82nd American Diabetes Association Conference Call

June 6, 2022

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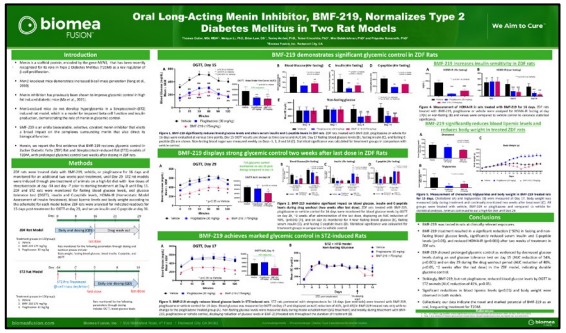
Oral Long Acting BMF-219 normalizes Type II Diabetes and displays significant effect on HbA1C in Animal Models

Results

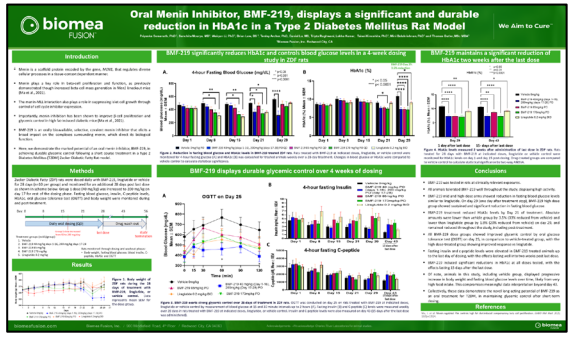
BMF-219 was able to normalize glucose levels in the majority of diabetic animals after as little as two weeks of treatment. The majority of the effect on glycemic control was maintained despite complete washout of BMF-219

Preclinical data support BMF-219 as an oral, long-acting treatment for diabetes with profound effects on HbA1C

Poster Presentations



Oral Long-Acting Menin Inhibitor, BMF-219, Normalizes Type 2 Diabetes Mellitus in Two Rat Models



Oral Menin Inhibitor, BMF-219, displays a significant and durable reduction in HbA1c in a Type 2 Diabetes Mellitus Rat Model

Next Steps

File IND by H2 2022

Initiate Phase I/II trial

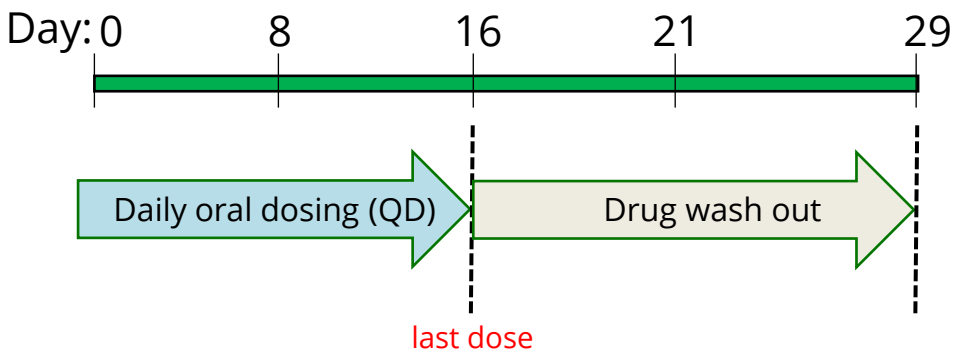
Conduct Additional Translational Work

Poster Presentation Date & Details

- Session Date: Jun 5, 2022, at 12 to 1 PM
- 851-P in category 12-F Clinical Therapeutics/New Technology—Other Therapeutic Agents.

Methods Section: Poster 851-P

ZDF Rat Model

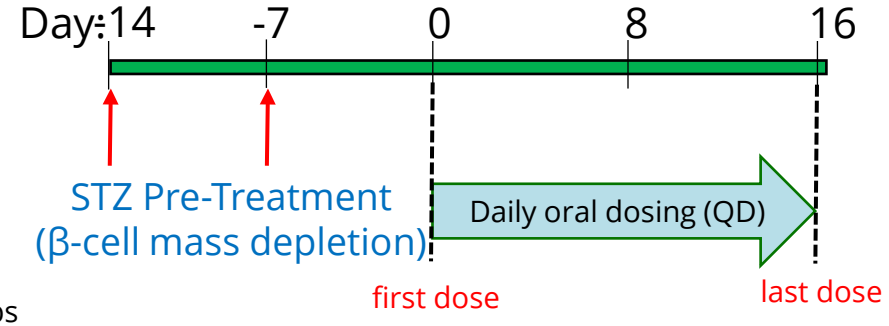


Treatment groups (n=10/group):

1. Vehicle
2. BMF-219 175 mg/kg
3. Pioglitazone 30 mg/kg

Rats monitored for the following parameters through dosing and washout phases include:
Body weight, fasting blood glucose, blood insulin, C-peptide, and OGTT

STZ Rat Model



Treatment groups (n=10/group):

1. Vehicle
2. BMF-219 175 mg/kg
3. Pioglitazone 30 mg/kg

Rats monitored for the following parameters through dosing include: OGTT, blood glucose levels

Detailed Description of Methods

ZDF rats were treated daily with BMF-219, vehicle, or pioglitazone for 16 days and monitored for an additional two weeks post-treatment, until Day 29. STZ rat models were induced through pre-treatment of animals on a high-fat diet with low doses of streptozotocin at day -14 and day -7 prior to starting treatment at Day 0 until Day 16. ZDF and STZ rats were monitored for fasting blood glucose levels, oral glucose tolerance test (OGTT), insulin and C-peptide levels, HOMA-IR (Homeostatic Model Assessment of Insulin Resistance), blood lipemic levels and body weight according to the schematic for each model below. ZDF rats were analyzed for indicated readouts for 15 days post-treatment for OGTT at day 29, and serum insulin and C-peptide at day 31.

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BMF-219 significantly reduces blood glucose levels

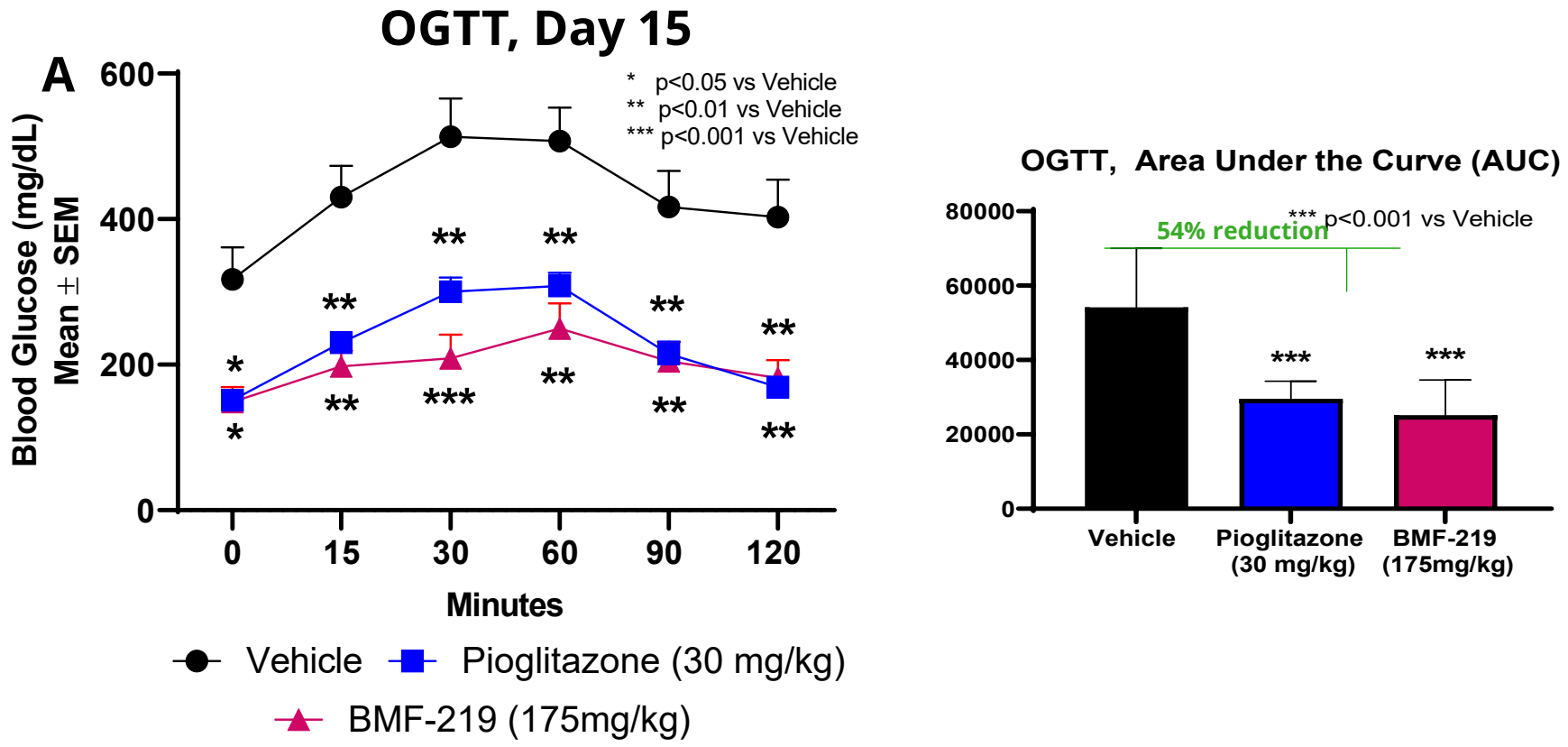


Figure 1. BMF-219 significantly reduces blood glucose levels and alters serum insulin and C-peptide levels in ZDF rats. ZDF rats treated with BMF-219, pioglitazone or vehicle for 16 days were evaluated at various time points. Day 15 OGTT results are shown as time course and AUC (A). Statistical significance was calculated for treatment groups in comparison with vehicle control.

BMF-219 demonstrates strong glycemic control in ZDF rats during treatment period

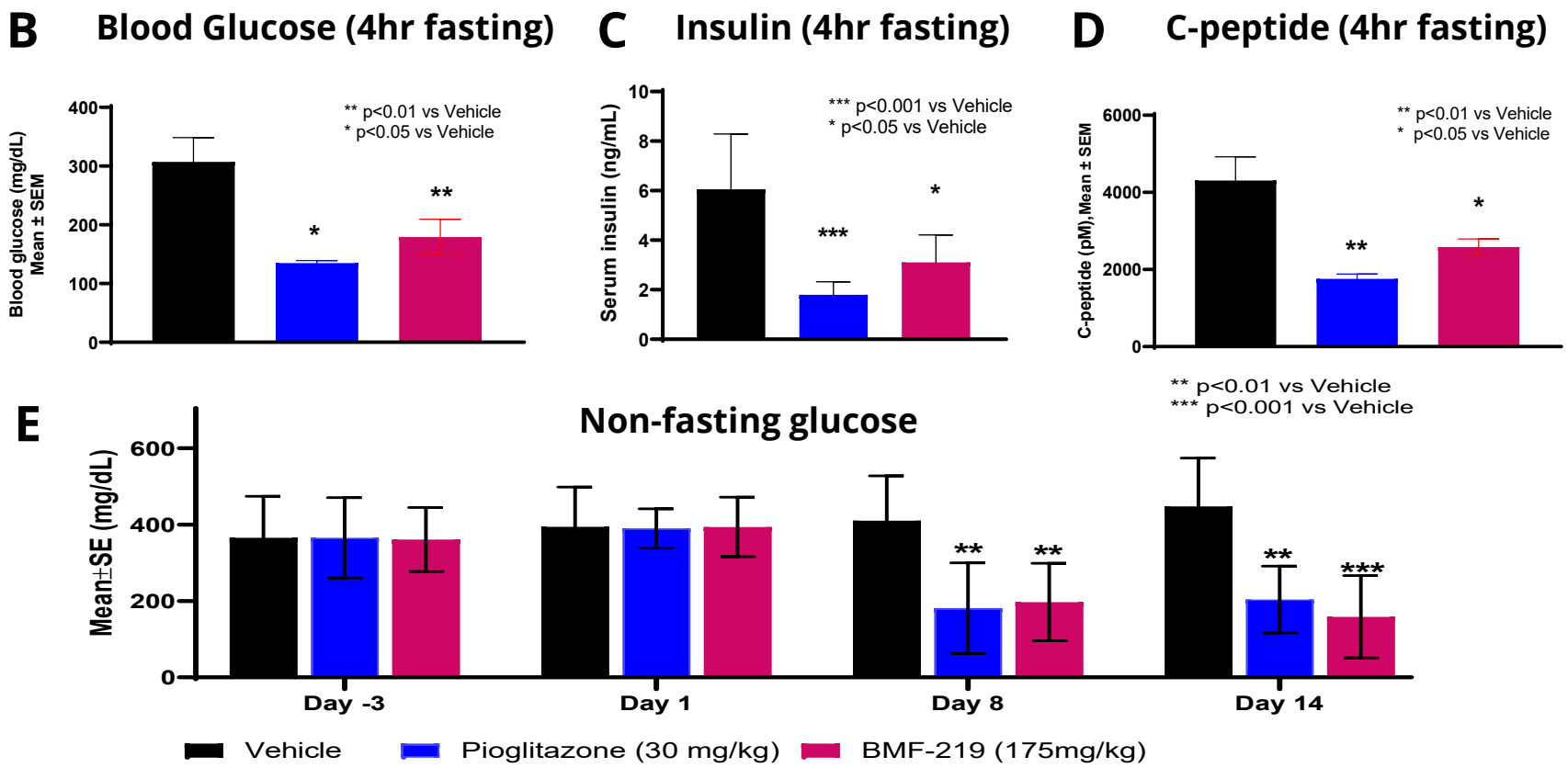


Figure 1. BMF-219 significantly reduces blood glucose levels and alters serum insulin and C-peptide levels in ZDF rats. ZDF rats treated with BMF-219, pioglitazone or vehicle for 16 days were evaluated at various time points. Day 15 OGTT results are shown as time course and AUC (A). Day 17 fasting blood glucose levels (B), fasting insulin (C), and fasting C-peptide (D) are shown. Non-fasting blood sugar was measured weekly on Days -3, 1, 8 and 14 (E). Statistical significance was calculated for treatment groups in comparison with vehicle control.

BMF-219 increases insulin sensitivity in ZDF rats

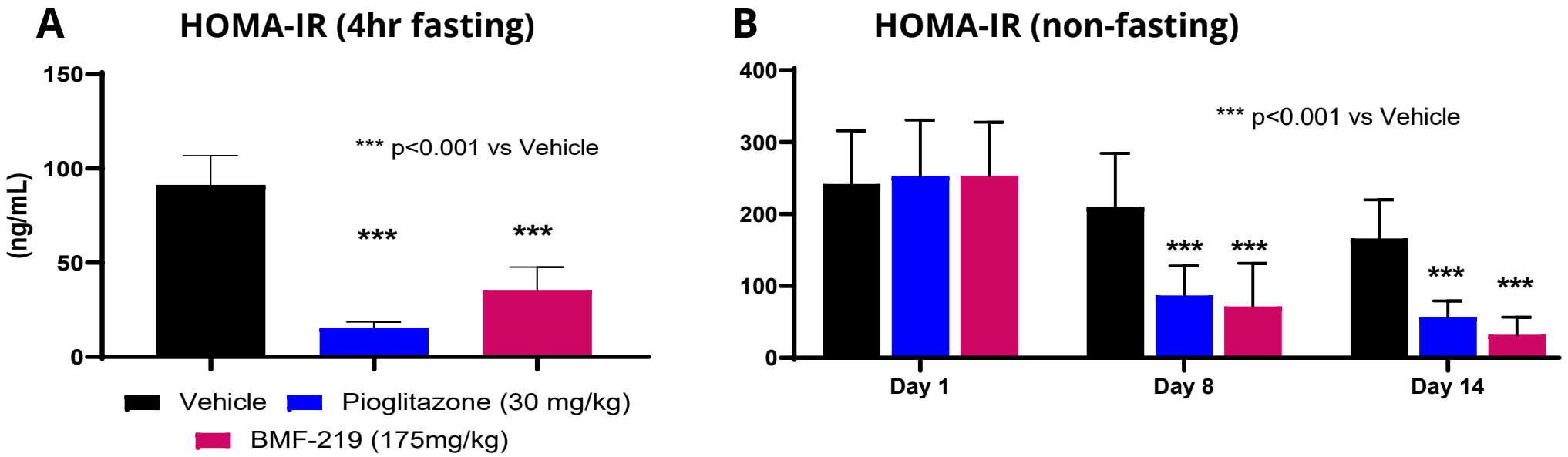
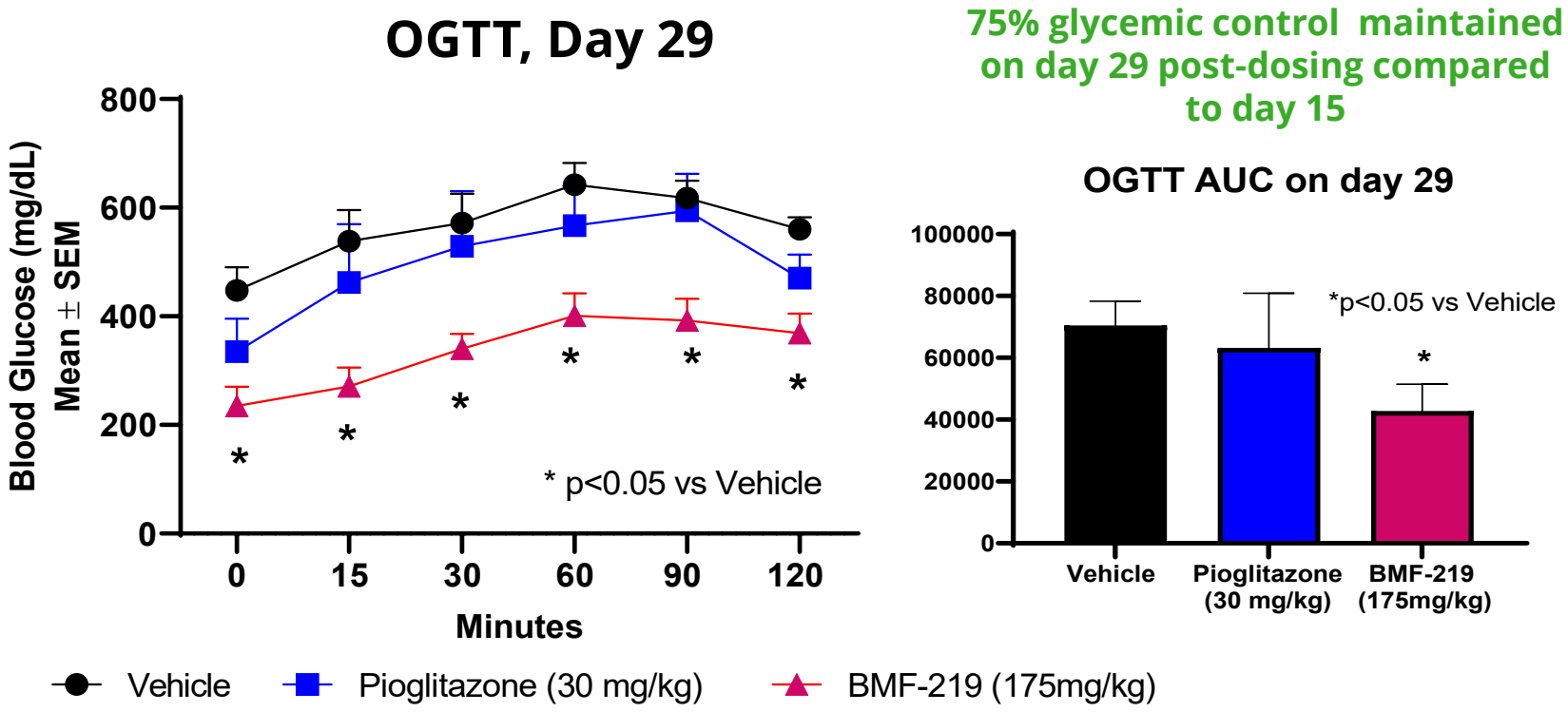


Figure 4. Measurement of HOMA-IR in rats treated with BMF-219 for 16 days. ZDF rats treated with BMF-219, pioglitazone or vehicle were analyzed for HOMA-IR 4 hour fasting at day 17(A) or non-fasting (B) and values were compared to vehicle control to calculate statistical significance.

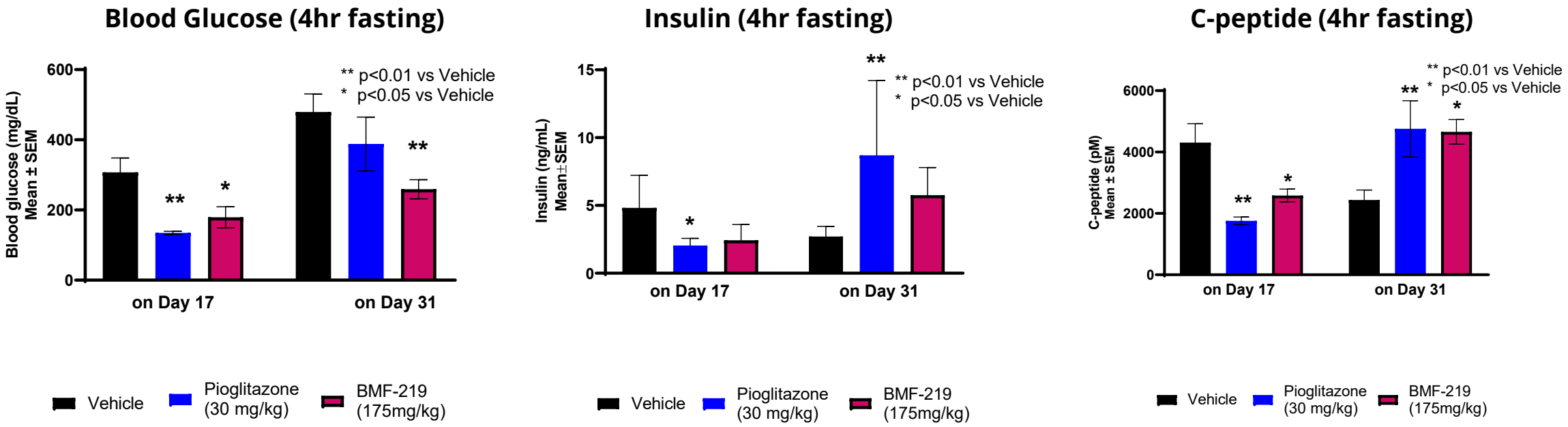
BMF-219 outperforms pioglitazone in OGTT at day 29, the 14th day of the treatment washout



75% glycemic control maintained on day 29 post-dosing compared to day 15

Figure 2. BMF-219 maintains significant impact on blood glucose, insulin and C-peptide levels during drug washout (two weeks after last dose). ZDF rats treated with BMF-219, pioglitazone or vehicle control for 16 days were monitored for blood glucose levels by OGTT on day 29, ~2 weeks after administration of the last dose, displaying an AUC reduction of 40%, ($p<0.05$) (A), and on day 31 monitored for 4-hour fasting blood glucose (B), fasting serum insulin (C), and fasting C-peptide levels (D). Statistical significance was calculated for treatment groups in comparison to vehicle control.

BMF-219 has significant impact on glucose, insulin, and C-peptide, even after 2 weeks of administration of last dose



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BMF-219 significantly reduces blood lipemic levels and reduces body weight in treated ZDF rats

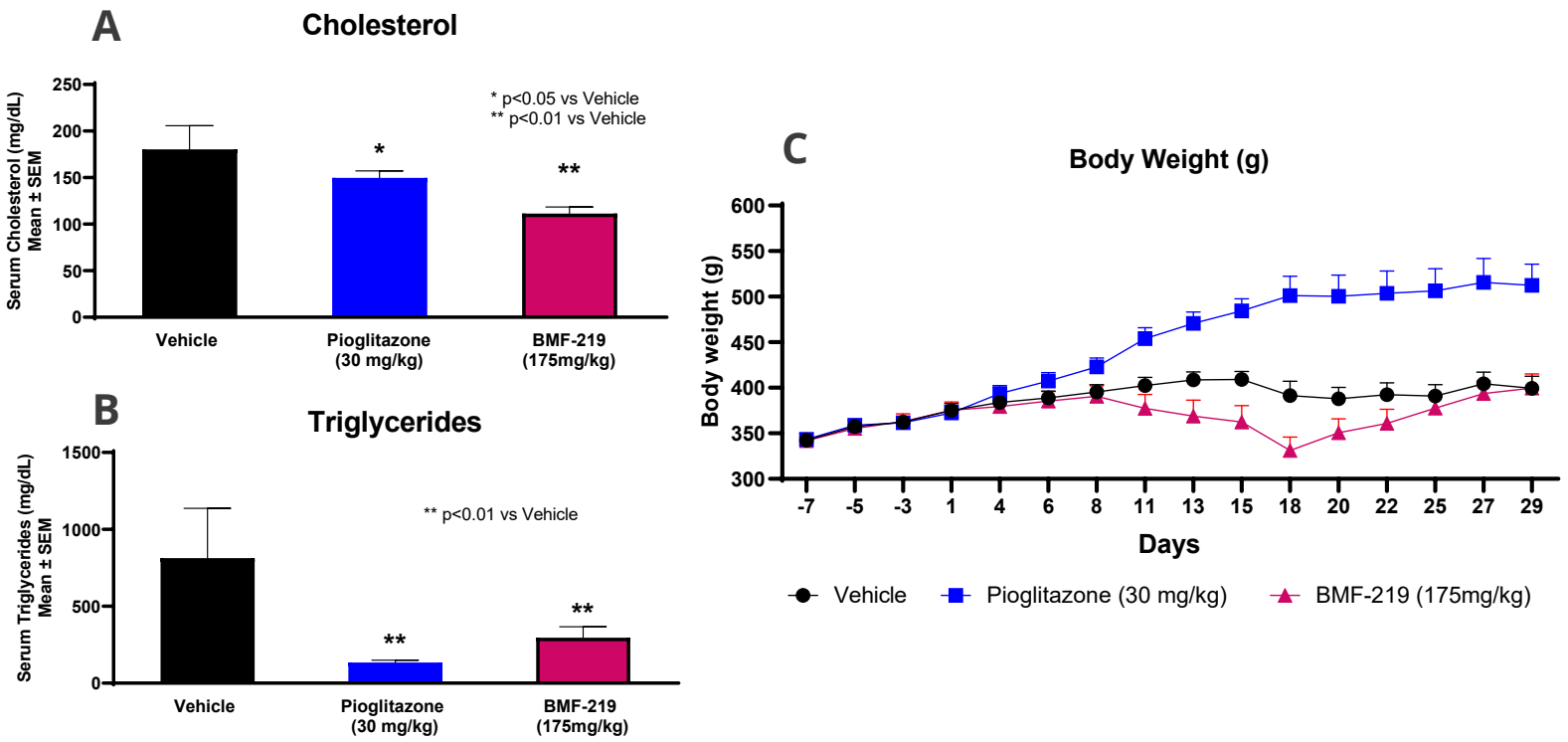
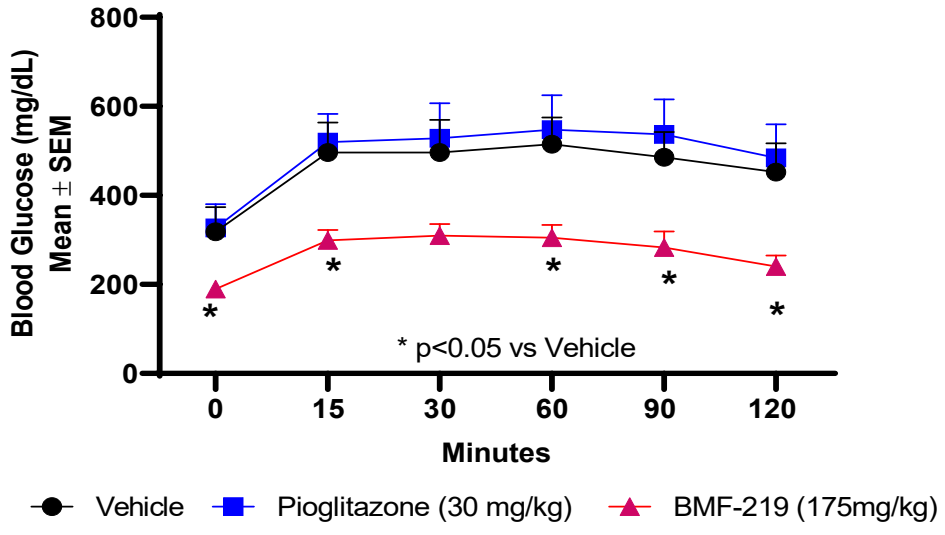


Figure 5. Measurement of cholesterol, triglycerides and body weight in BMF-219 treated rats for 16 days. Cholesterol (A) and triglycerides (B) were measured at Day 17. Body weight was measured daily during treatment and continually monitored two weeks after treatment (C). All groups were treated with vehicle, BMF-219 or pioglitazone and compared to vehicle for statistical analyses. Animals continued to eat a high fat diet until Day 29.

BMF-219 Demonstrates Preclinical Proof of Concept in Challenging Diabetes Model, outperforming pioglitazone

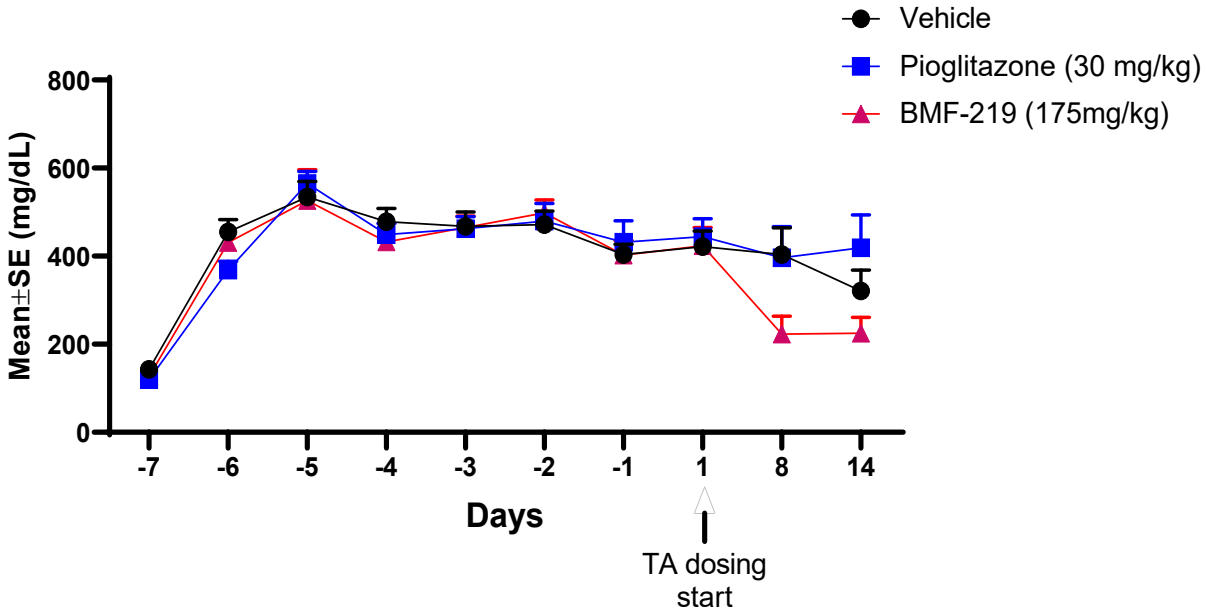
BMF-219 Achieves Glycemic Control in STZ Rat Model

Oral Glucose Tolerance Test (Day 17)



BMF-219 achieves lower glucose level than pioglitazone at all timepoints in OGTT (day 17) in STZ rat model

Non-Fasting Glucose



BMF-219 achieves lower non-fasting glucose than pioglitazone at day 8 and day 14 in STZ rat model

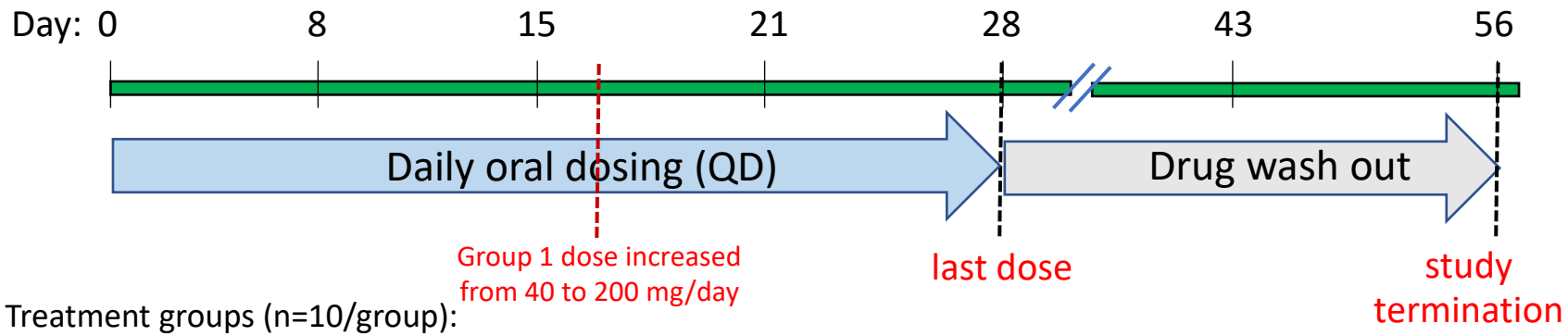
Poster Presentation Date & Details

- Session Date: Jun 5, 2022 at 12 to 1 PM

- 113-LB in category 12-F Clinical Therapeutics/New Technology—Other Therapeutic Agents

Methods Section: Poster 113-LP

ZDF Rat Model



Treatment groups (n=10/group):

1. Vehicle
2. BMF-219 40 mg/kg days 1-16, 200 mg/kg days 17-28
3. BMF-219 85 mg/kg
4. BMF-219 170 mg/kg
5. Liraglutide 0.2 mg/kg

Rats monitored through dosing and washout phases:

- Body weight, fasting blood glucose, blood insulin, C-peptide, HbA1c and OGTT

Detailed Description of Methods

Zucker Diabetic Fatty (ZDF) rats were dosed daily with BMF-219, liraglutide or vehicle for 28 days (n=10 per group) and monitored for an additional 28 days post last dose as shown in scheme below. Group 1 dose (40 mg/kg) was increased to 200 mg/kg on day 17 for rest of the dosing phase. Fasting blood glucose, insulin, C-peptide levels, HbA1c, oral glucose tolerance test (OGTT) and body weight were monitored during and post-treatment.

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BMF-219 displays body weight reduction at proper dose of 200mg

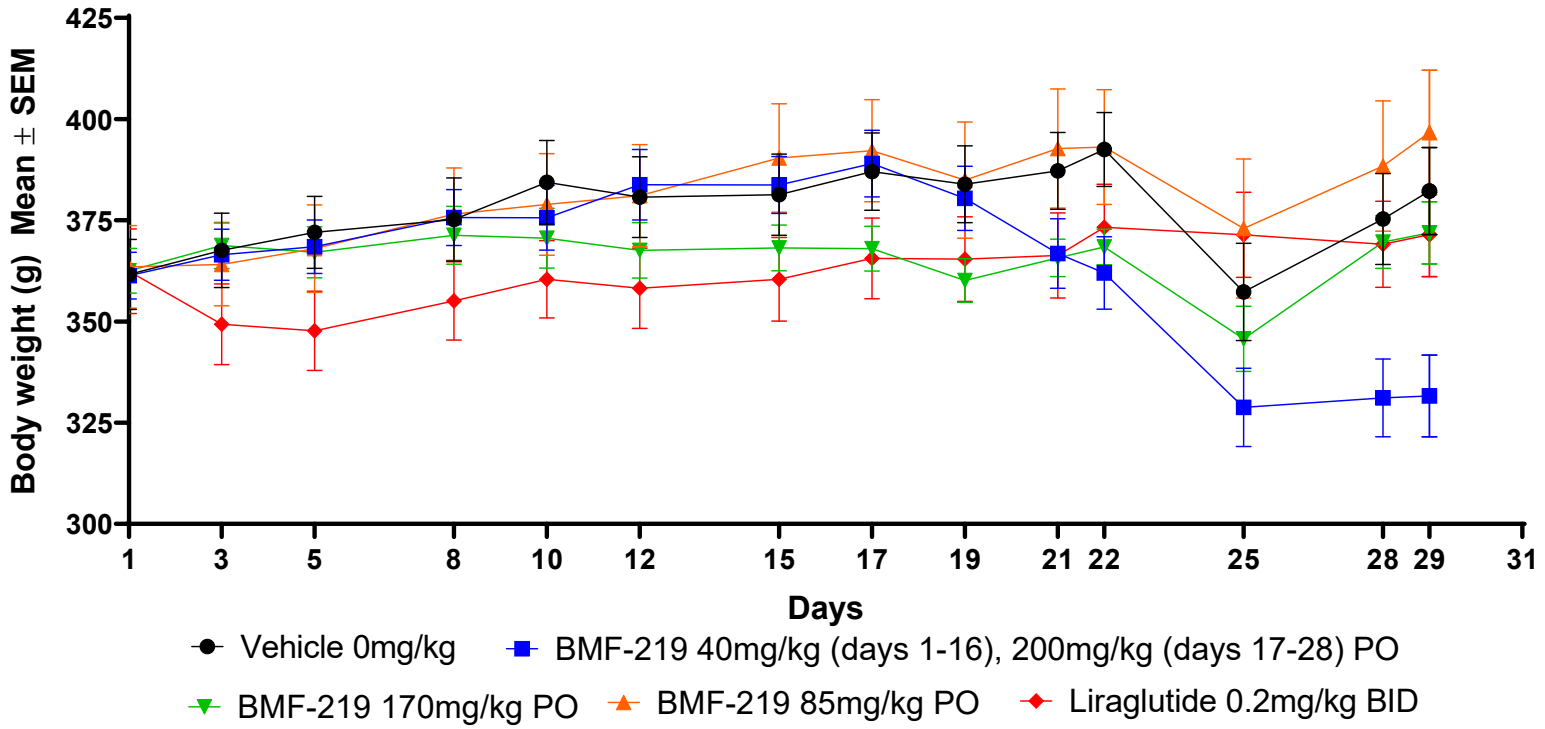


Figure 1. Body weight of ZDF rats during the 28 days of treatment with BMF-219, liraglutide, or vehicle control. Data represents mean SEM for the dose group.

BMF-219 significantly reduces HbA1c (-3.5%) and controls blood glucose levels in a 4-week dosing study in ZDF rats

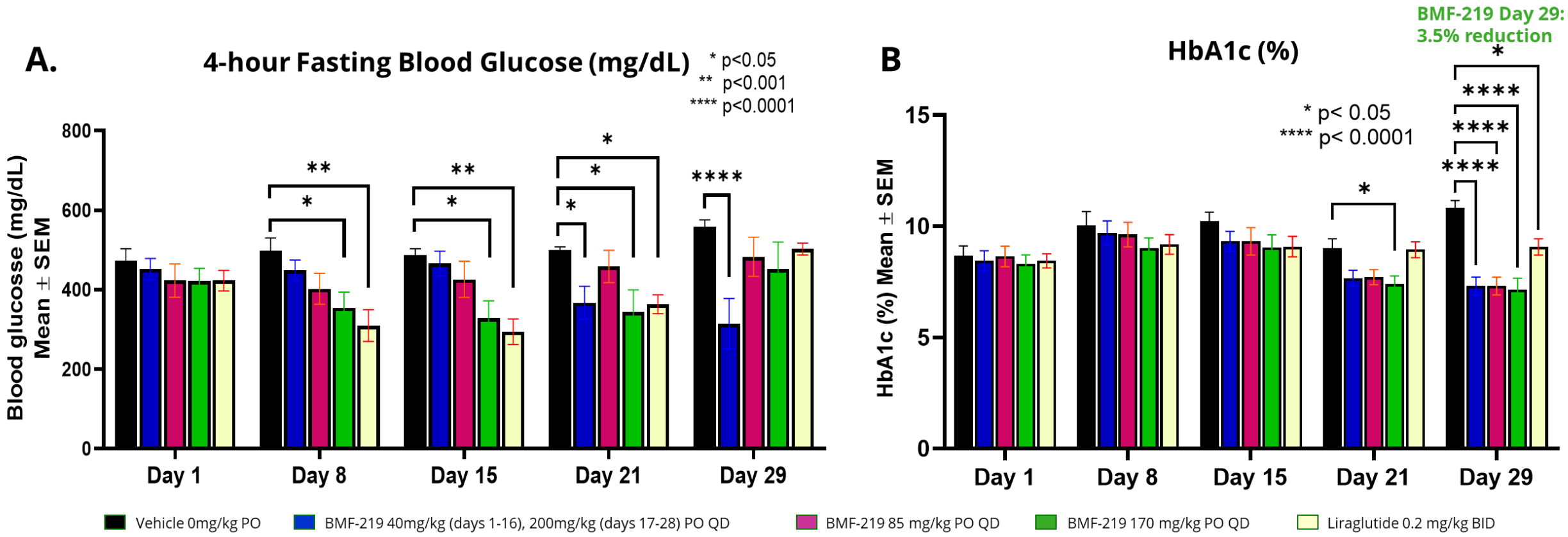
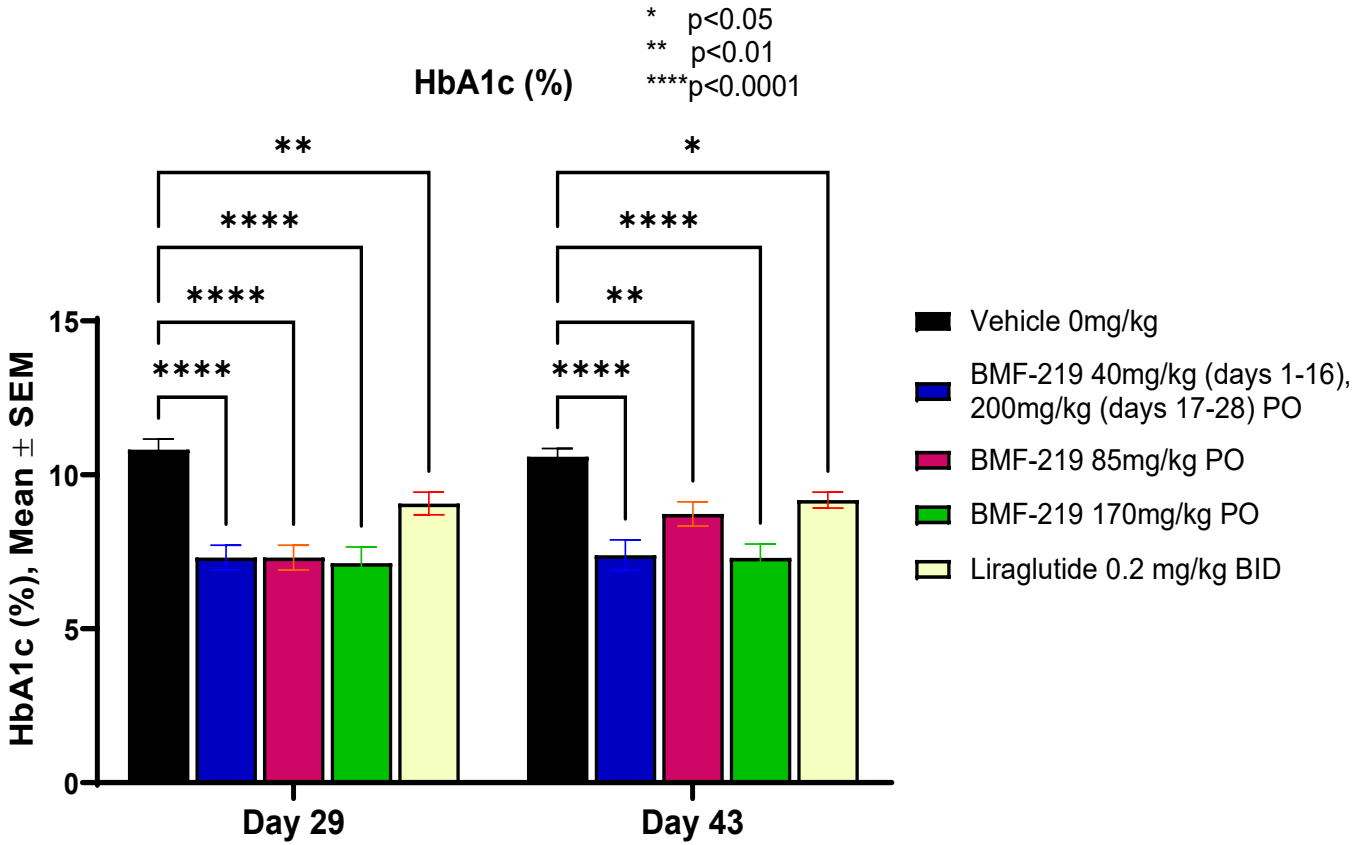


Figure 2. Reduction in fasting blood glucose and HbA1c levels in BMF-219 treated ZDF rats. Rats treated with BMF-219 at indicated doses, liraglutide, or vehicle control were monitored for 4-hour fasting glucose (A) and HbA1c (B) was calculated for treated animals weekly over a 28-day treatment. Changes in blood glucose or HbA1c were compared to vehicle control to calculate statistical significance.

BMF-219 significantly reduces HbA1c in a 4-week dosing study in ZDF rats and MAINTAINS the effect during a two week follow up.

BMF-219 Reduces HbA1c After 28 days of Treatment and Maintains Effect After 14-day Washout



BMF-219 demonstrated significant decrease in HbA1c vs. control starting on day 21 of treatment

BMF-219 treated group demonstrated significant weight reduction starting at day 25

HbA1c reduction in BMF-219 highest dose groups maintained through washout period

BMF-219 displays strong glycemic control over 4 weeks of dosing

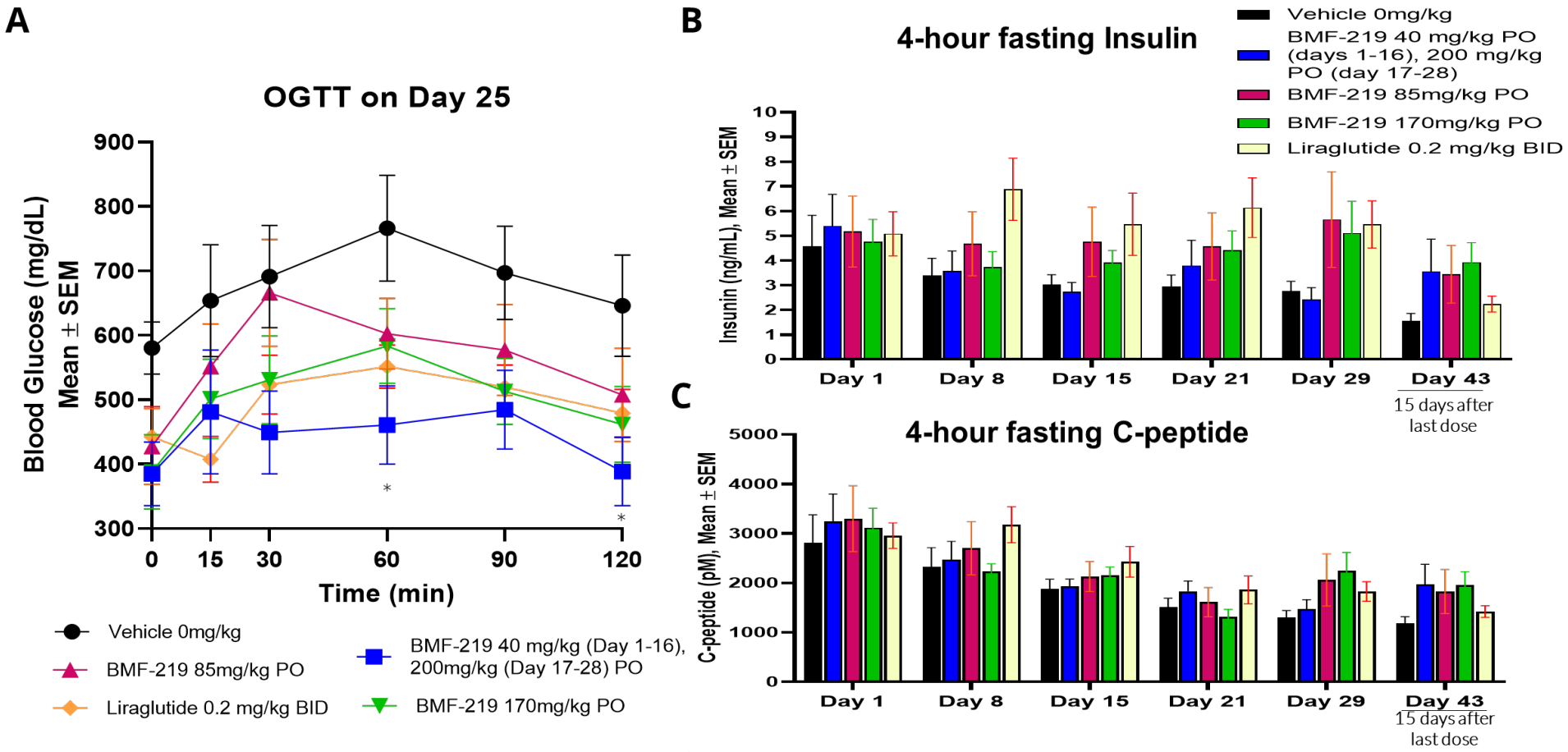


Figure 3. BMF-219 exerts strong glycemic control over 28-days of treatment in ZDF rats. OGTT was conducted on day 25 on rats treated with BMF-219 at indicated doses, liraglutide or vehicle control by measurement of blood glucose at 15 and 30 minute intervals up to 2 hours (A). Fasting insulin (B) and C-peptide (C) levels were measured weekly over 28 days in rats treated with BMF-219 at indicated doses, liraglutide, or vehicle control. Insulin and C-peptide levels were also measured on day 43 (15 days after the last dose was administered).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