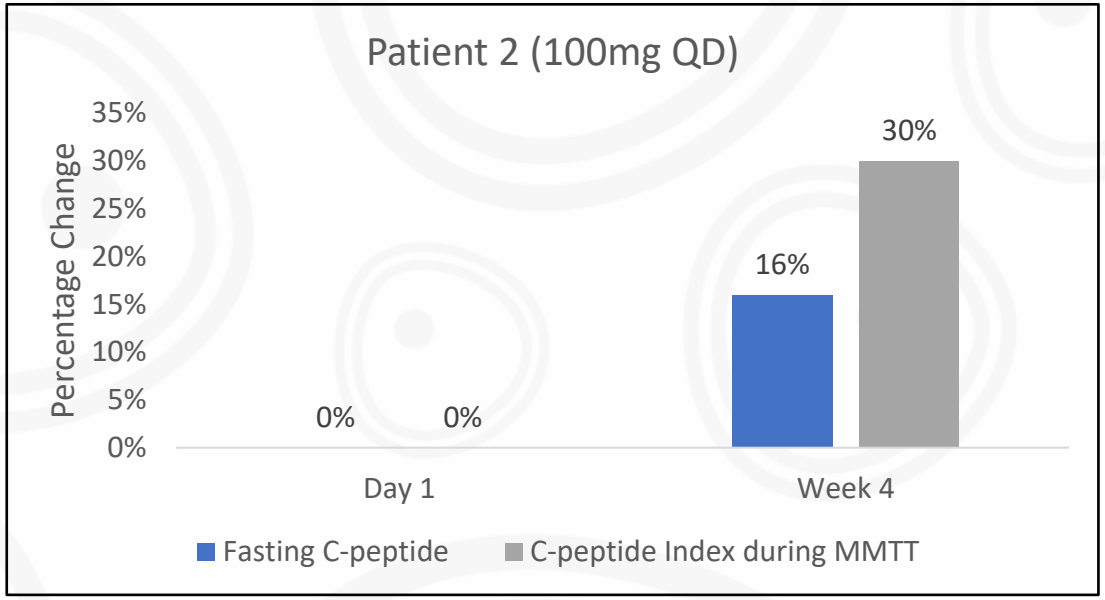
→ **100 mg QD, n=50**
→ **200 mg QD, n=50**
→ **Matched placebo, n=50**

BMF-219 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
- BMF-219 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; BMF-219 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

First Data Readout of Initial Healthy Volunteers and Type 2 Diabetes Cohorts

March 28, 2023

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First Data Readout of Initial Healthy Volunteer and Type 2 Diabetes Cohorts

March 28, 2023

Summary of Results

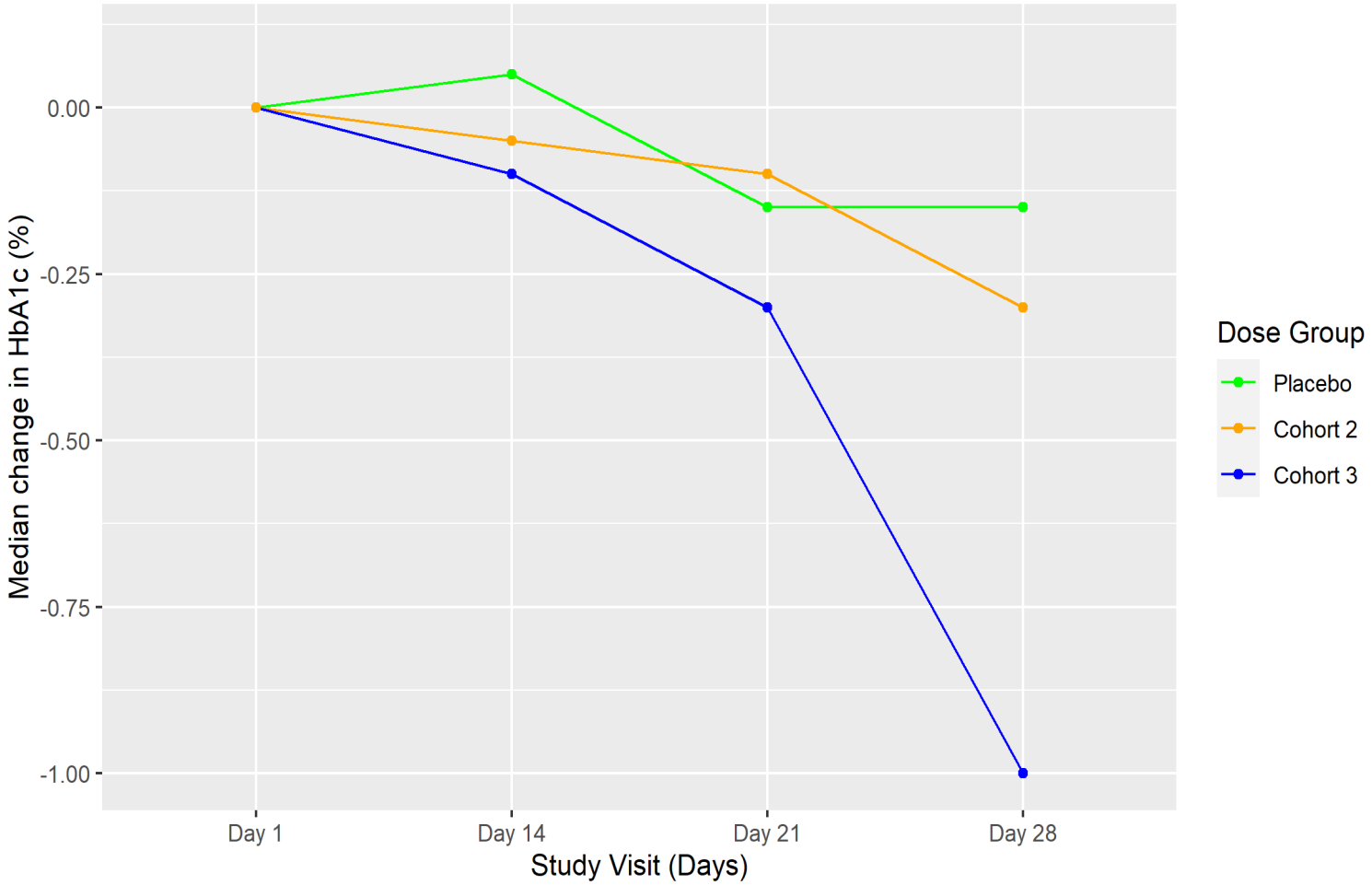
	Cohort 2		Cohort 3	
	BMF-219	**Placebo**	**BMF-219**	**Placebo**
Number of Subjects	10	2	10	2
Exposure: C_{max} (ng/mL)/ AUC (hr*ng/mL)	34.8 / 84.3	-	94.2 / 224	-
Median (Mean) HbA1c % at Baseline	7.9 (8.0)	8.4 (8.4)	7.8 (8.1)	7.8 (7.8)
Median (Mean) Change in HbA1c % at Week 4	**-0.3 (-0.25)**	-0.1 (-0.1)	**-1.0 (-0.81)**	-0.15 (-0.15**)**

Note: **Cohort 2** – 100 mg BMF-219 or placebo daily for 4 weeks taken with food
Cohort 3 – 100 mg BMF-219 or placebo daily for 4 weeks taken without food

COVALENT-111 Baseline Patient Characteristics

	Cohort 2		Cohort 3	
	BMF-219	**Placebo**	**BMF-219**	**Placebo**
Number of Subjects	10	2	10	2
Age (min, max)	35, 60	40, 53	38, 63	35, 61
Sex (M, F)	7, 3	2, 0	6, 4	2, 0
Time since T2DM diagnosis (min, max)	4 yrs, 14 yrs	~1 yrs, 5 yrs	6 mo, 9 yrs	9 mo, 9 yrs
Concurrent Medications for T2DM	▪ Metformin (7/10) ▪ Janumet (1/10) ▪ Jardiance [Metformin + Empagliflozin] (1/10) ▪ Synjardy [Metformin + Empagliflozin] (1/10)	▪ Metformin alone (1/2) ▪ Janumet [Metformin + Sitagliptin] (1/2)	▪ Metformin alone (9/10) ▪ Janumet and Farxiga [Dapagliflozin] (1/10)	▪ Metformin (2/2)

Observed HbA1c Lowering of BMF-219



Cohort 2

Response Rate

70% of patients responded to BMF-219

HbA1c (all pts)

Median Baseline: 7.9%

Median Δ: - 0.3% (at week 4)

Cohort 3

Response Rate

89% of patients responded to BMF-219

HbA1c (all pts)

Median Baseline: 7.8%

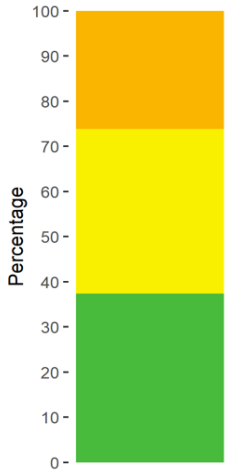
Median Δ: - 1.0% (at week 4)

COVALENT-111 HbA1c Summary Results at Week 4

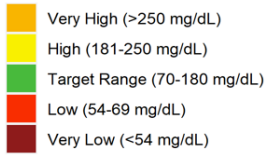
	Cohort 2		Cohort 3	
	BMF-219	**Placebo**	**BMF-219**	**Placebo**
Number of Subjects	10	2	10	2
HbA1c (%) at Baseline	7.1 – 9.1		7.0 – 9.8	
Median HbA1c (Mean) (%) at Baseline	7.9 (8.0)	8.4 (8.4)	**7.8 (8.1)**	7.8 (7.8)
Number of Subjects with Reduction in HbA1c at week 4	7/10 (70%)	1/2	**8/9 (89%)***	1/2
≥0.5% Reduction in HbA1c at Week 4	3/10 (30%)	1/2	**7/9 (78%)***	0
≥1% Reduction in HbA1c at Week 4	0	0	**5/9 (56%)***	0
Median Change in HbA1c at Week 4 (Mean) (%)	-0.3 (-0.25)	-0.1 (-0.1)	**-1.0 (-0.81)**	-0.15 (-0.15)

*Note: The active group denominator in Cohort 3 is 9 because the week 4 sample for one patient was unable to process.

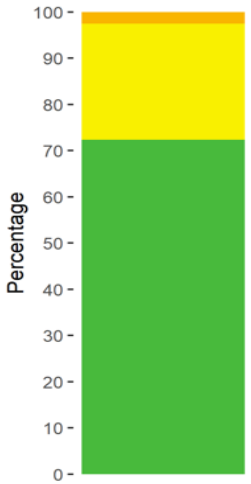
Case Report Cohort 3 Patient Results (Patient A): Glycemic Parameters



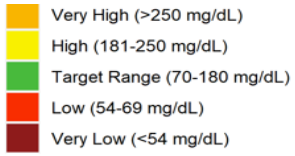
Continuous Glucose Monitoring
Baseline



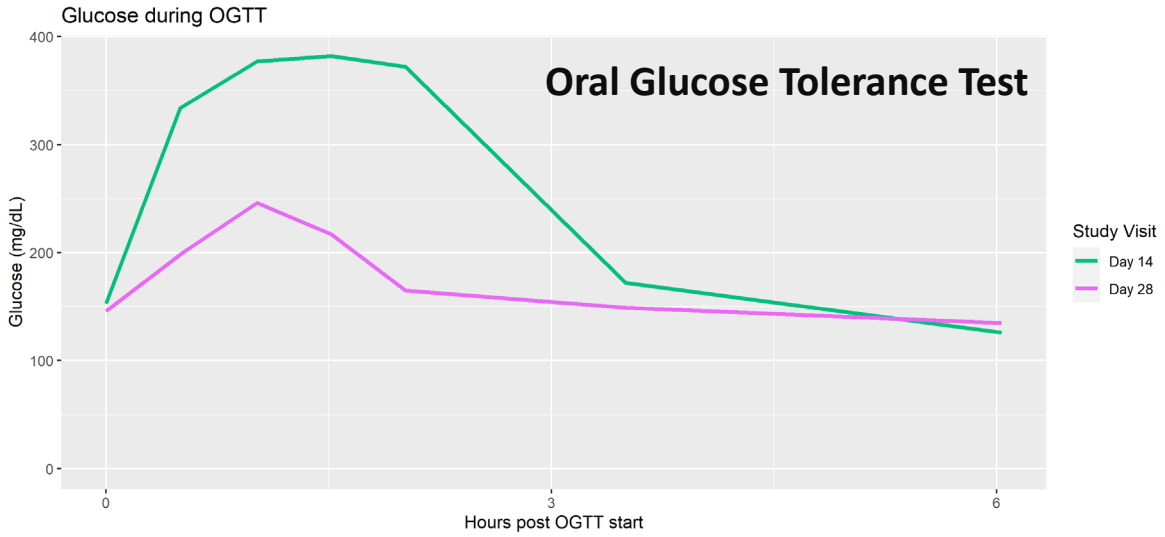
- Average glucose 205 mg/dL
- 37% time in Target Range

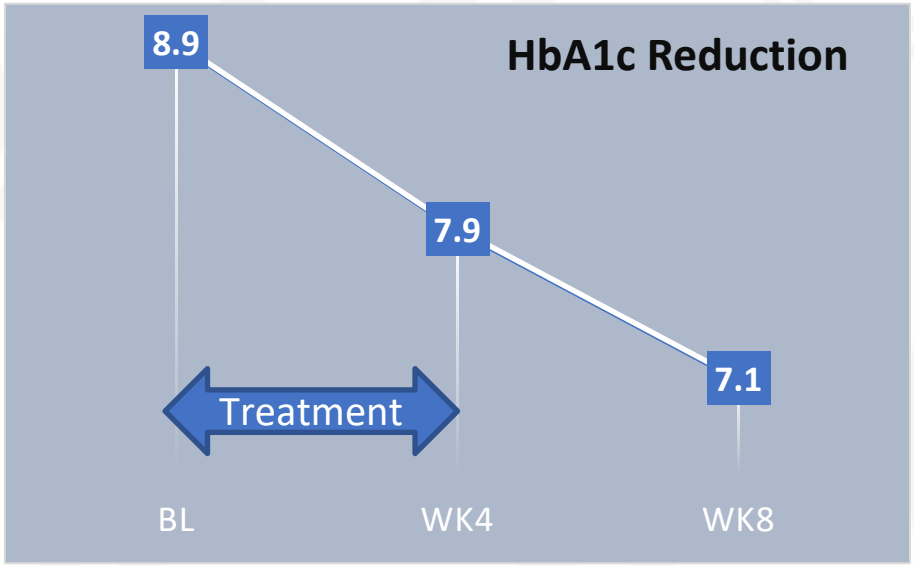


Continuous Glucose Monitoring
Week 4

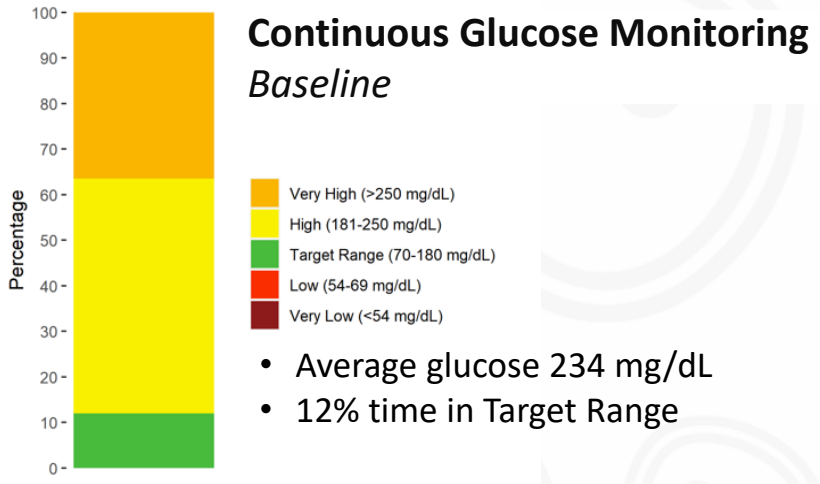


- Average glucose 169 mg/dL
- 72% time in Target Range



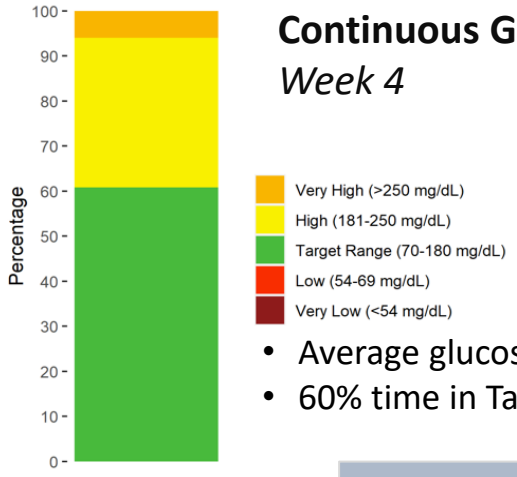


Case Report Cohort 3 Patient Results (Patient B): Glycemic Parameters



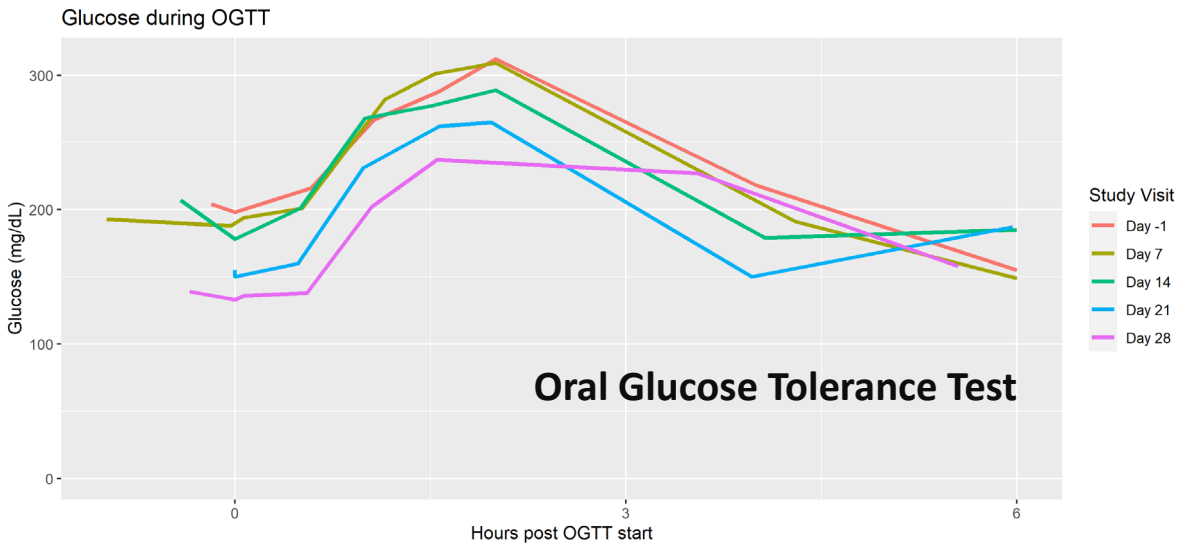
Continuous Glucose Monitoring
Baseline

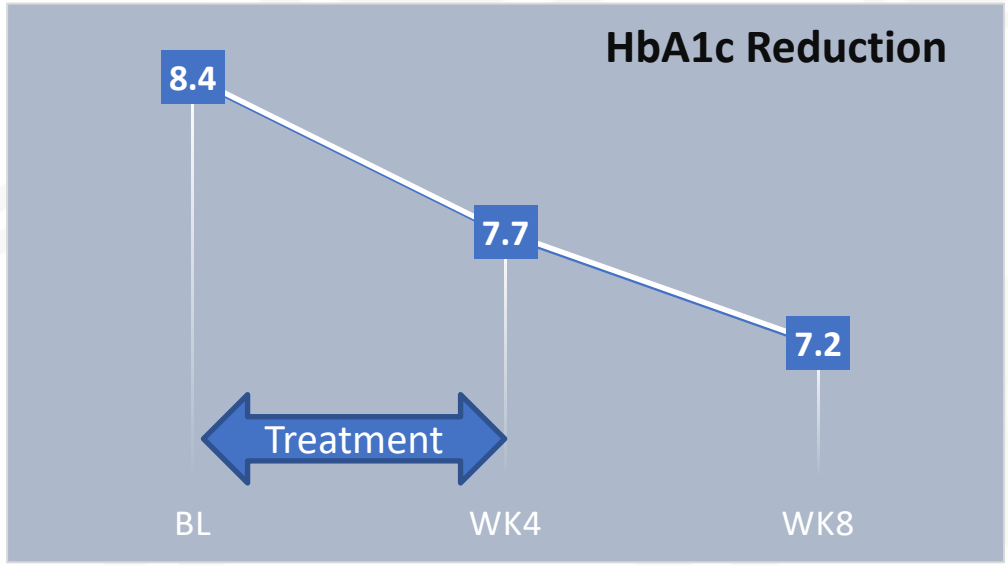
- Average glucose 234 mg/dL
- 12% time in Target Range



Continuous Glucose Monitoring
Week 4

- Average glucose 174 mg/dL
- 60% time in Target Range





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COVALENT-111 Cohort 1 All Treatment Emergent Adverse Events (TEAEs) (Healthy Volunteers, n=16; *100 mg once daily for 14 days*)

Preferred Term for TEAE	BMF-219 (N=12)	Placebo (N=4)	Total (N=16)
Subjects with ≥1 TEAE	2 (16.7%)	1 (25%)	3 (18.8%)
Headache	1 (8.3%)	1 (25%)	2 (12.5%)
Sharp left eye pain	1 (8.3%)	0	1 (6.3%)

*All TEAEs were Grade 1

COVALENT-111 Cohort 2 & 3 All TEAEs (Type 2 Diabetes n=24; 100 mg once daily dosing X 4 weeks)

Preferred Term for TEAE	BMF-219 (N=20)	Placebo (N=4)	Total (N=24)
Subjects with ≥1 TEAE	7 (35%)	2 (50%)	9 (38%)
Abdominal bloating	2 (10%)	0	2 (8.4%)
Elevated pancreatic polypeptide in plasma	0	2 (50%)	2 (8.4%)
Cough	1 (5%)	1 (25%)	2 (8.4%)
Elevated GGT	1 (5%)	0	1 (4.2%)
Elevated AST	1 (5%)	0	1 (4.2%)
Elevated ALT	1 (5%)	0	1 (4.2%)
Sore throat	1 (5%)	0	1 (4.2%)
Non-specific GI symptoms	1 (5%)	0	1 (4.2%)
Decreased interleukin-6	1 (5%)	0	1 (4.2%)
Swollen lymph nodes	0	1 (25%)	1 (4.2%)
Elevated lipase	1 (5%)	0	1 (4.2%)
Intermittent headaches	1 (5%)	0	1 (4.2%)
Contact dermatitis	1 (5%)	0	1 (4.2%)

All TEAEs are Grade 1 except Elevated Lipase (Grade 2)

Summary of Data

Safety

- BMF-219 demonstrated a well-tolerated safety profile
- No dose discontinuations
- All 20 subjects completed 4 weeks of treatment and continue in 5-month follow-up period
- No severe or serious TEAEs were observed
- No episodes of symptomatic hypoglycemia occurred in any patients

Efficacy

Cohort 3 highlights

- 89% pts achieved a reduction in HbA1c
- 78% pts achieved ≥ 0.5% reduction in HbA1c
- 56% pts achieved ≥ 1% reduction in HbA1c
- Positive trend in OGTT and CGM parameters

Preliminary Results of Healthy Volunteer (HV) and Type 2 Diabetes Mellitus (T2DM) 100mg Cohorts

June 26, 2023 ADA

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COVALENT-111 Data Readout ADA 2023 - June 26, 2023

Table 1: Results Summary at Week 12

	Cohort 2		Cohort 3	
	BMF-219	**Placebo**	**BMF-219**	**Placebo**
Number of Patients	10	2	10	2
HbA1c (%) at Baseline	7.1 – 9.1		7.0 – 9.8	
Exposure: C_{max} (ng/mL)/ AUC (hr*ng/mL)	34.8 / 84.3	-	94.2 / 224	-
Median (Mean) HbA1c % at Baseline	7.9 (8.0)	8.4 (8.4)	7.8 (8.1)	7.8 (7.8)
Number of Patients with Reduction in HbA1c at **Week 12**	6/10 (60%)	1/2	9/10 (90%)*	1/2
≥0.5% Reduction in HbA1c at **Week 12** (%)	4/10 (40%)	1/2	8/10 (80%)*	0
≥1% Reduction in HbA1c at **Week 12** (%)	3/10 (30%)	0	4/10 (40%)*	0
Median (Mean) Change in HbA1c at **Week 12**	-0.1 (-0.1)	0.2 (0.2)	-0.8 (-1.0)	0 (0)
Top 50% Mean Change in HbA1c at **Week 12**	-0.9	NA	-1.5	NA

*Note: Linear imputation used for single data point with results available before and after missing data.
Cohort 2 – 100 mg BMF-219 or placebo daily for 4 weeks taken with food
Cohort 3 – 100 mg BMF-219 or placebo daily for 4 weeks taken without food

Table 1 The top 50% of patients in Cohort 2 had a mean reduction in HbA1c of 0.9% at week 12 while the top 50% of Cohort 3 patients demonstrated a mean reduction of 1.5%. Cohort 2 patients had ~3 fold lower BMF-219 exposure than Cohort 3 patients.

COVALENT-111 Data Readout ADA 2023 - June 26, 2023

Figure 1: HbA1c Results in Cohort 1 (HVs)

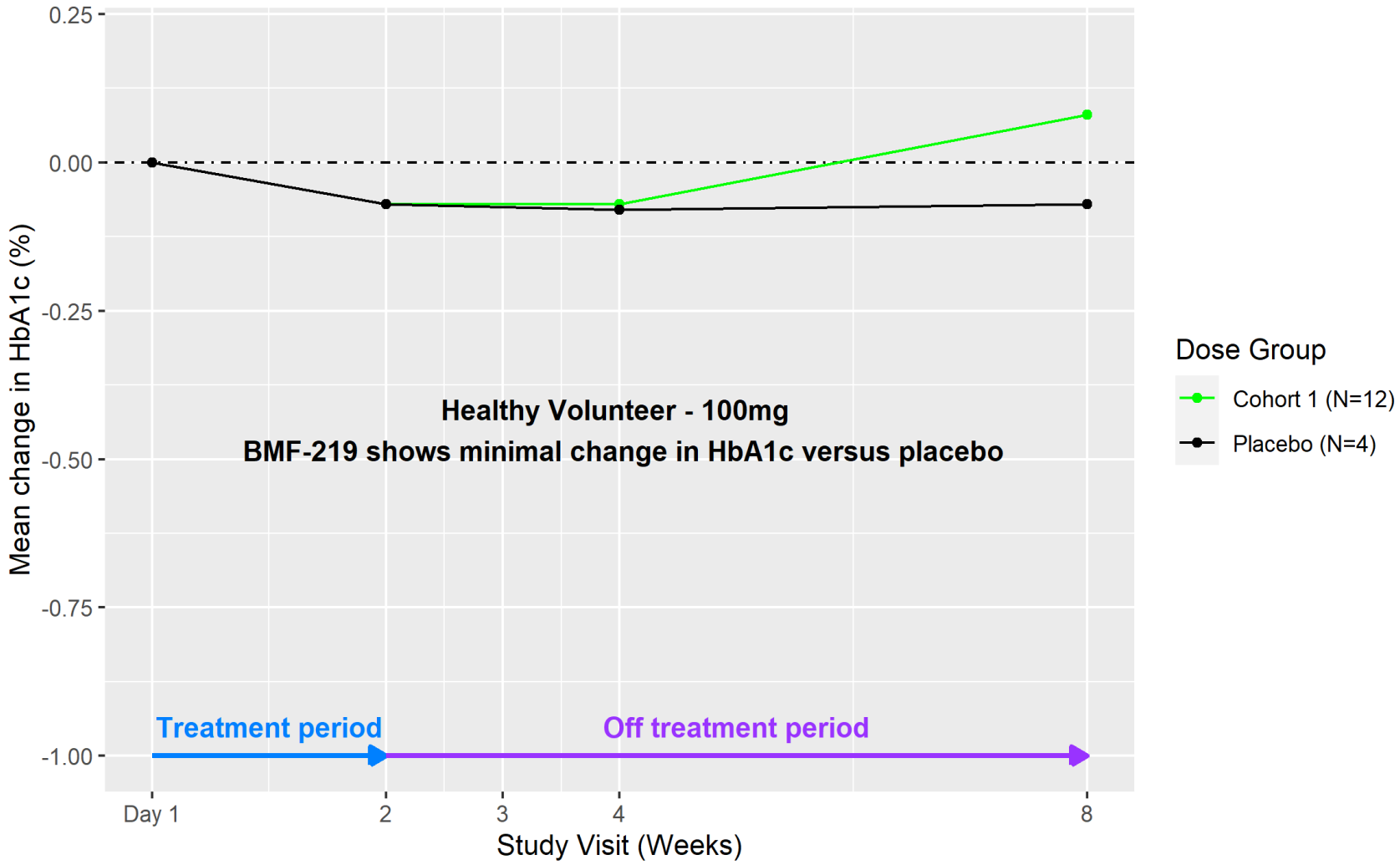


Figure 1. Minimal change was observed in HbA1c in healthy volunteers (HVs) during 14 days of treatment and 6-week follow-up.

Figure 2: Change in HbA1C for all patients and Top 50% at Week 12

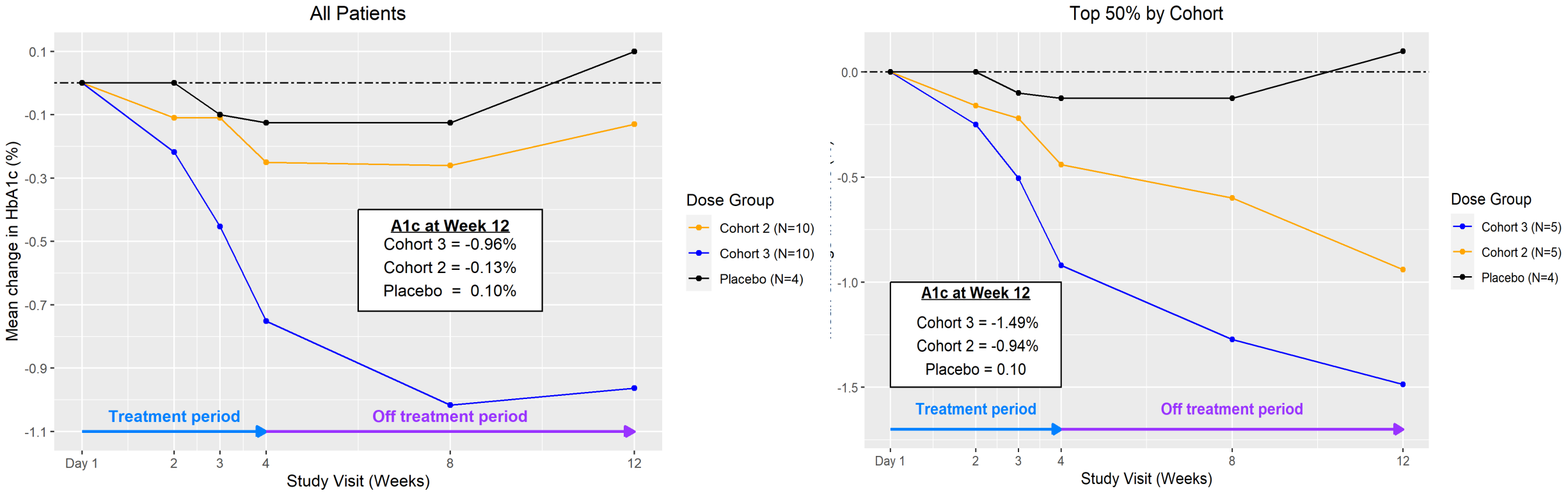


Figure 2 The top 50% of responders after 4-weeks of treatment in Cohorts 2 and 3 demonstrated durable and ongoing reduction in HbA1c while off treatment up to Week 12; a continued reduction in HbA1c was observed in Cohort 2 (additional 114%) and in Cohort 3 (additional 62%).

Figure 3: Patients achieving an HbA1c reduction to ≤ 7% during 4-week treatment and 8-week follow-up

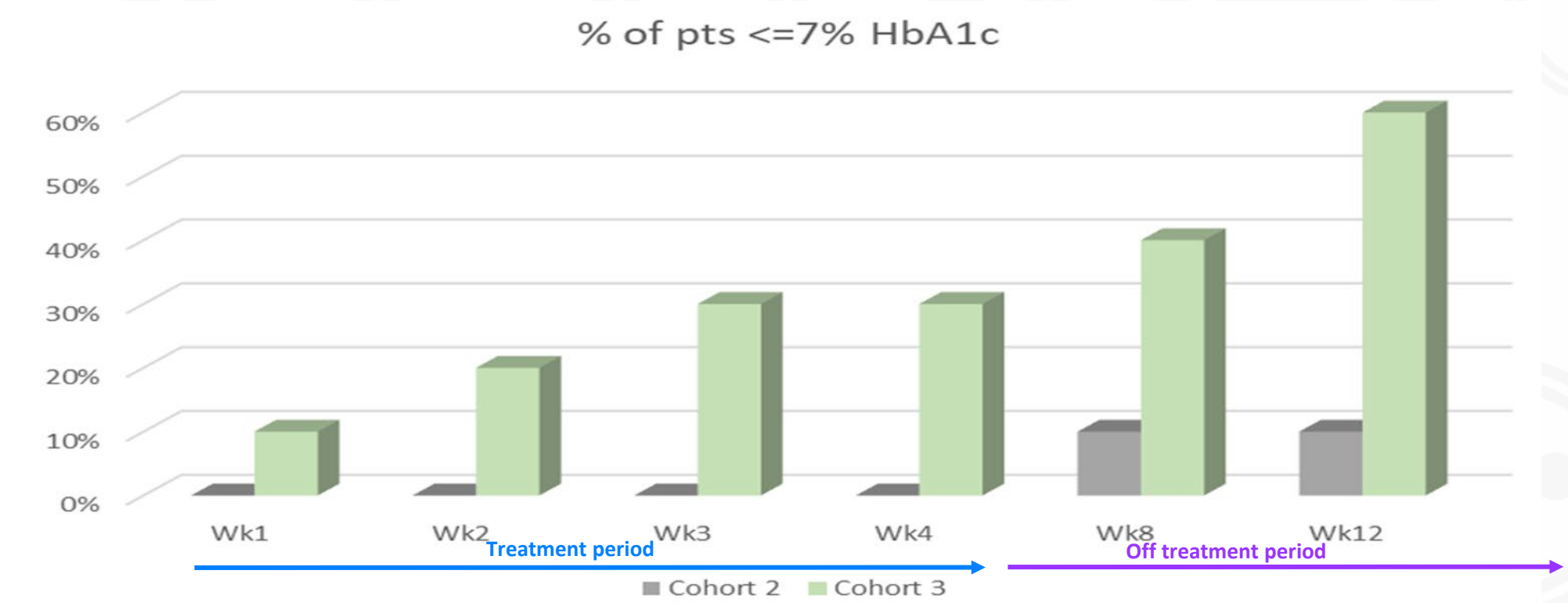


Figure 3. After 4-weeks of BMF-219 once daily dosing both cohorts demonstrated an increasing proportion of patients achieving a target HbA1c ≤ 7% and maintained through Week 12.

Figure 4: Mean AUC of C-peptide and HOMA-B during OGTT

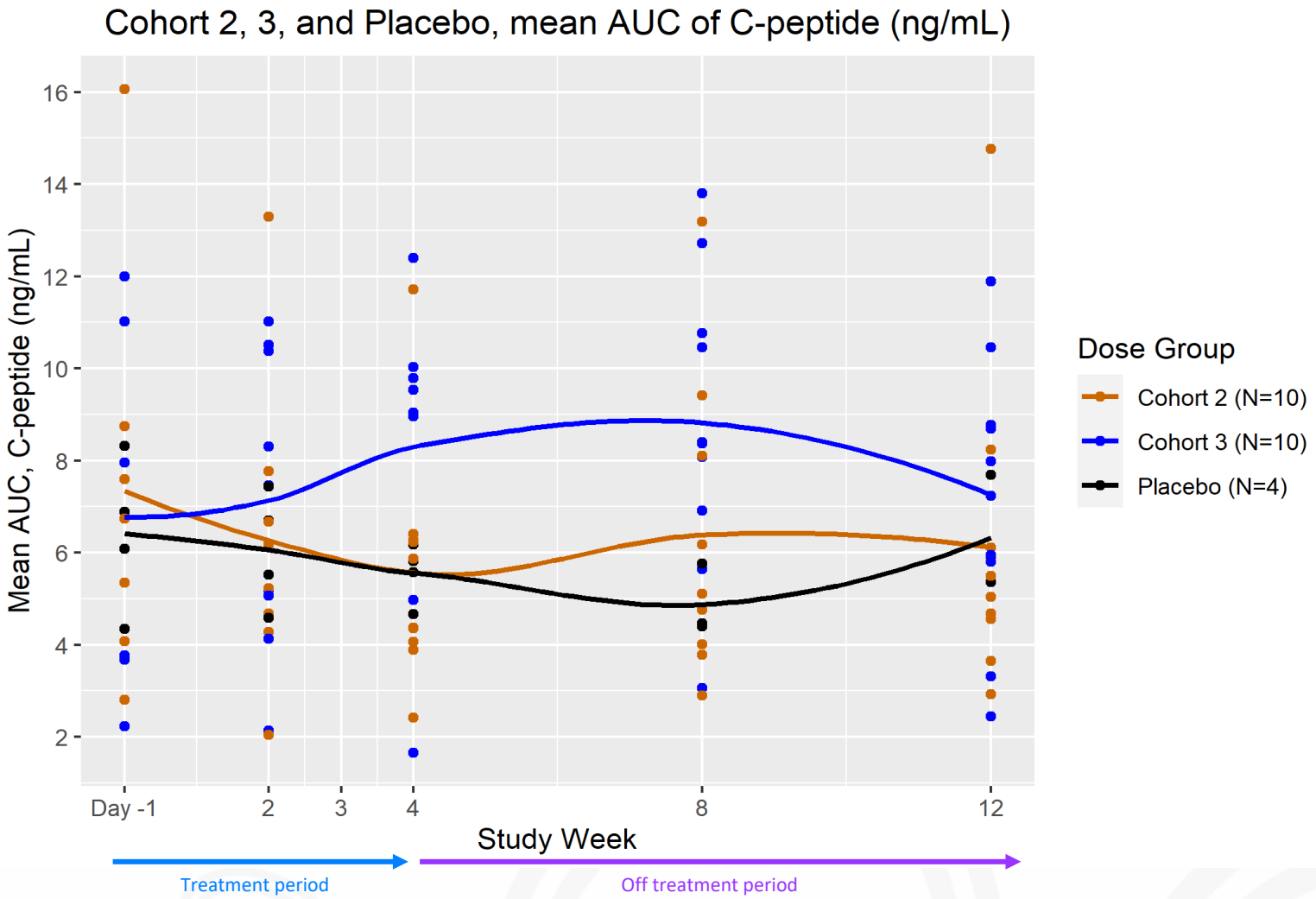


Figure 4.
Top panel (Left) The mean AUC of C-peptide increased during OGTT for Cohort 3 compared to placebo.

Figure 4: Mean AUC of C-peptide and HOMA-B during OGTT

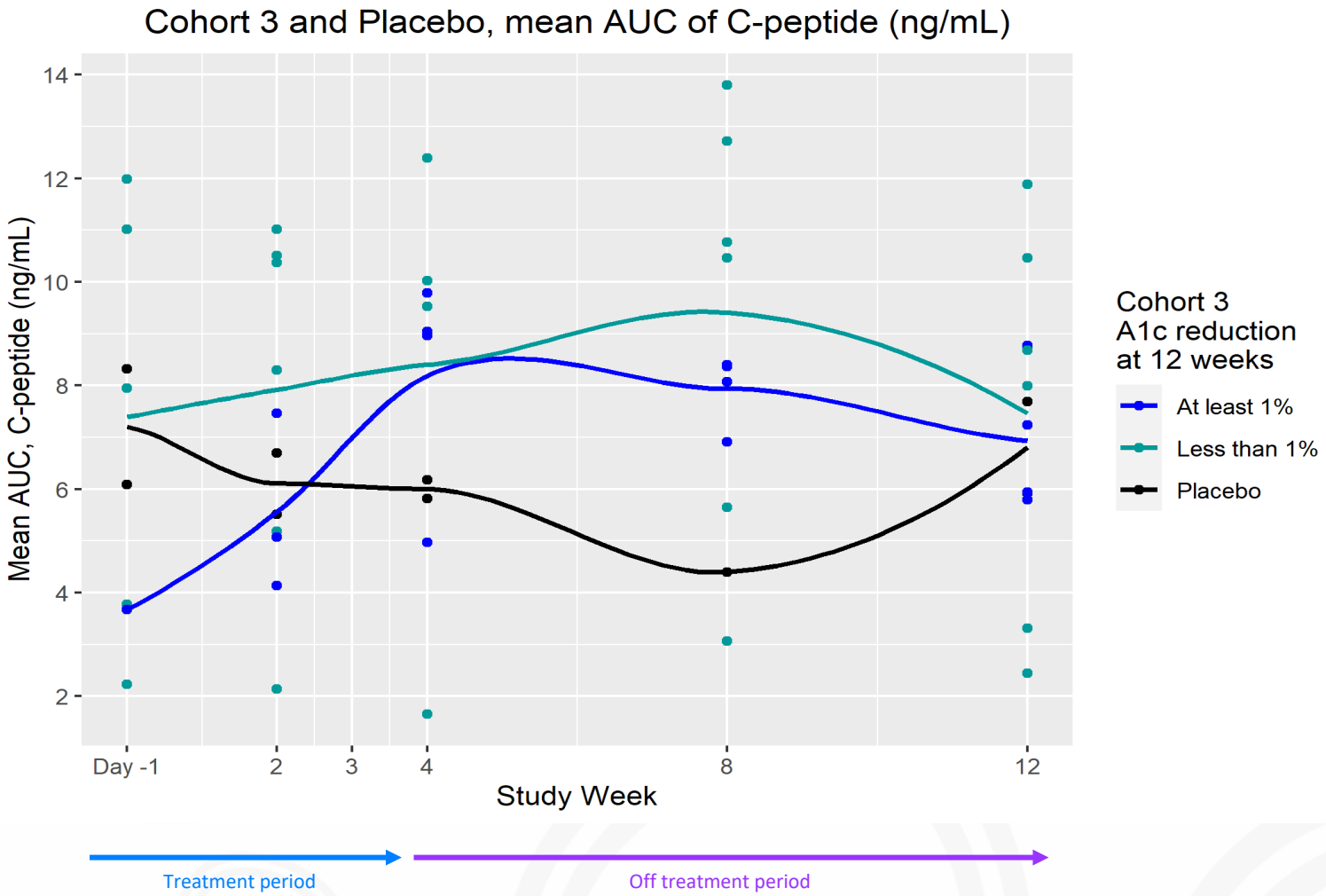


Figure 4.
Top panel (Right) Cohort 3 patients with ≥1% reduction in HbA1c showed a greater increase in C-peptide production

Figure 4: Mean AUC of C-peptide and HOMA-B during OGTT

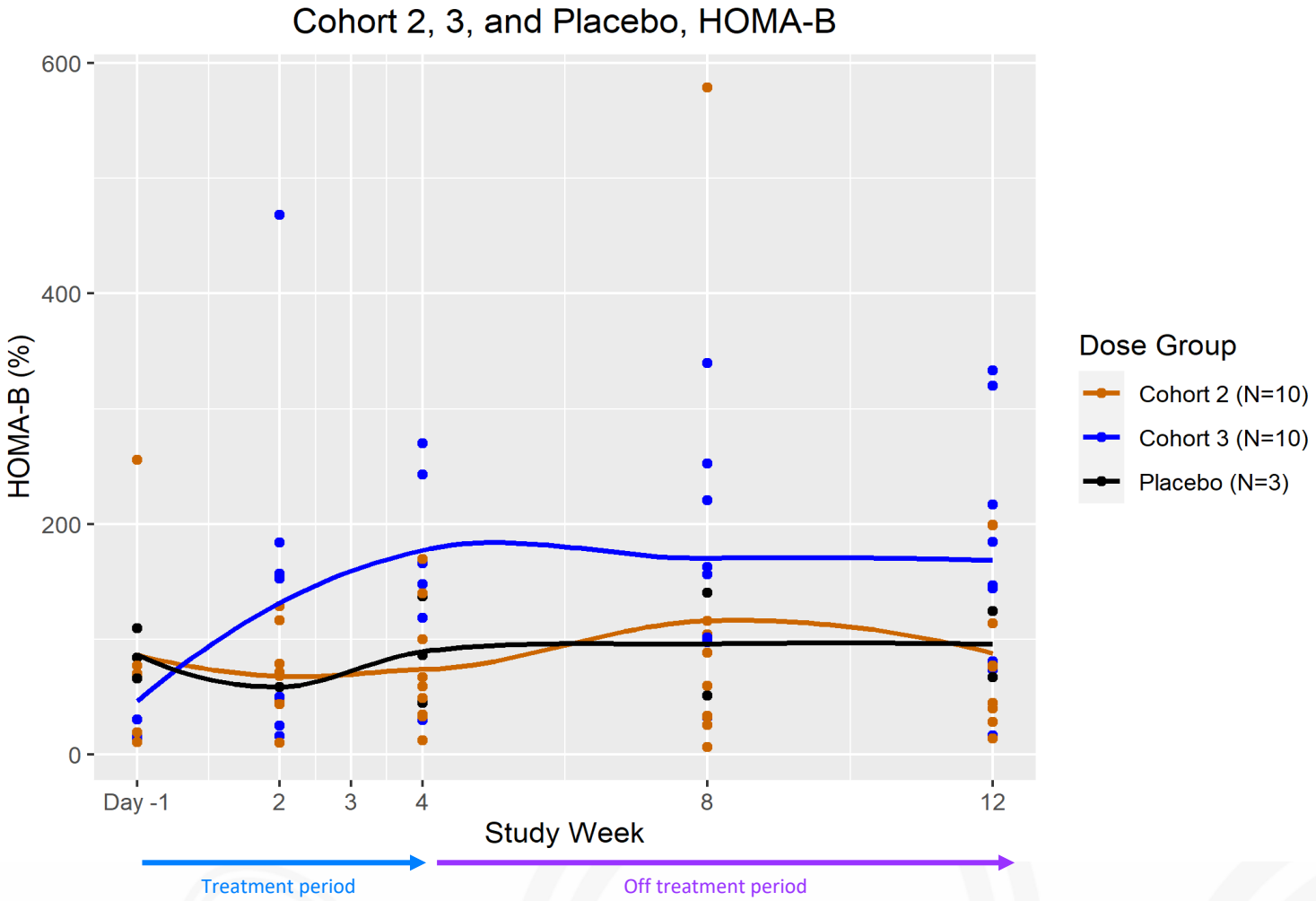


Figure 4.
Lower panel An increase in HOMA B was observed in Cohort 3

Figure 5: Change in HbA1c ordered by Baseline HbA1c, BMI, and Time since Diagnosis (Weeks 4 and 12)

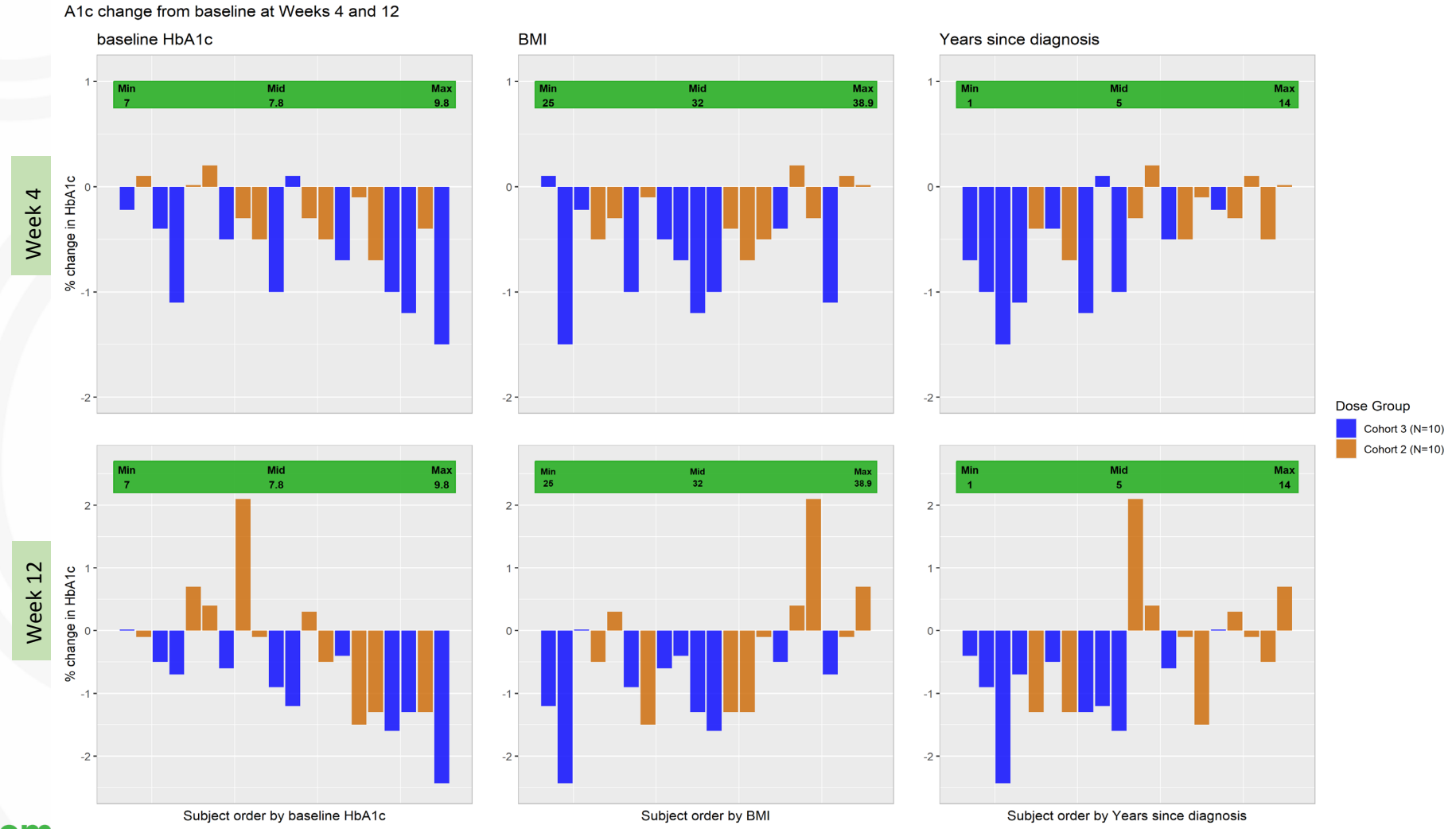
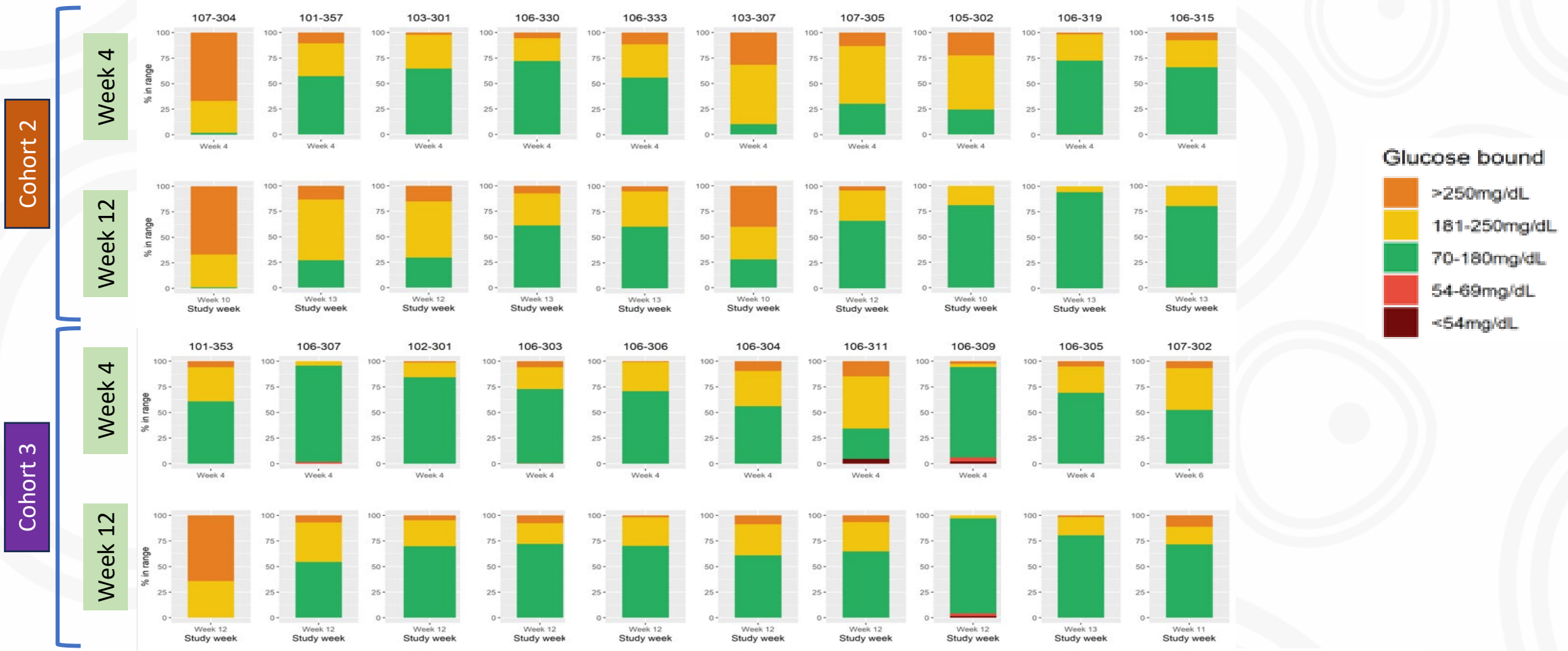


Figure 5.
Left panels. Patients with higher baseline HbA1c tended to have a greater reduction.
Middle panels. Patients in Cohort 3 tended to have lower BMI and a greater reduction in HbA1c.
Right panels. Patients in Cohort 3 tended to have more recently diagnosed T2D (≤5 yrs) and had a greater reduction in HbA1c.

Figure 6: CGM Time In Range (TIR) at Weeks 4 and 12 (Cohorts 2 and 3) (normal glucose range 70 to 180 mg/dL)



Upper Panel (Cohort 2) 6 of 10 (60%) patients maintained or improved TIR while off treatment.
Lower Panel (Cohort 3) 7 of 10 (70%) patients maintained or improved TIR while off treatment.

Figure 7: Change in lipid levels at Weeks 4 and 12

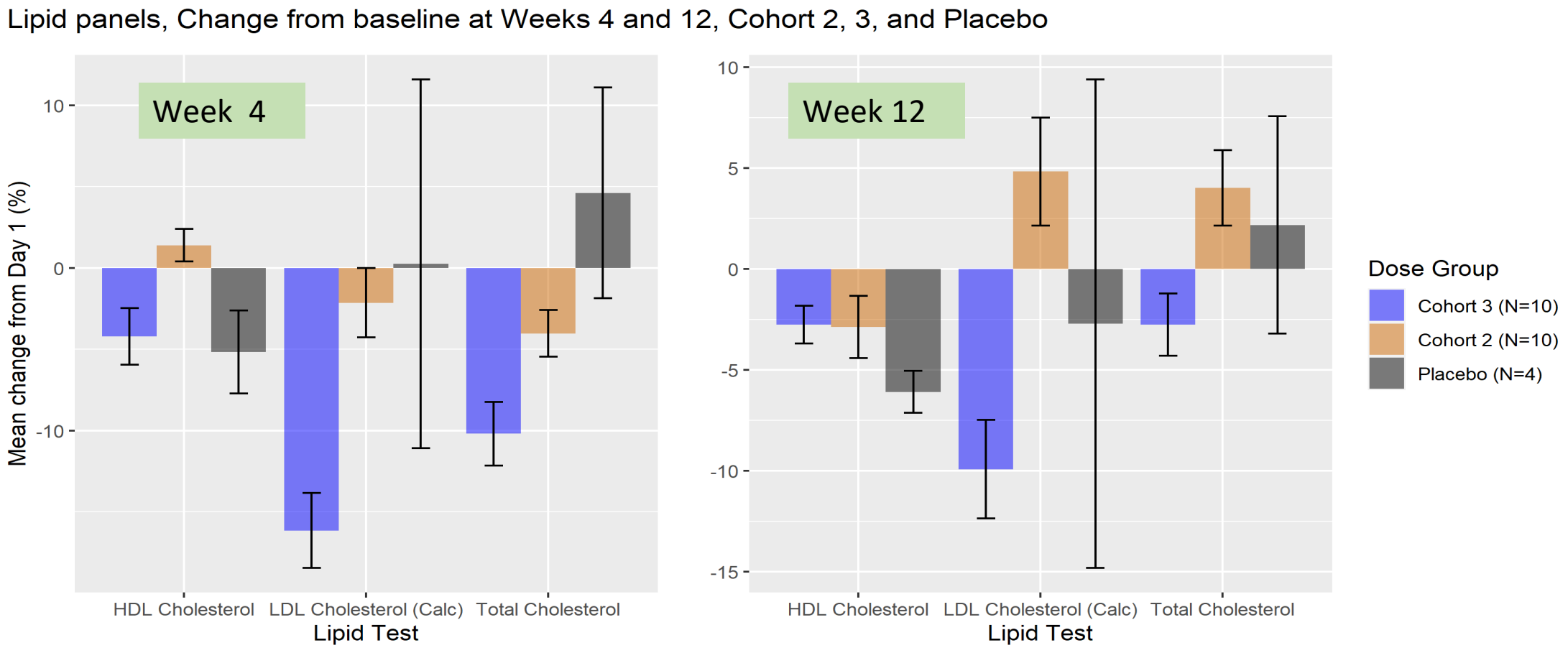


Figure 7. A positive trend was observed in both LDL and total cholesterol levels in Cohort 3.

Summary of Data

Efficacy Data: At Week 12 (8 weeks after completion of 28 days of treatment), BMF-219 demonstrated:

- The majority of patients continued to show a reduction in HbA1c, despite cessation of therapy. During the off-treatment period, both cohorts demonstrated a continued improvement in the proportion of patients [Cohort 2 (10%) and Cohort 3 (60%)] with a target HbA1c ≤7% through week 12.
- Top 50% of patients after 28-day dosing, achieved an HbA1c reduction of 1.49% in Cohort 3 (100 mg fasted) and 0.94% in Cohort 2 (100 mg fed) from baseline
- BMF-219 elicited increases in C-peptide and HOMA-B during the treatment and off-treatment period
- While off treatment, the majority of patients experienced a durable overall improvement in Time In Range in CGM (6/10 in Cohort 2 and 7/10 in Cohort 3)
- No meaningful change in weight relative to baseline
- Favorable trend in LDL and total cholesterol in Cohort 3

Safety Data:

- BMF-219 demonstrated a generally well-tolerated safety profile with no severe or serious AEs
- No symptomatic hypoglycemia
- No dose discontinuation or modification
- No meaningful change in hemoglobin levels

Next Steps:

- Complete dose escalation, identify optimal dose levels, and initiate dose expansion
- Explore longer duration of treatment (for up to 12 weeks)

BMF-219: A Novel Therapeutic Agent to Reestablish Functional Beta Cells and Provide Long-Term Glycemic Control

Dec 8, 2023 WCIRDC Oral Presentation

Background

- **Menin is a scaffold protein** with multiple functions, including the **regulation of gene transcription and cellular signaling**
- Through interacting with its binding partners, menin acts as an important regulator of glycemic control, whereby **inhibition of menin activity enhances beta cell proliferation and function**
- **BMF-219 is an oral covalent menin inhibitor** in clinical development for the management of T2D and T1D
- In **preclinical models of diabetes**, BMF-219 showed durable glycemic control following short-term treatment in ZDF and STZ rat models[1,2]
- In a **multiple ascending dose (MAD) cohorts in patients with T2D**, 4 weeks of BMF-219 100 mg once daily improved glycemic control at Week 12 (8 weeks after the final dose) and was generally safe and well tolerated[3]

1. Butler T. et al. *Diabetes.* 2022; 71 (Supplement_1): 851–P.
2. Somanath P. et al. *Diabetes.* 2022; 71 (Supplement_1): 113–LB.
3. Rodriguez J. et al. *Diabetes.* 2023; 72(Supplement_1): 91-LB

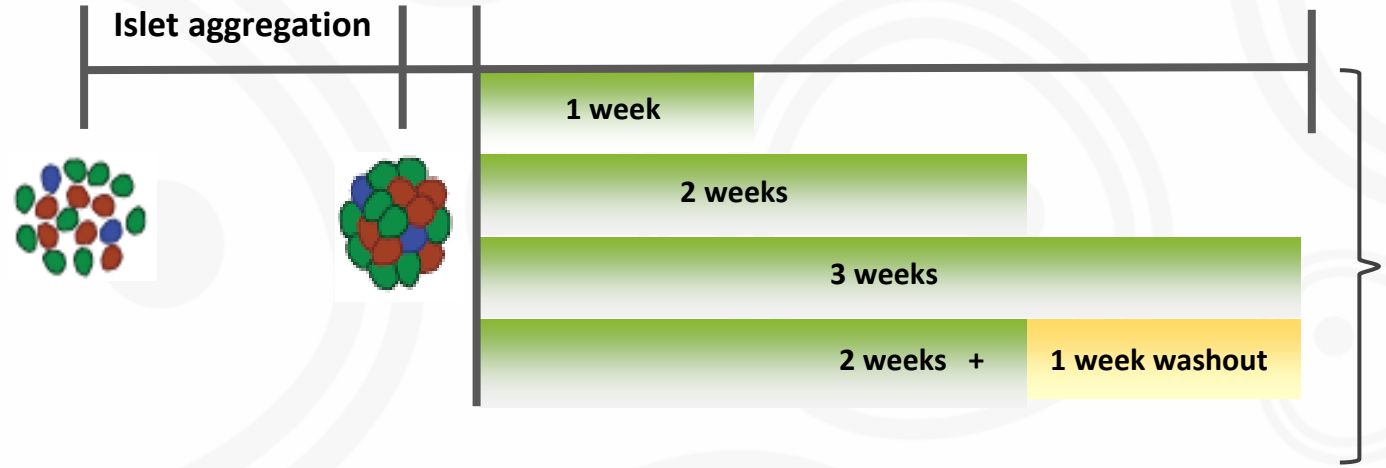
Aims

- To assess the effects of BMF-219 in human donor islet microtissues
- To assess the safety and efficacy of BMF-219 100 mg once daily for 4 weeks at Week 26 (22 weeks after final dose)

Ex-vivo human islet microtissues: Study design

Cadaver-derived human islets (without diabetes)

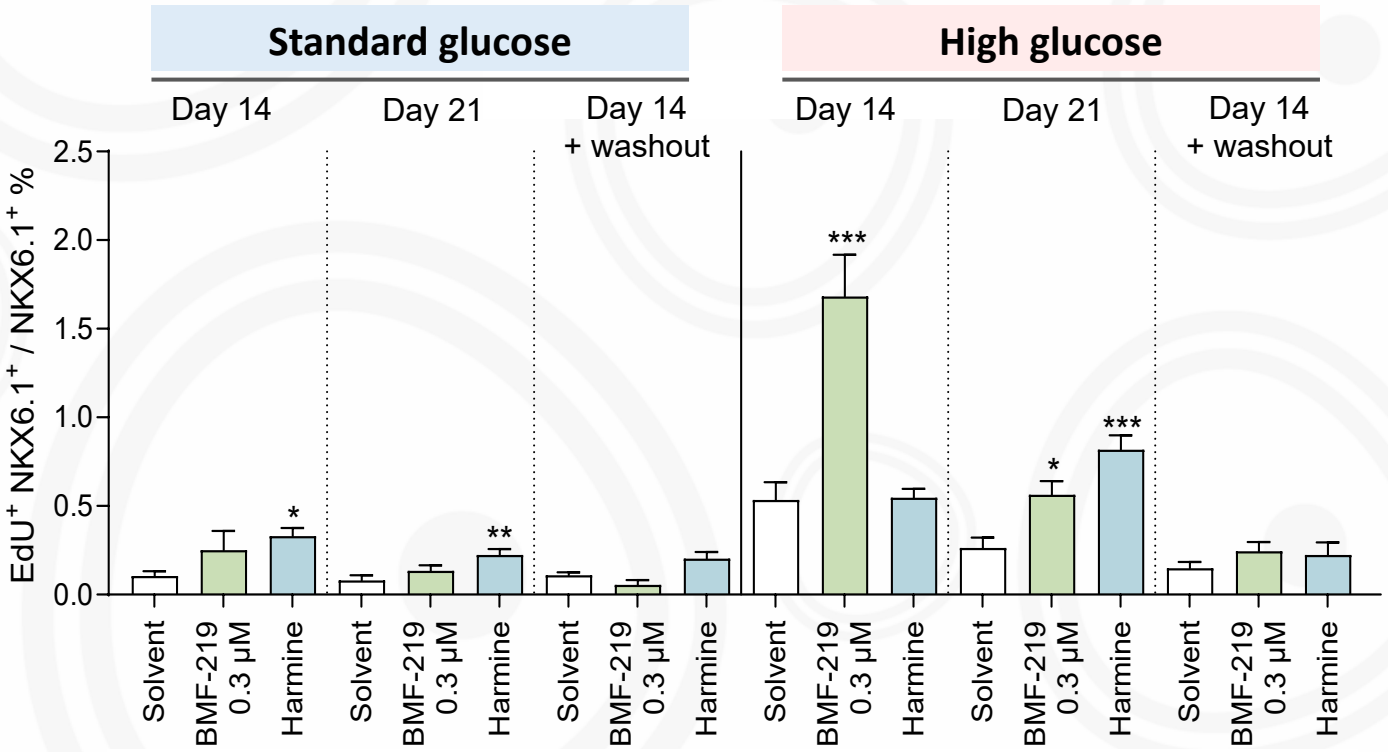
- BMF-219, harmine, or vehicle control for 1-3 weeks (+/- washout)
- Assayed under standard (5.5 mM) and high (8.0 mM) glucose



- Beta cell proliferation
- Beta cell insulin content

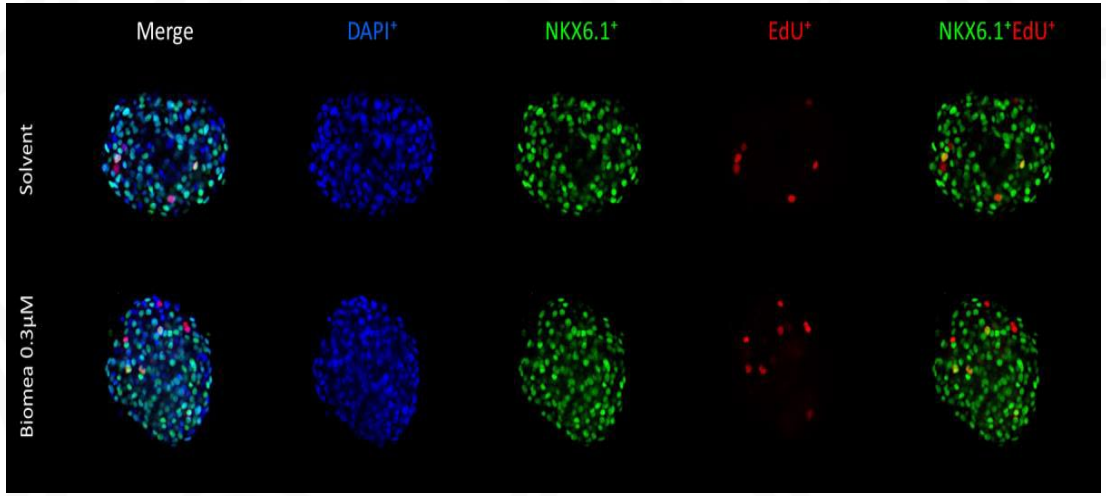
Human islet microtissues: Beta cell proliferation (Donor 1)

Proliferating beta cells as a fraction of total beta cells



Data represent mean ±SEM of 1 donor with n = 6-10 technical replicates.
One-way ANOVA with Dunnett's post hoc test rel. to DMSO control. *p < 0.05, **p < 0.01, ***p < 0.001

Day 14, high glucose

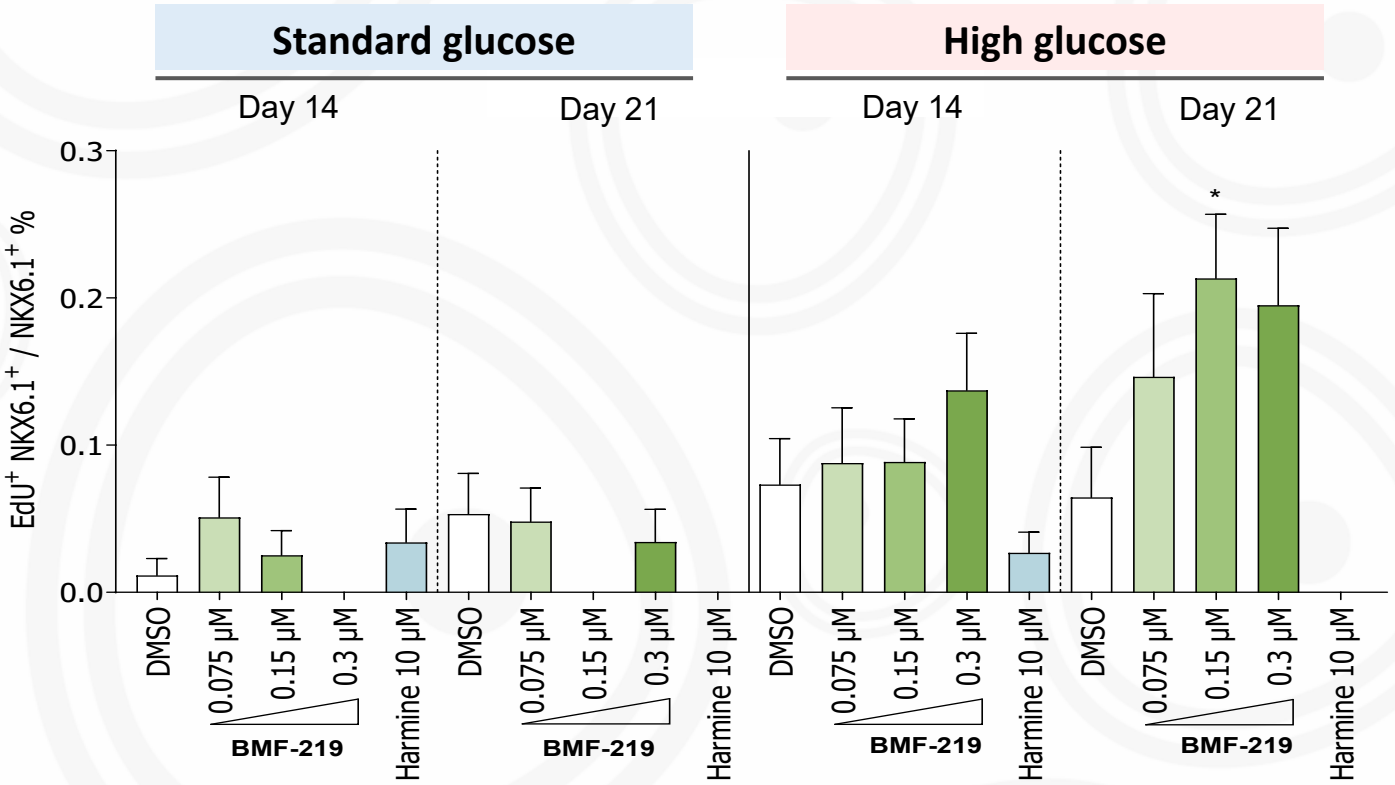


Donor 1	Age	BMI	HbA_{1c}
	19	23.2	5.8

Proliferation observed only under elevated glucose conditions and with continuous drug exposure

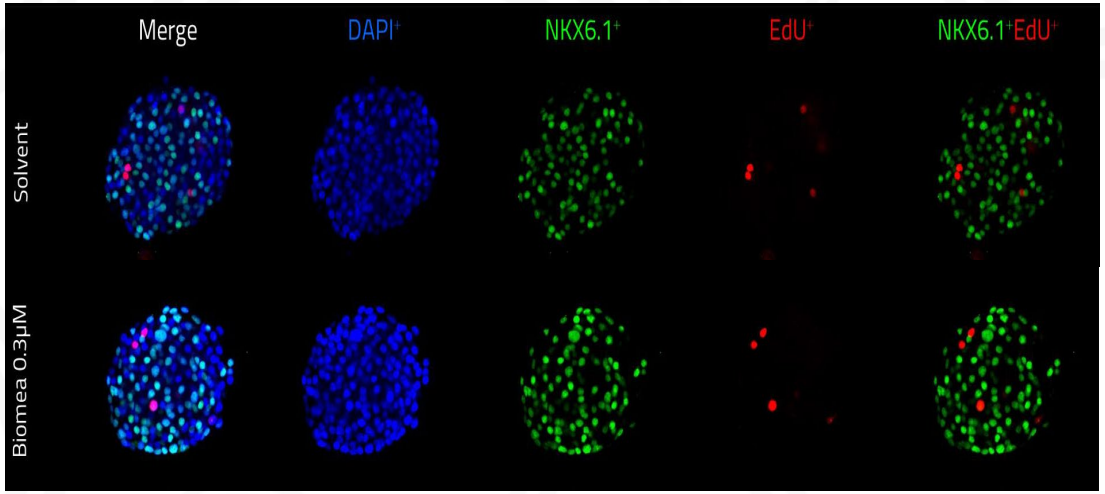
Human islet microtissues: Beta cell proliferation (Donor 2)

Proliferating beta cells as a 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

Day 14, High glucose



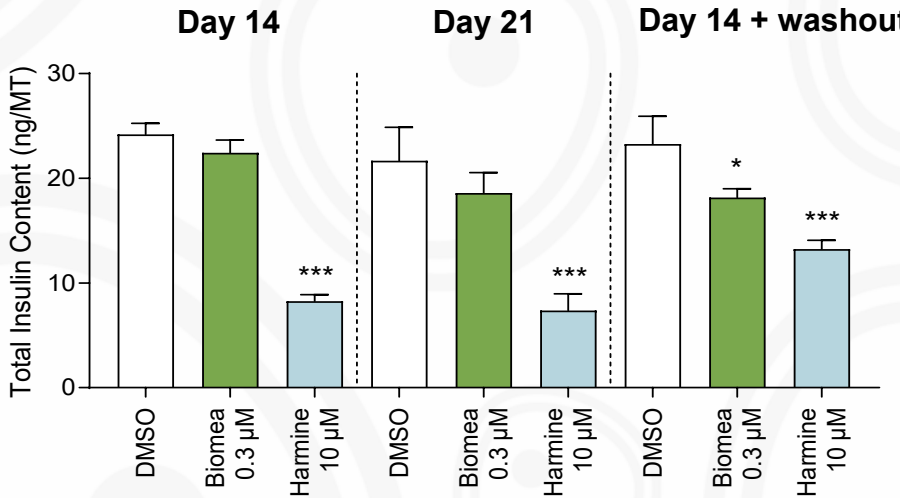
Donor 2	Age	BMI	HbA_{1c}
	32	25.0	5.2

Proliferation observed only under elevated glucose conditions and with continuous drug exposure

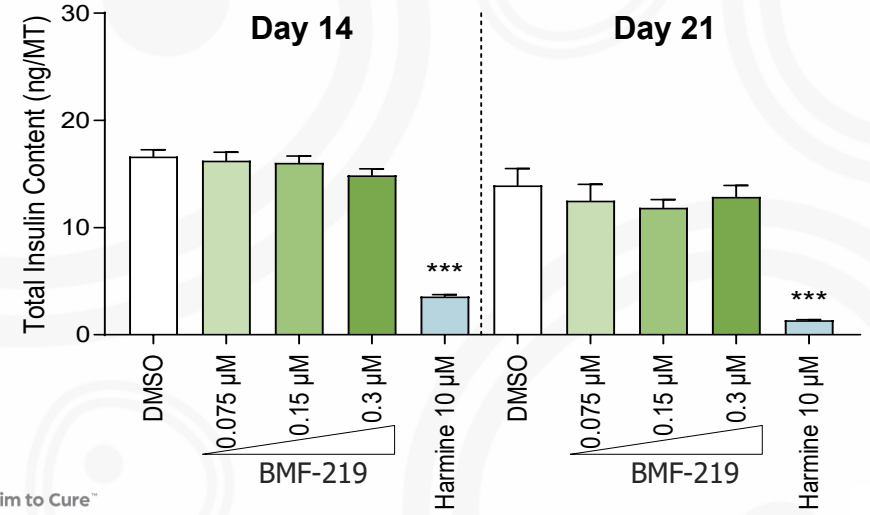
Human islet microtissues: Beta cell insulin content

Standard glucose

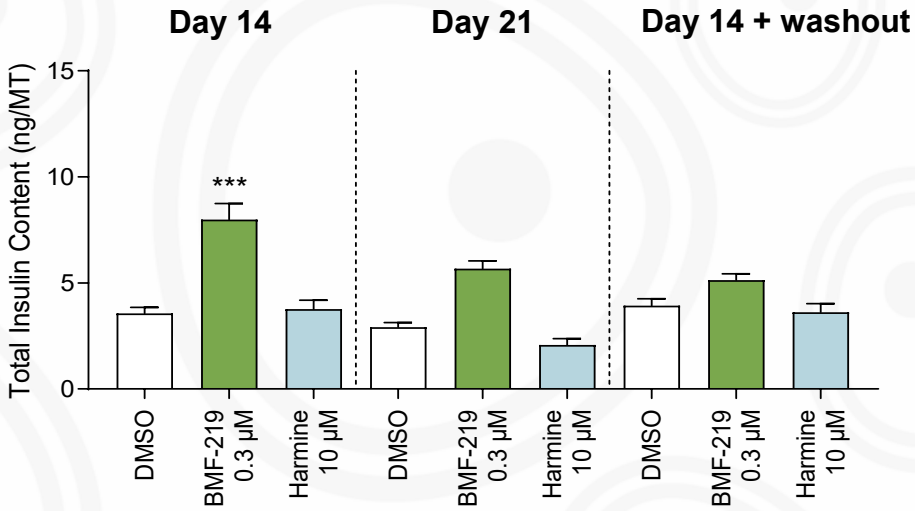
Donor 1

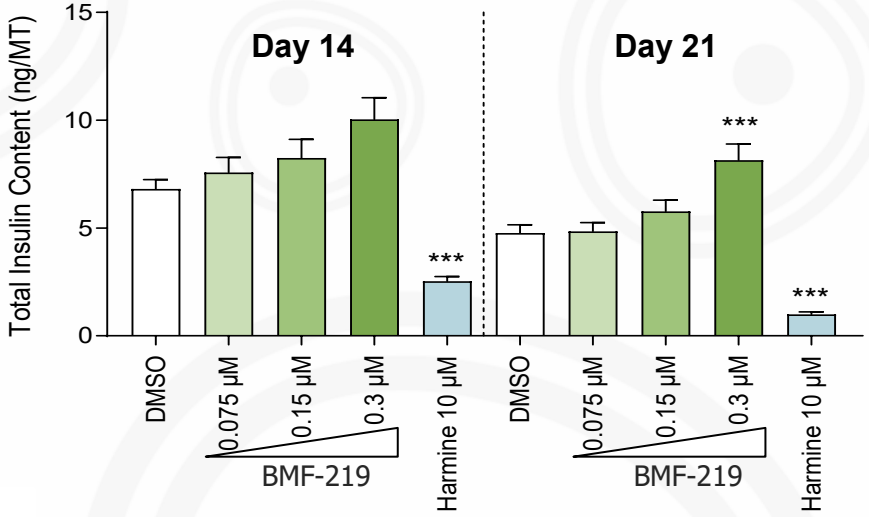


Donor 2



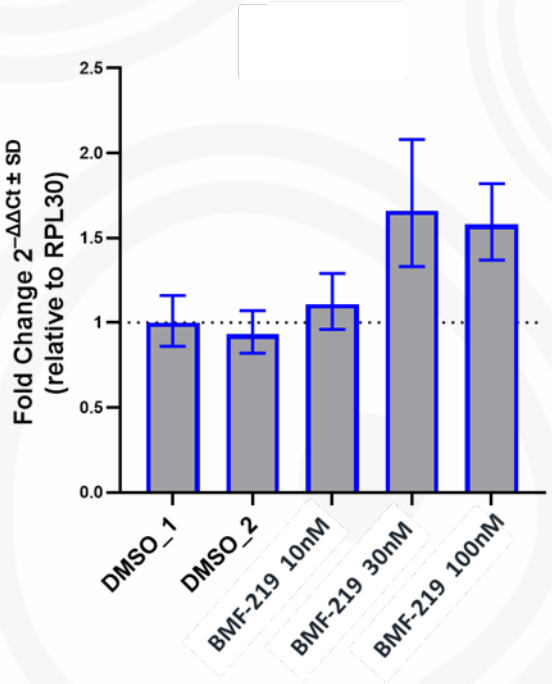
High glucose



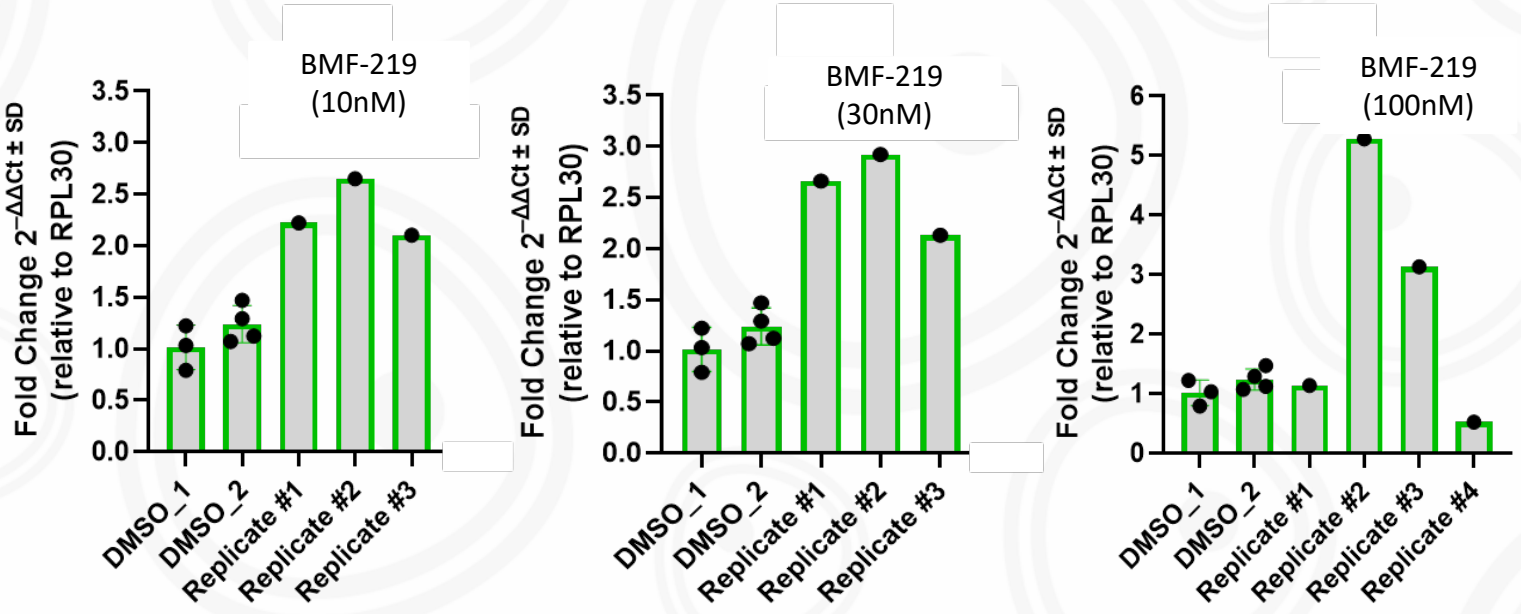


Human islets: CCNA2 and PbK gene expression

CCNA2 gene expression



PbK gene expression



- BMF-219 resulted in **increased CCNA2 and PbK expression**, similar to literature results from menin knockdown experiments
- **CCNA2 and PbK expression** have been shown to **support proliferation of beta cells**, resulting in an increase in beta cell mass

Covalent-111 Study

Key eligibility criteria and study design

Eligibility Criteria

- T2D, age 18-65 yr
- Duration of diabetes 15 yr or less
- HbA_{1c} 7.0-10.0%, inclusive
- Treated with diet/exercise ± up to 3 antihyperglycemic agents (insulin secretagogues and insulin excluded)

COVALENT-111 T2D MAD Cohorts

50 mg QD, without food
x 4 weeks

100 mg QD, without food
x 4 weeks

100 mg QD, with food
x 4 weeks

BMF-219 (n=10) and placebo (n=2) per cohort

200 mg QD, without food
x 4 weeks

200 mg QD, with food
x 4 weeks

100 mg BID, without food
x 4 weeks

200 mg QD x 2 weeks	**400 mg QD** x 2 weeks

without food

4 weeks dosing + 22 weeks follow-up

Study objectives of T2D multiple ascending dose cohorts

Primary Objective:

To assess the **safety and tolerability** of multiple ascending oral doses of BMF-219

Key Secondary Objectives:

- To determine the **pharmacokinetics** following multiple ascending doses of BMF-219
- To determine the impact of multiple ascending doses of BMF-219 on **glycemic parameters**
- To assess changes in **beta-cell function** after multiple ascending doses of BMF-219

Covalent-111 Study

Baseline characteristics and demographics

	BMF-219 100mg QD without food (n=10)	BMF-219 100mg QD with food (n=10)	Placebo (n=6)
Age (year, min-max)	52 (38-63)	51 (35-60)	46 (31-61)
Sex (n, M/F)	6/4	7/3	6/0
Duration of diabetes (year, min-max)	4.2 (0.5-9.0)	8.7 (4.0-14.0)	4.2 (1.0, 10.0)
HbA_{1c} (%-point, SD)	8.1 (0.9)	8.0 (0.6)	8.3 (0.7)
Diet and exercise alone (n, %)	0 (0%)	1 (10%)	0 (0%)
1 antihyperglycemic agent (n, %)	9 (90%)	7 (70%)	5 (83%)
2 antihyperglycemic agent (n, %)	0 (0%)	2 (20%)	1 (17%)
3 antihyperglycemic agent (n, %)	1 (10%)	0	0 (0%)

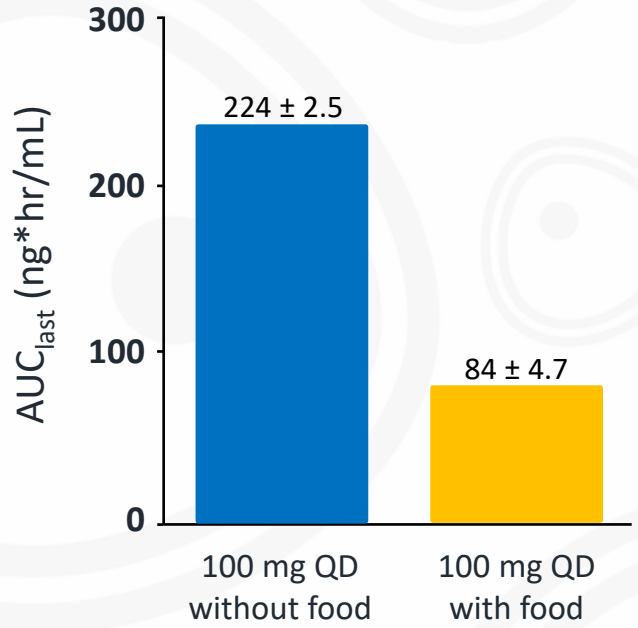
COVALENT-111 Study

Greater BMF-219 exposure at Week 4 resulted in greater reduction in HbA_{1c} at Week 26

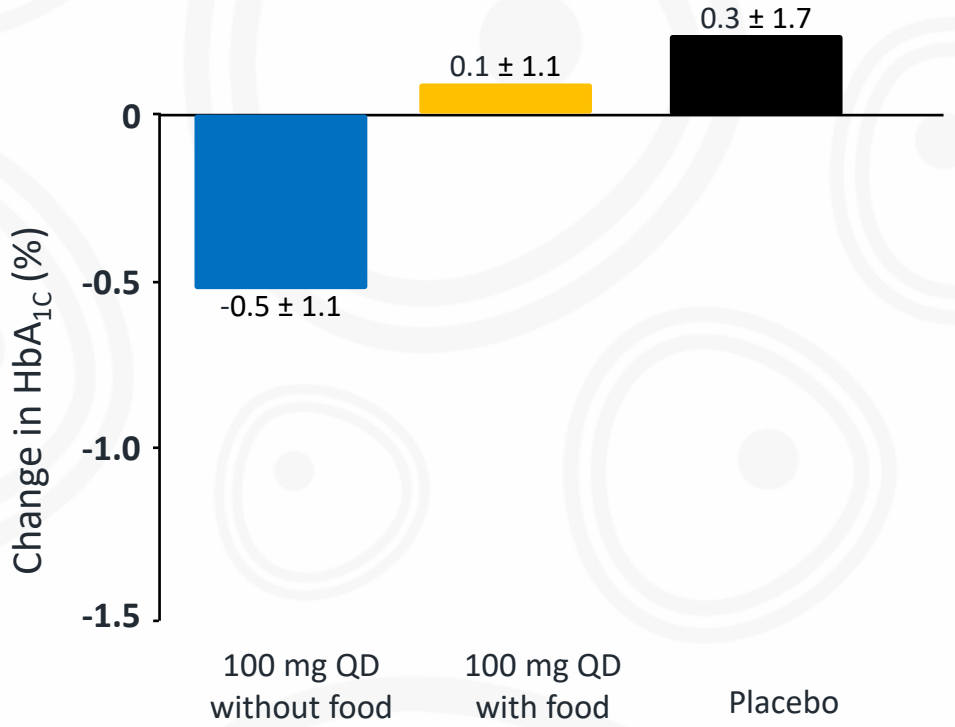
100 mg QD without food

100 mg QD with food

BMF-219 mean AUC_{last} at Week 4



Change in HbA_{1c} at Week 26



COVALENT-111 Study

Glycemic results summary at Week 26

	BMF-219 100mg QD without food (n=10)	BMF-219 100mg QD with food (n=10)	Placebo (n=6)
Mean change in HbA_{1c}	-0.5%	0.1%	0.3%
Placebo adjusted mean change in HbA_{1c}	-0.8%	-0.2%	-
Percent of participants with ≥1.0% reduction in HbA_{1c}	20%	20%	0%

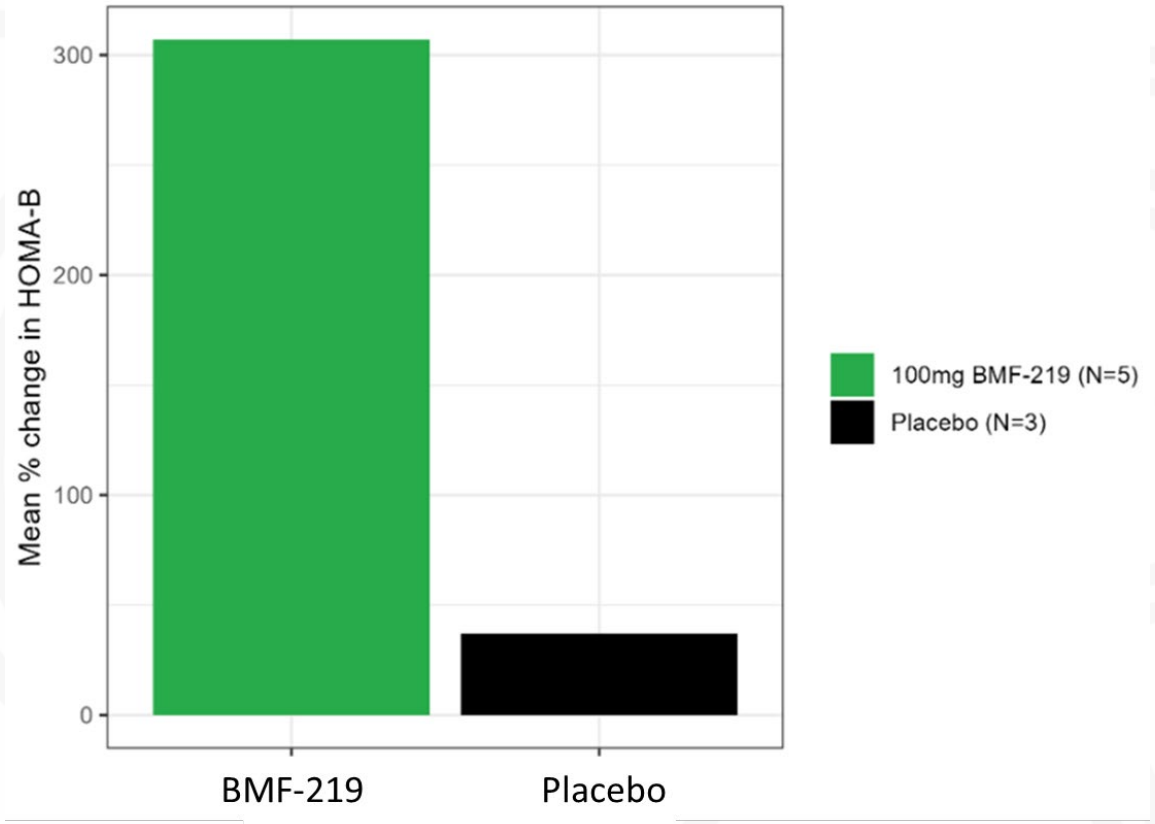
Percent of participants with any reduction in HbA_{1c}: 80% (BMF-219 100mg QD without food) and 40% (BMF-219 100mg QD with food)

COVALENT-111 Study

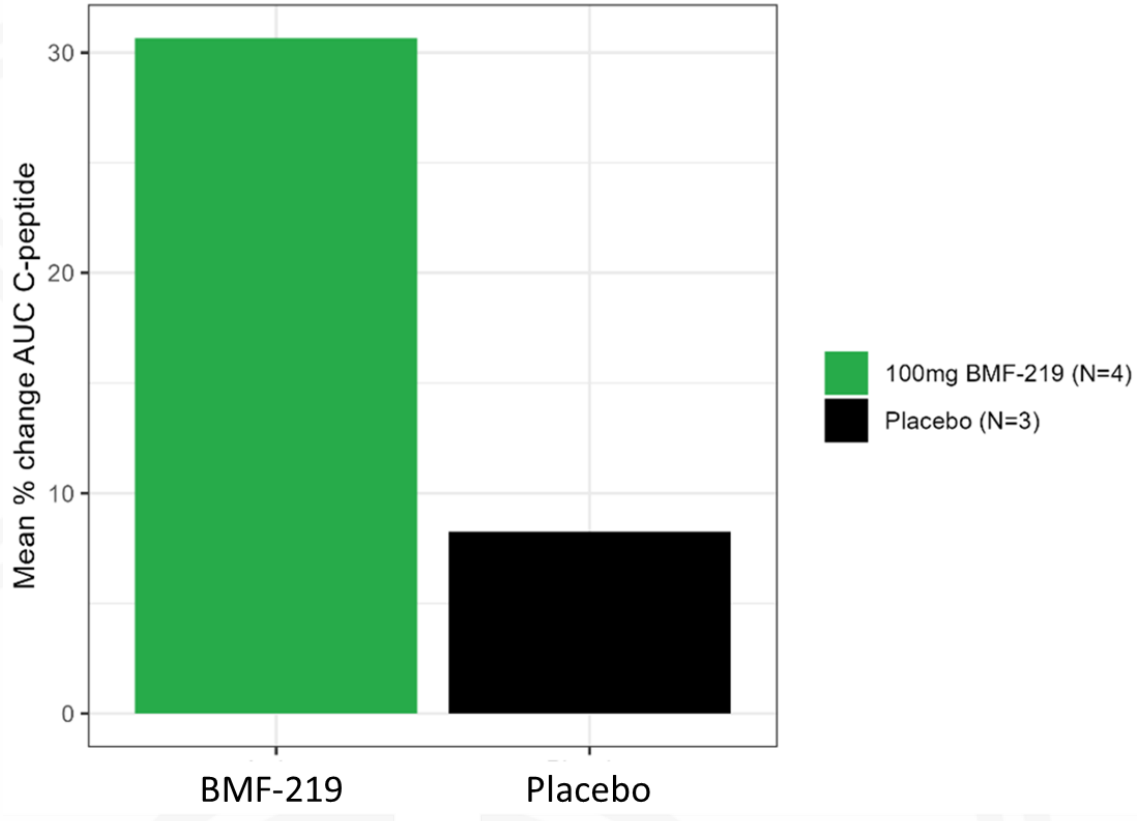
% increase in HOMA-B and C-peptide AUC in responders

Patients with HbA_{1c} reduction ≥0.5% at Week 26 and baseline HOMA-B <200

% change HOMA-B



% change C-peptide AUC



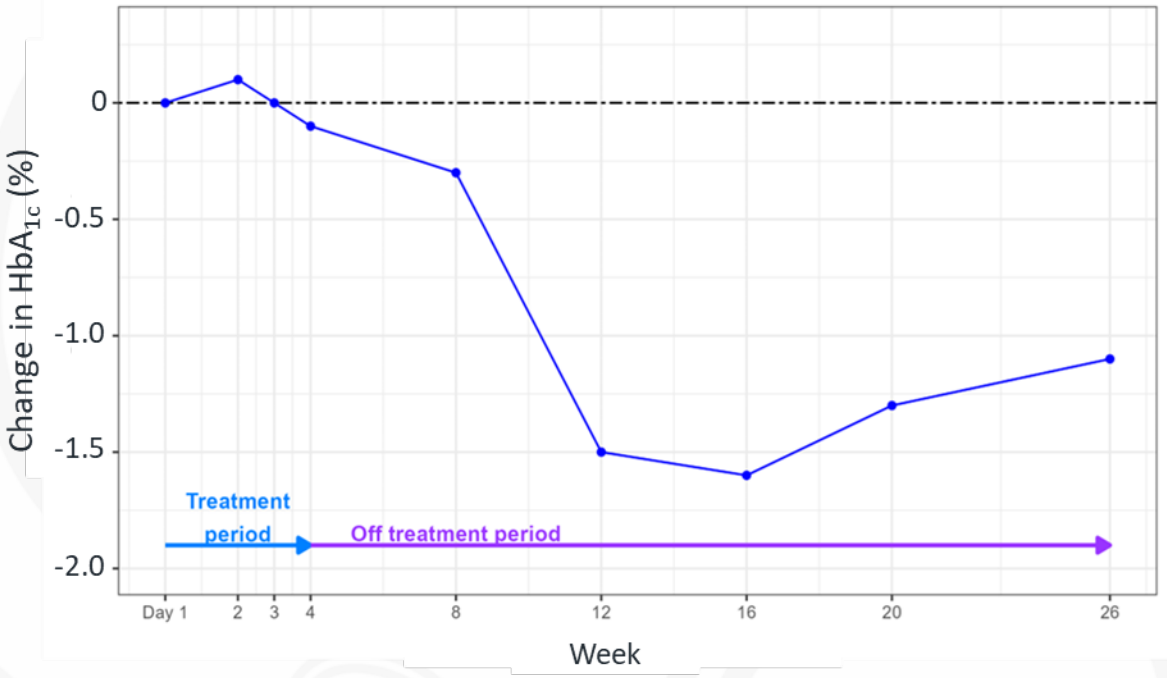
COVALENT-111 Study

Case Study 1: 45-year-old man with 9-year history of T2D

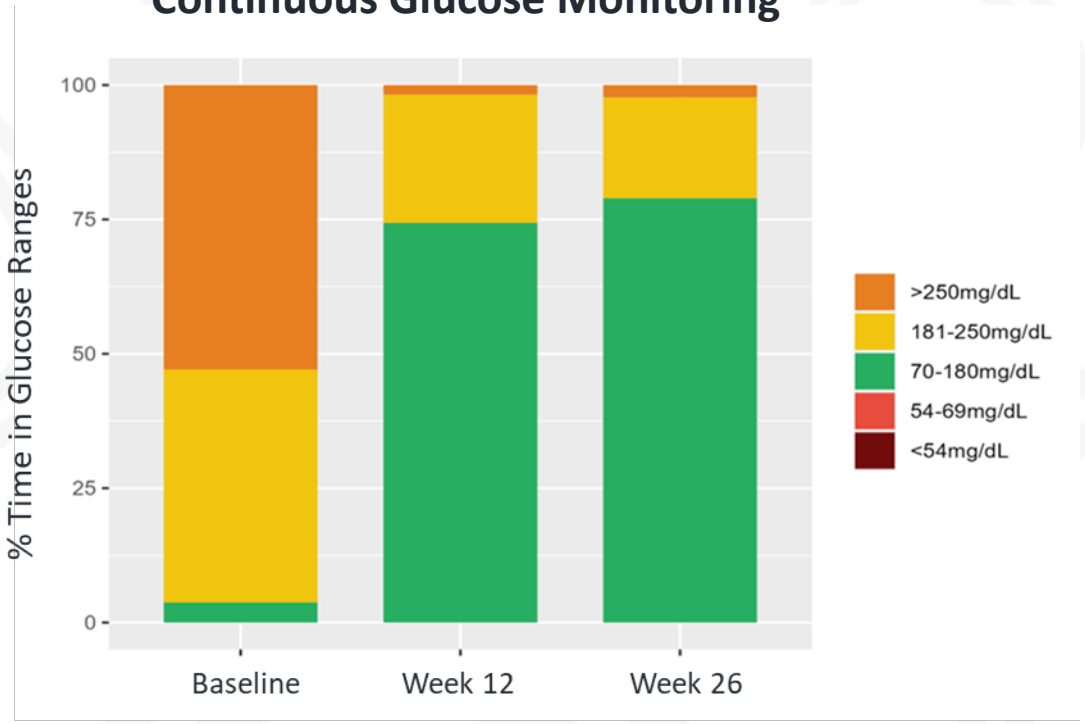
- 45-year-old man with 9-year history of T2D
- Metformin 500 mg BID
- HbA_{1c} 8.4%; FPG 216 mg/dL; BMI 29.6 kg/m^2

- BMF-219 100 mg once daily with food for 4 weeks
- CGM at Week 26 with >75% $TIR_{70\text{-}180\ mg/dL}$
- No tolerability issues or related adverse events

Change in HbA_{1c} (%)



Continuous Glucose Monitoring



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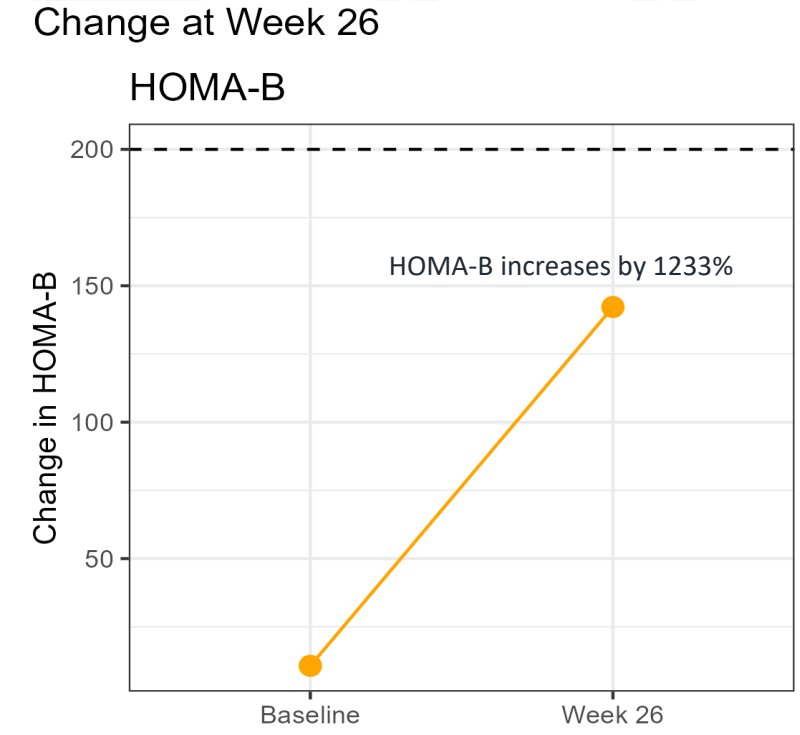
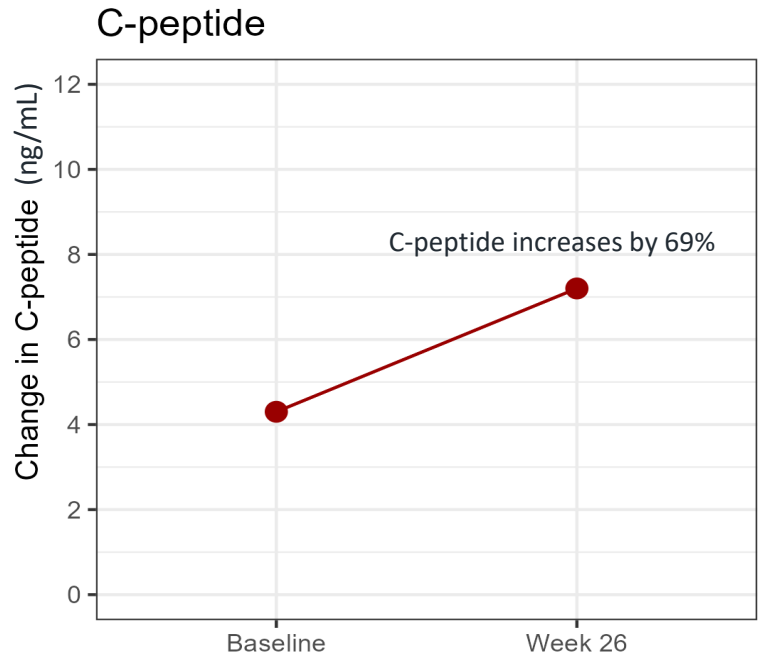




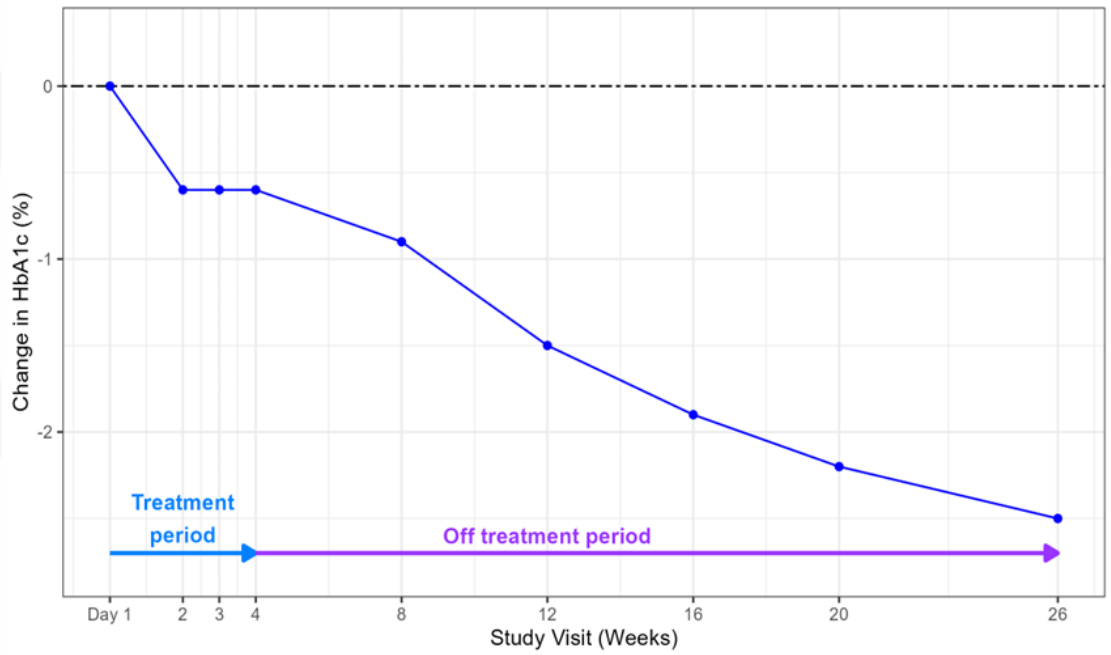
COVALENT-111 Study

Case Study 2: 29-year-old man with 4-year history of T2D

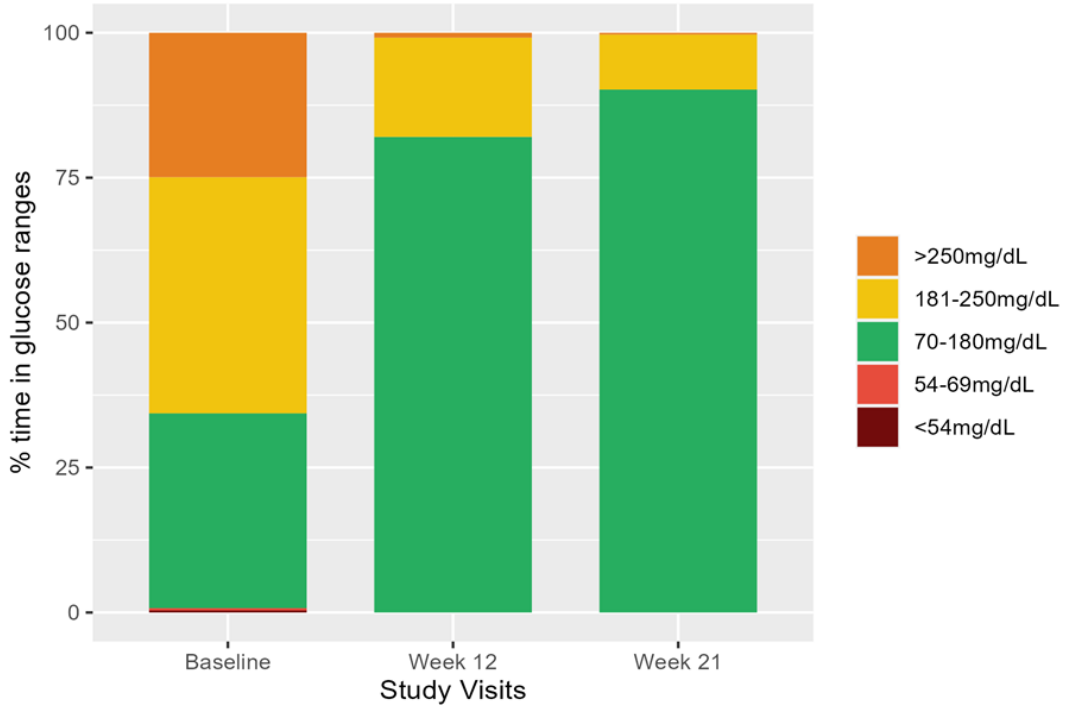
- 29-year-old man with 4-year history of T2D
- Metformin and empagliflozin
- HbA_{1c} 9.5%; FPG 146 mg/dL; BMI 25.6 kg/m^2

- BMF-219 200 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

Change in HbA_{1c} (%)



Continuous Glucose Monitoring



COVALENT-111 Study

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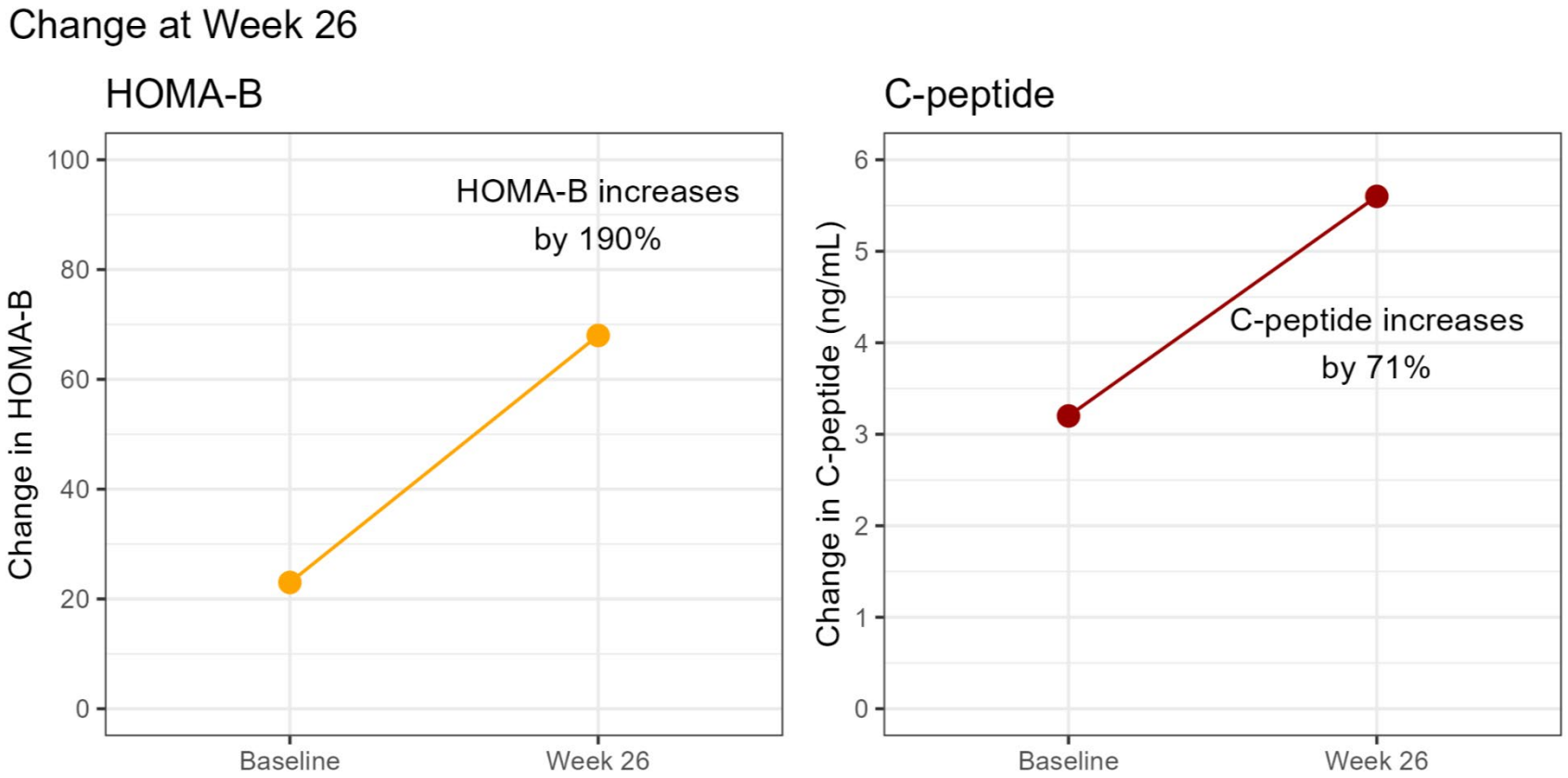


biomea FUSION We Aim to Cure™

COVALENT-111 Study

Safety and tolerability

- BMF-219 was generally well tolerated and safe
- There were no severe or serious adverse events reported
- No dose discontinuations or modifications
- No symptomatic or clinically significant hypoglycemia
- All patients completed 4 weeks of dosing and followed through Week 26

Summary and Conclusions

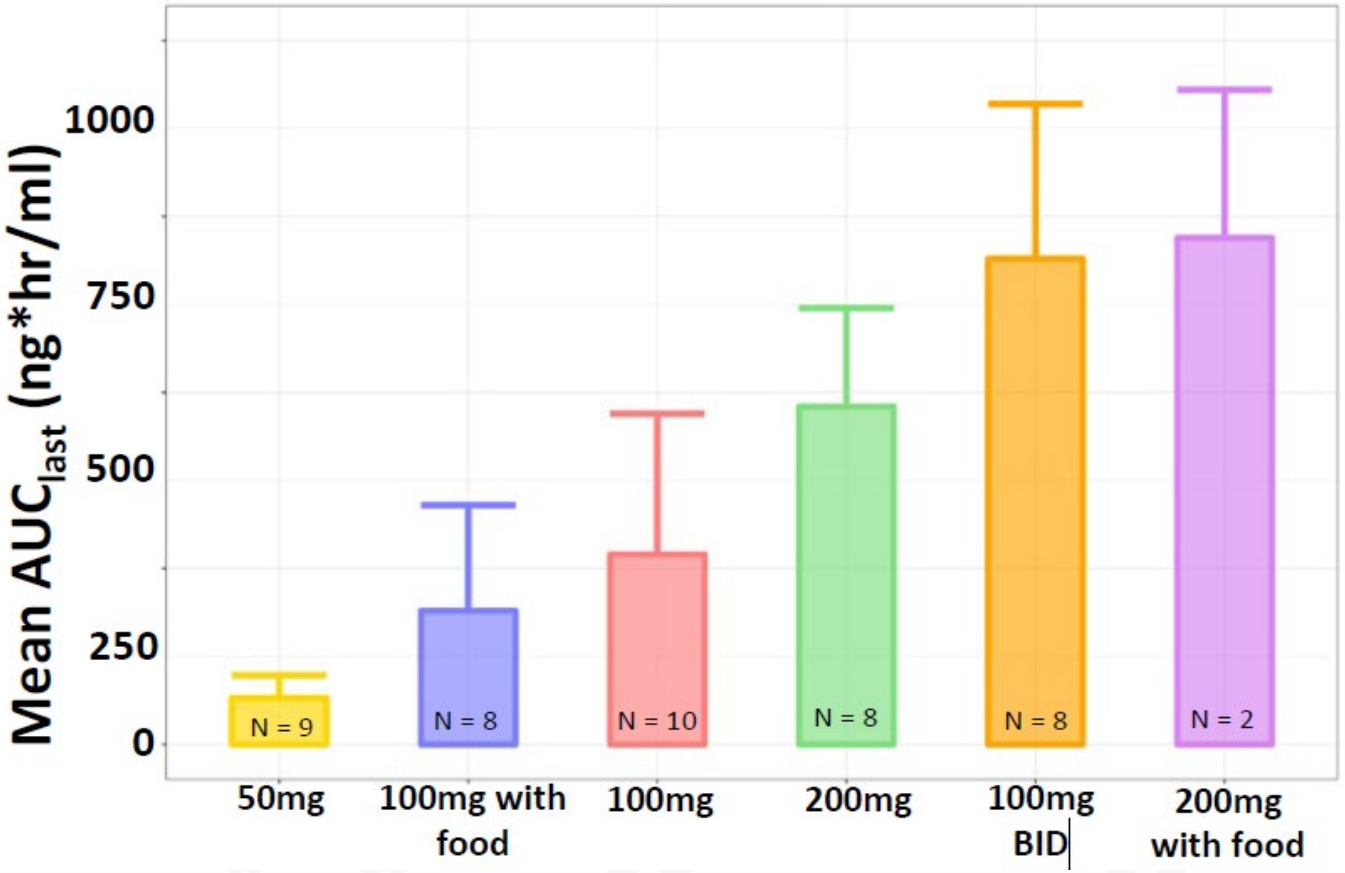
- In ex-vivo cultured human islet microtissues, BMF-219 enhanced beta cell proliferation and increased beta cell insulin content in a glucose-dependent manner
- In patients with T2D, 4 weeks of BMF-219 100 mg once-daily resulted in clinically meaningful improvements in glycemic control at Week 26 (22 weeks after the final dose)
- These combined results support BMF-219's key mechanism of action of beta cell proliferation and support the novel disease-modifying potential of short-term BMF-219 therapy
- At Week 26, BMF-219 200 mg once-daily for 4 weeks resulted in approximately 40% (4/11) of participants achieving ≥1.0% reduction in HbA_{1c} (nearly doubling the effect achieved at Week 26 with the 100 mg dose)
- Next steps: Higher BMF-219 doses and longer exposure (8-12 weeks) are being assessed in an ongoing Phase 2 trial in T2D and a study in T1D has been initiated

Key Observations from the Dose-Escalation Portion of COVALENT-111, a Phase 1/2 Trial of the Covalent Menin Inhibitor BMF-219 in Patients with Type 2 Diabetes

March 6-9, 2024 ATTD

Dose-Dependent PK Response Demonstrated

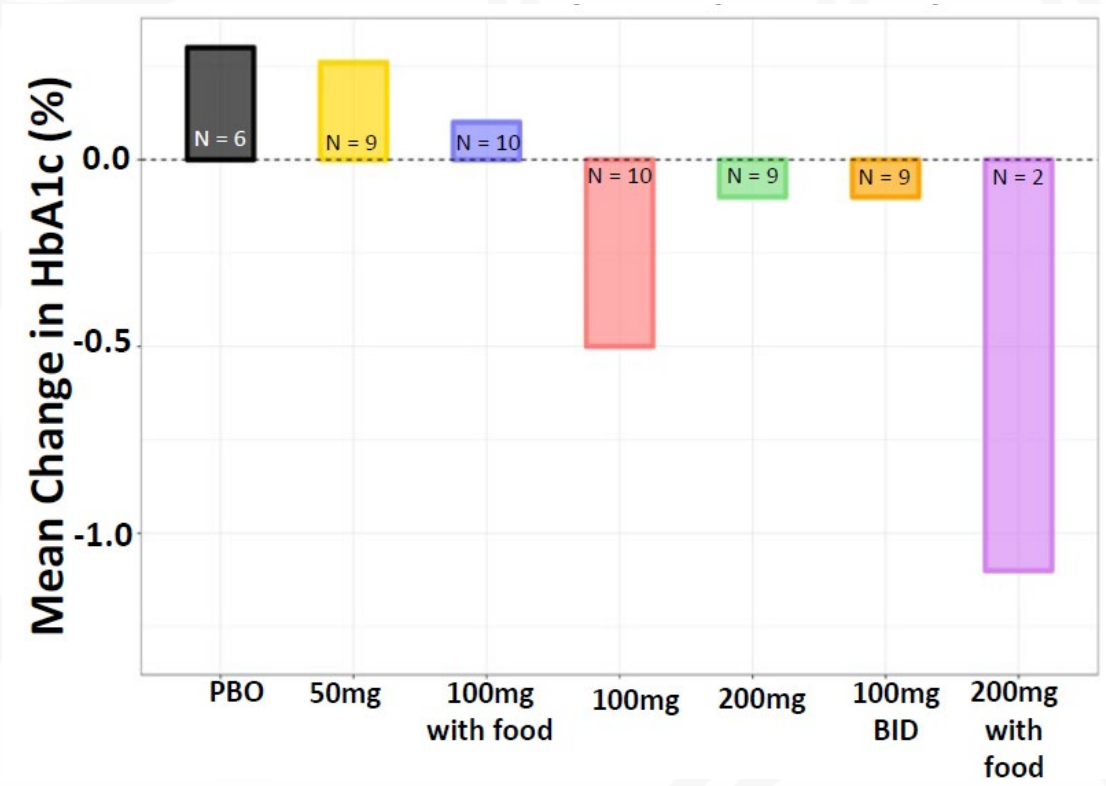
PK Response Across Cohorts (Week 4)



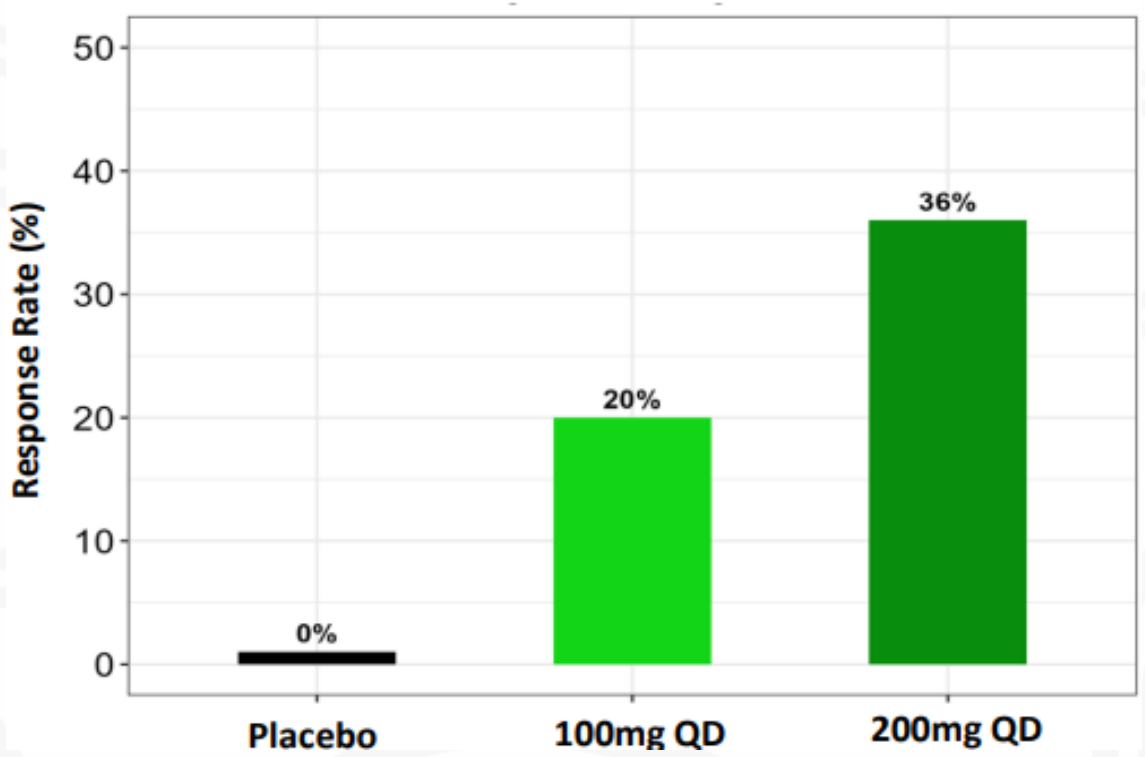
- Dose-dependent PK response is demonstrated across different dose cohorts
- Increase in AUC is shown in higher dose cohort (200mg QD)

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

Mean HbA1c Response (Week 26)



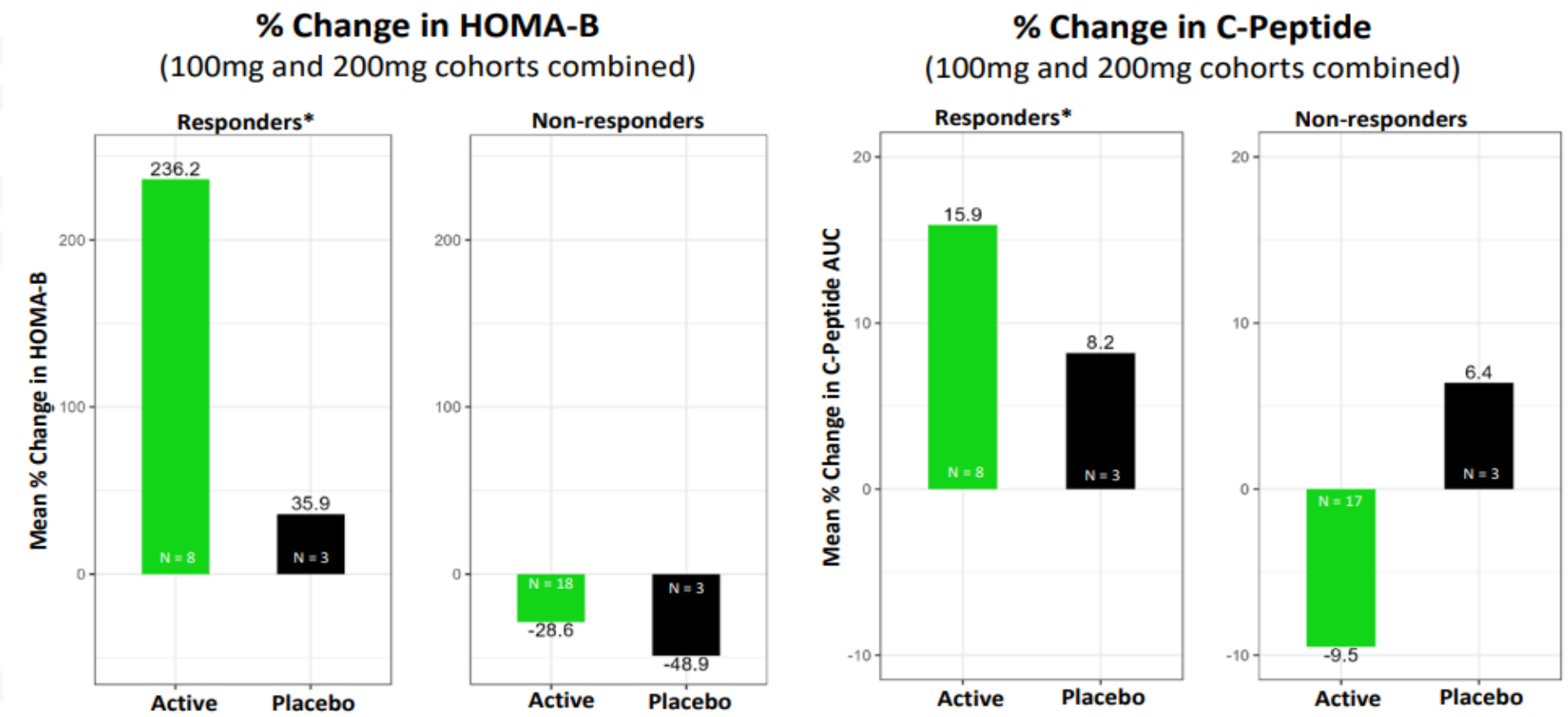
Proportion with ≥ 1% HbA1c Reduction (Week 26)



Variability in patient response (Mean Change) reflects variability in proliferation capacity within a 4-week treatment window.

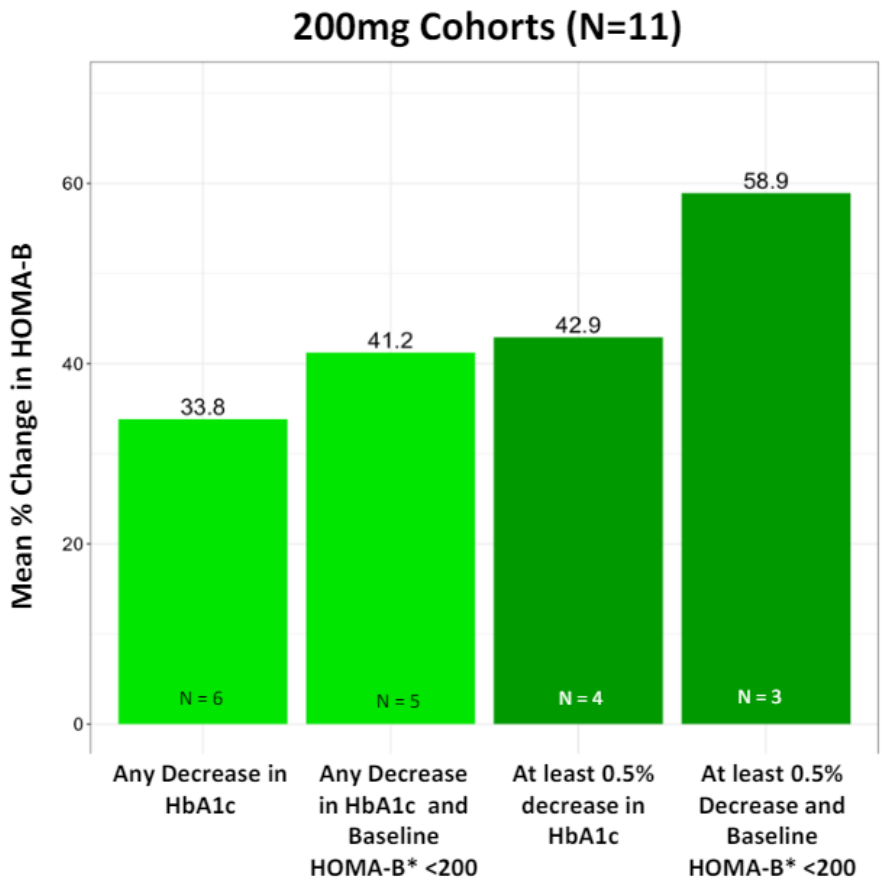
Evidence of Beta Cell Proliferation Supported by Increase in HOMA-B and C-Peptide

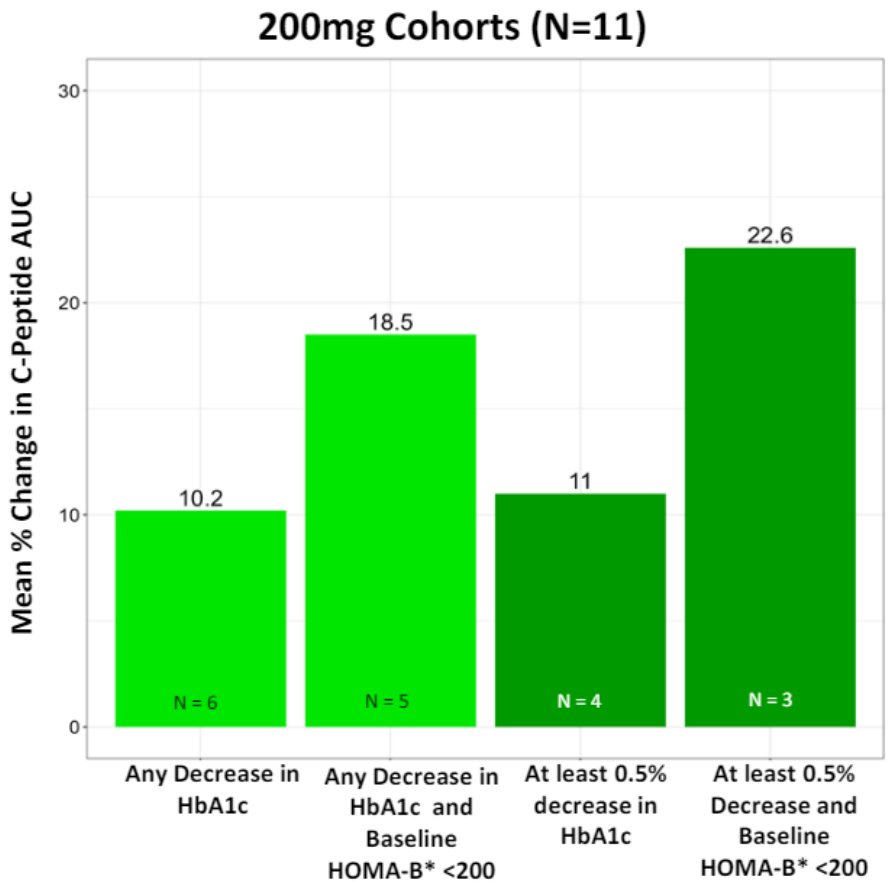
at Week 26



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

HOMA-B and C-Peptide Increases with Magnitude of HbA1C Reduction





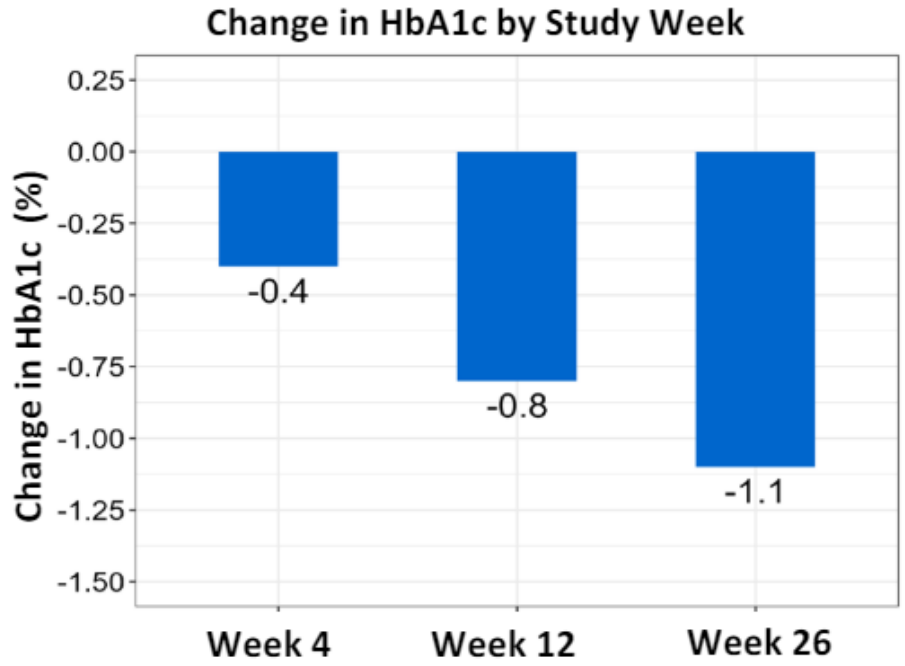
HOMA-B and C-peptide at Week 26 increases with magnitude of reduction in HbA1C and in patients with baseline HOMA-B <200 with BMF-219 200mg once daily dosing for 4 weeks.

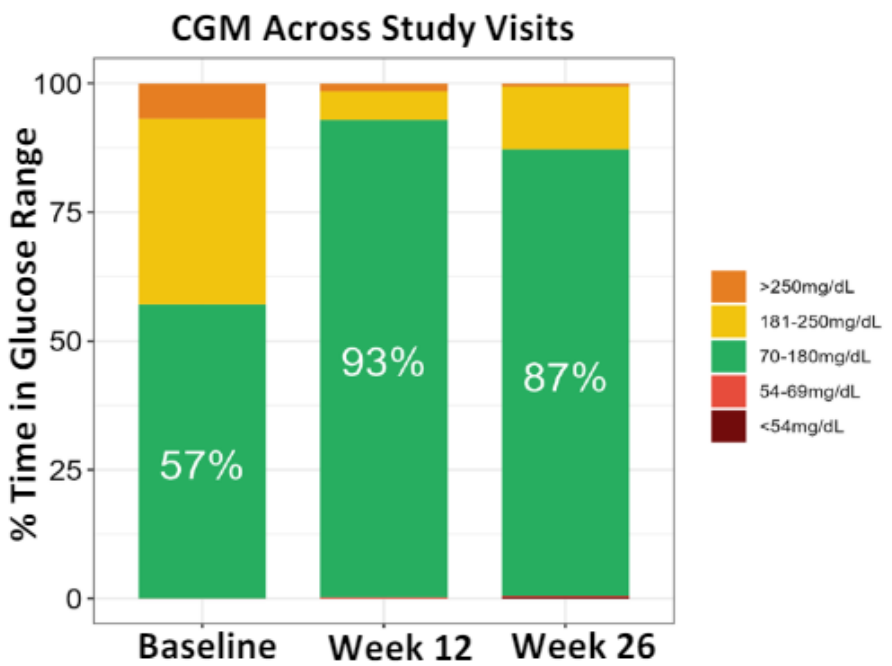
*HOMA-B<200 is considered beta cell deficient

Case Study: 61-year-old woman with 10-year history of T2D

- 61-year-old woman with 10-year history of T2D
- Metformin 500 mg BID; liraglutide 1.2mg QD (GLP-1 RA); canagliflozin 500 mg QD (SGLT2i)
- HbA_{1c} 7.9%; FPG 163 mg/dL; BMI 29.4 kg/m^2

- BMF-219 200 mg QD with food for 4 weeks
- Metformin, liraglutide (GLP-1 RA), and canagliflozin (SGLT2i) continued
- No serious adverse events reported



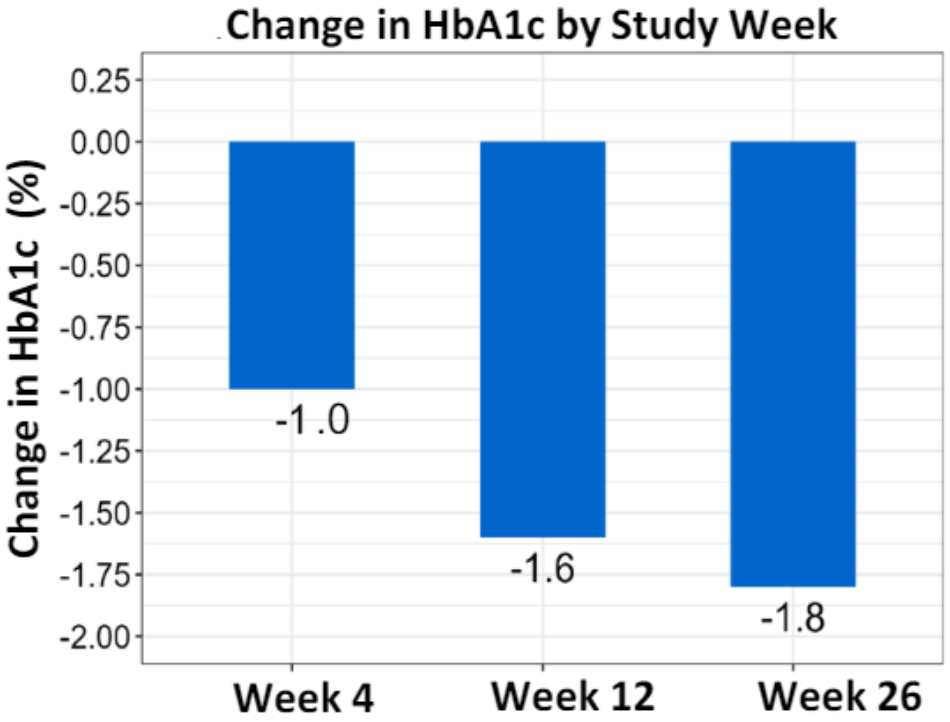


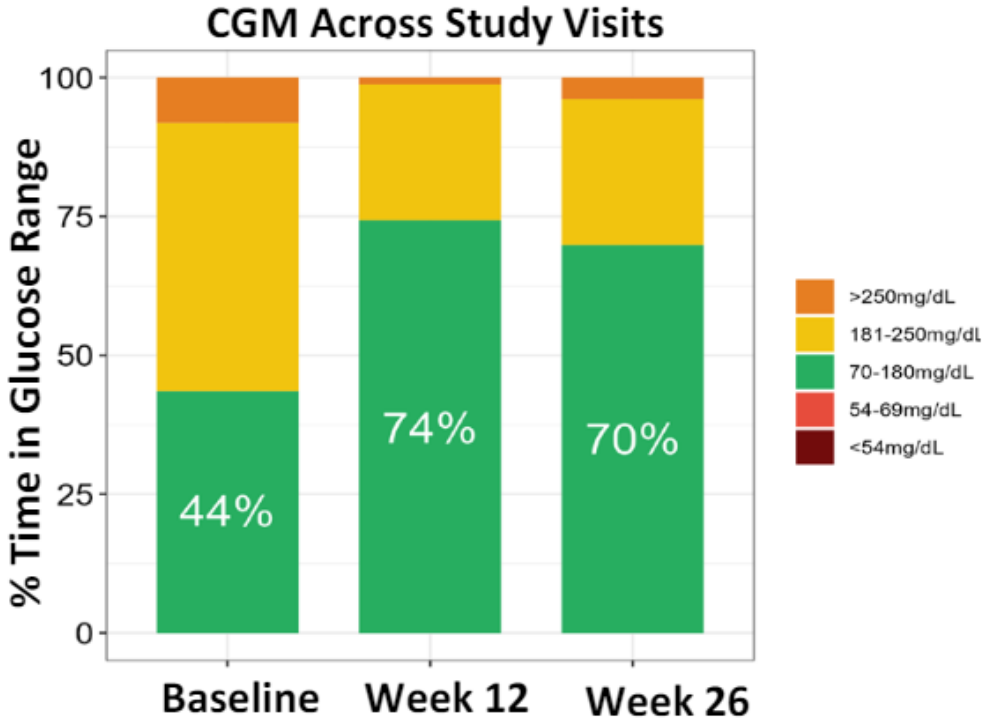
A patient with a 10-year history of T2D and on triple-agent regimen (metformin, GLP1 RA, and SGLT2i) at baseline, experienced a 1.1% reduction in HbA1c and an increase of 30% in TIR compared to baseline at Week 26

Case Study: 51-year-old man with 5-year history of T2D

- 51-year-old man with 5-year history of T2D
- Metformin 500mg BID
- HbA_{1c} 8.9%; FPG 184mg/dL; BMI 32.1 kg/m^2

- BMF-219 100mg QD without food for 4 weeks
- Metformin continued
- No adverse events reported



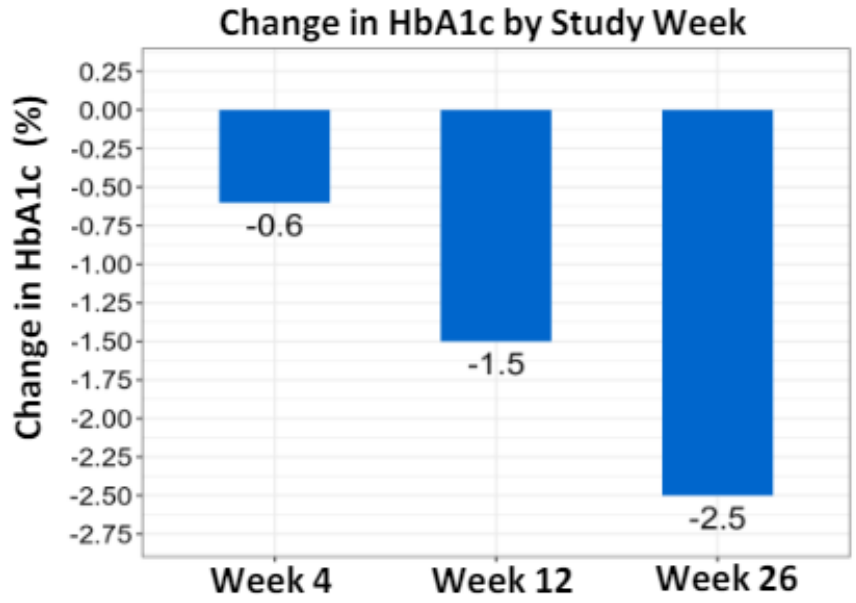


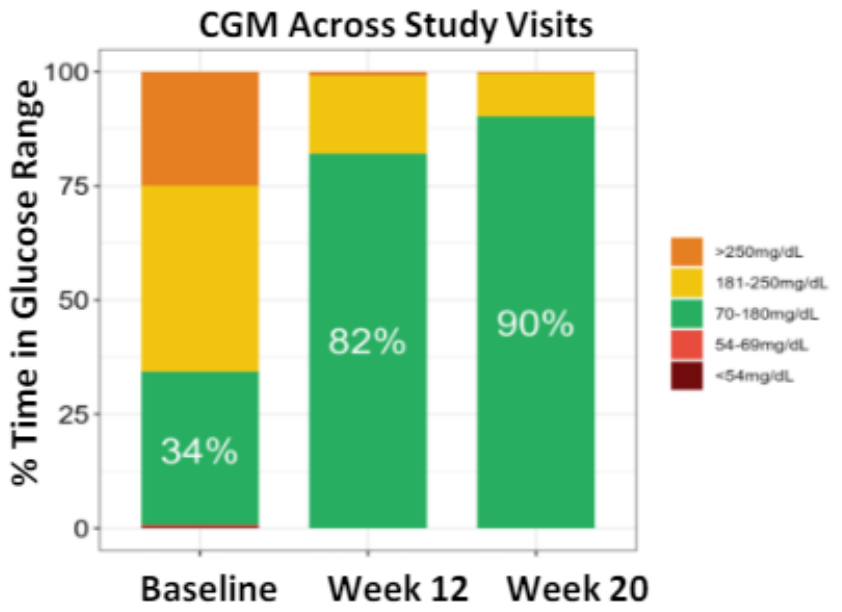
A case study demonstrating continued improvement in HbA1C and improved Time In Range on CGM (after completion of 4 weeks of once daily oral treatment), indicating a durable glycemic control.

Case Study: 29-year-old man with 4-year history of T2D

- 29-year-old man with 4-year history of T2D
- Metformin 500 mg BID, empagliflozin 25 mg BID
- HbA_{1c} 9.5%; FPG 134 mg/dL; BMI 25.6 kg/m^2
- CGM TIR 34%

- BMF-219 200 mg QD without food for 4 weeks
- Metformin and SGLT2i continued
- No adverse events reported
- At (Week 26), HbA1c 7.0% (change from baseline [CFB], -2.2%), FPG 105 mg/dL (CFB, -24 mg/dL), TIR 90% (CFB, +65%).





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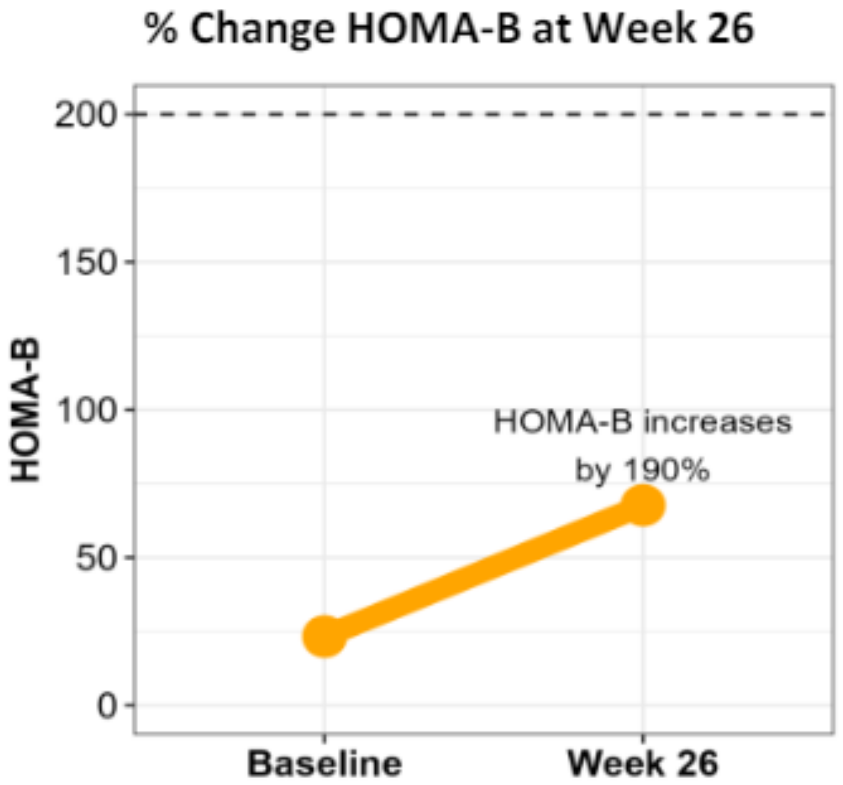
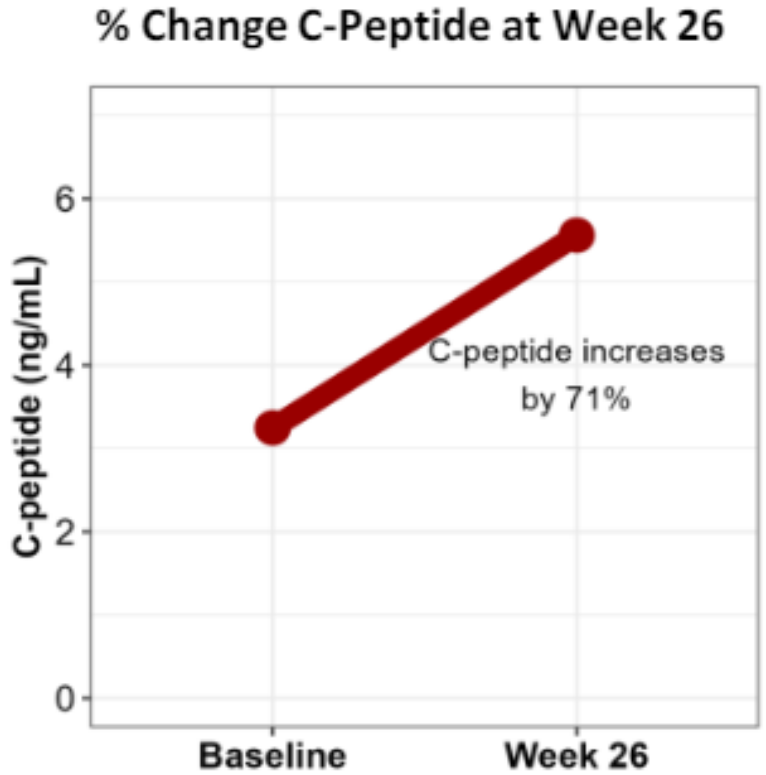
Case Study: 29-year-old man with 4-year history of T2D

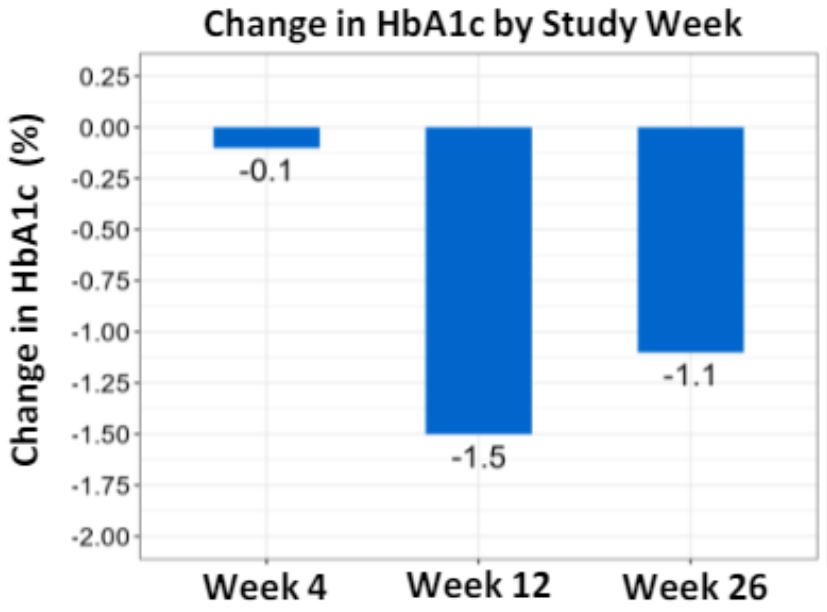


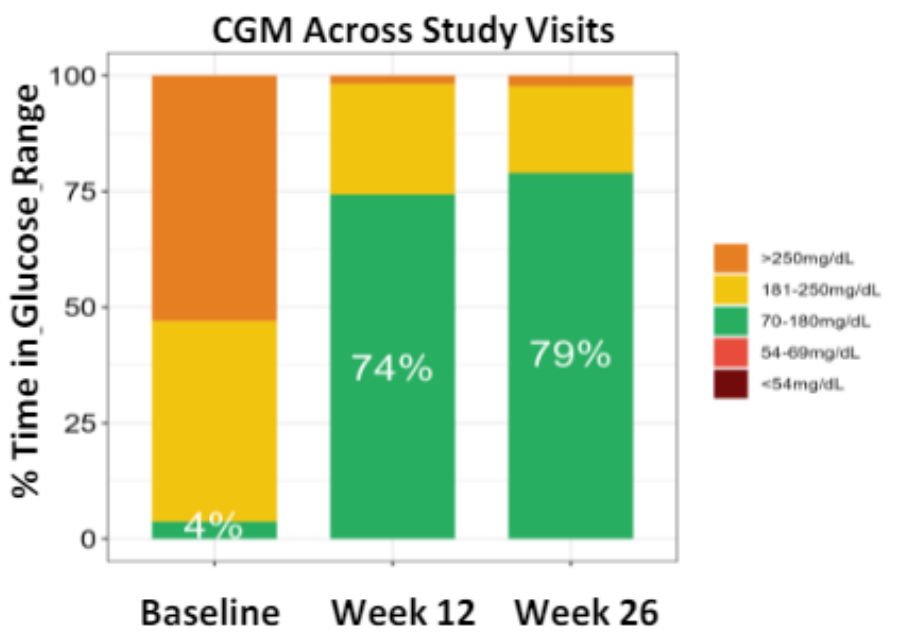


Case Study: 45-year-old man with 10-year history of T2D

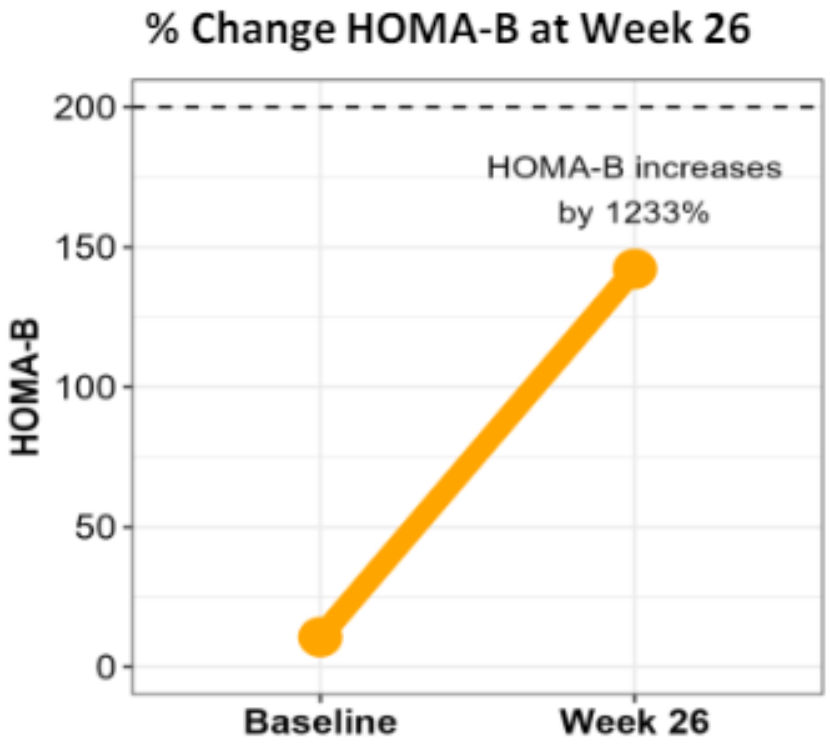
- 45-year-old man with 10-year history of T2D
- Metformin 500 mg BID
- HbA_{1c} 8.6%; FPG 235 mg/dL; BMI 29.6 kg/m^2
- CGM TIR 4%

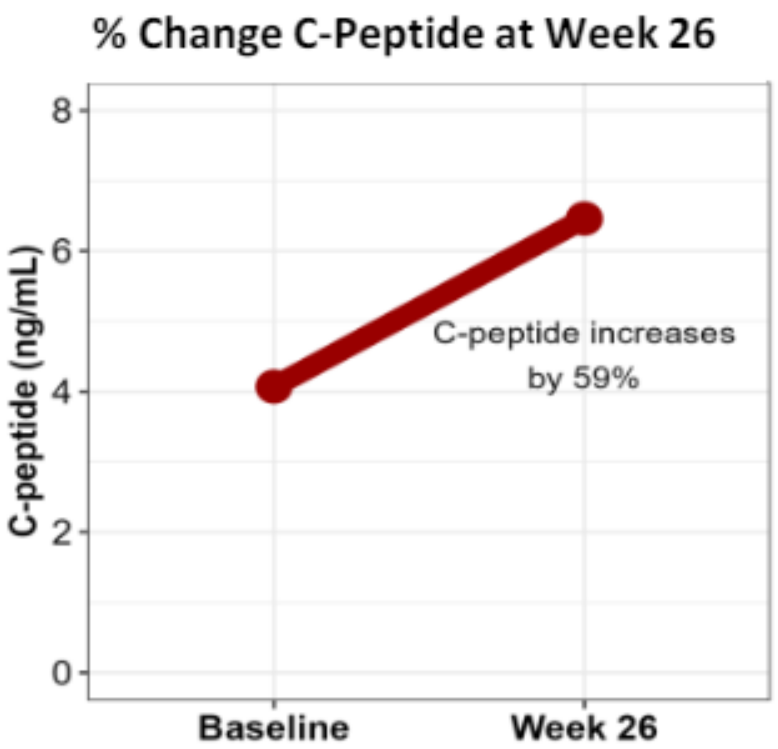
- BMF-219 100 mg QD with food for 4 weeks
- Metformin continued
- No adverse events reported
- At (Week 26), HbA1c 7.5% (CFB, -1.1%), FPG 144 mg/dL (CFB, -91 mg/dL), TIR 79% (CFB, +73%), HOMA B (CFB, 12-fold increase).





Case Study: 45-year-old man with 10-year history of T2D





Summary

- BMF-219 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 BMF-219, 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 first 3 Arms of 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:

- Initial 26-week data of the Expansion Phase expected in 2H24

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THANK YOU

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