

BIOMEA CONFERENCE CALL

Preclinical Data Combining icovamenib
with a GLP-1-Based Therapy &
Biomea's Oral GLP-1 RA Candidate BMF-650

October 30, 2024

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Agenda

Introduction

Ramses Erdtmann
Chief Operating Officer & Co-Founder of Biomea

Executive Summary

Thomas Butler
Chief Executive Officer, Chairman of the Board & Co-Founder of Biomea

GLP-1 Based Therapy Background & Overview

Juan Frias, M.D.
Chief Medical Director of Biomea

Icovamenib in combination with GLP-1 Based Therapy

Mini Balakrishnan, Ph.D.
Executive Director of Biology, Biomea

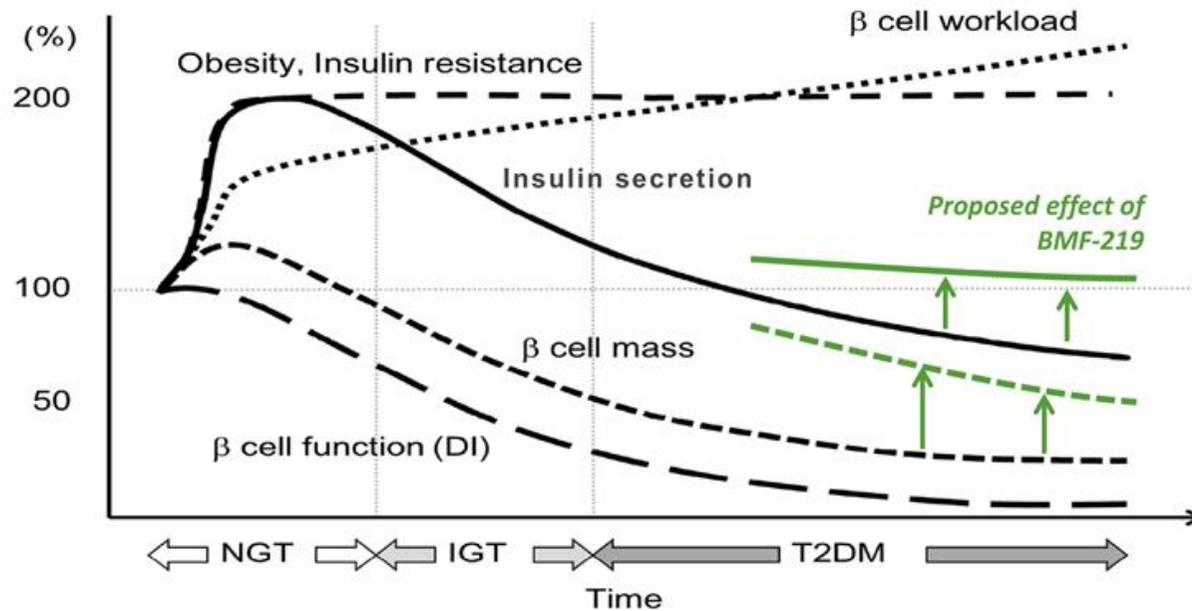
BMF-650 Preclinical Summary

Thorsten Kirschberg, Ph.D.
Executive Vice President of Chemistry, Biomea

Closing Remarks

Thomas Butler
Chief Executive Officer, Chairman of the Board & Co-Founder of Biomea

Type 2 Diabetes Progression is Driven by Loss of Beta Cell Mass



Type 1 and type 2 diabetes both result in beta cell loss and reduction in beta cell mass.

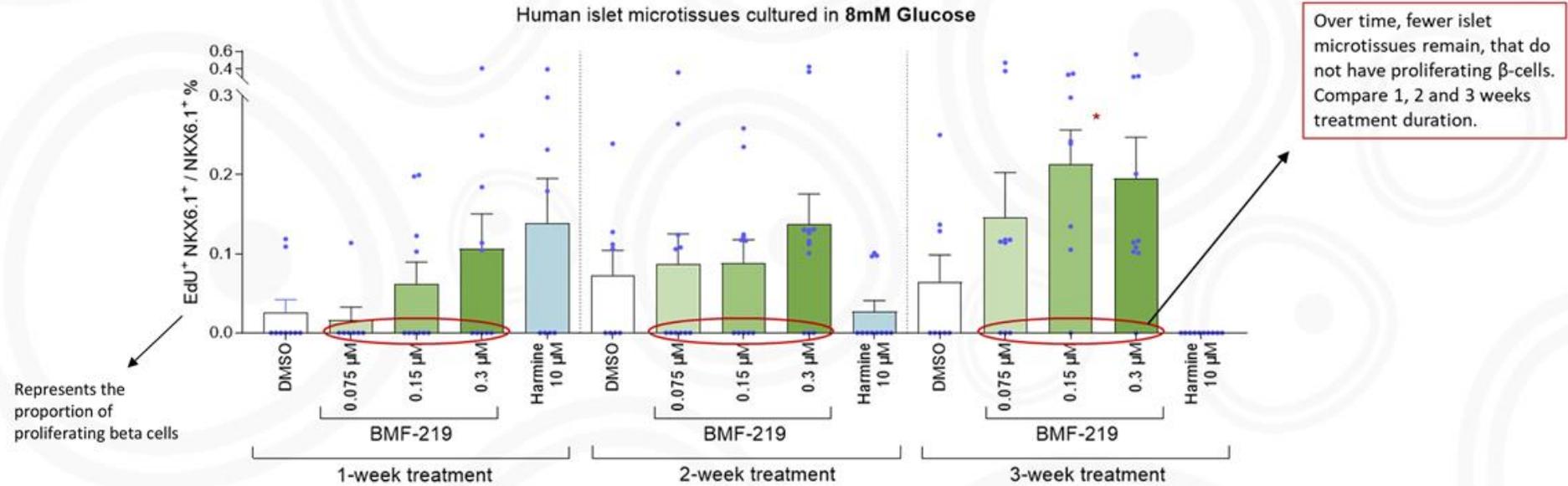
Current diabetes therapies are generally **not** observed to address the decrease in beta cell mass and beta cell health.

Normal glucose tolerance (NGT) followed by impaired glucose tolerance (IGT) followed by type 2 diabetes mellitus (T2DM) insulin resistance has been observed to lead to an increase in beta cell workload which may ultimately lead to beta cell failure and death, and the progression of type 2 diabetes.

[*Int. J. Mol. Sci. 2016, 17, 744; doi:10.3390/ijms17050744](https://doi.org/10.3390/ijms17050744)

Longer Dosing and Higher Dose Concentration Resulted in Greater Proportion of Proliferating Human Islet Beta Cells

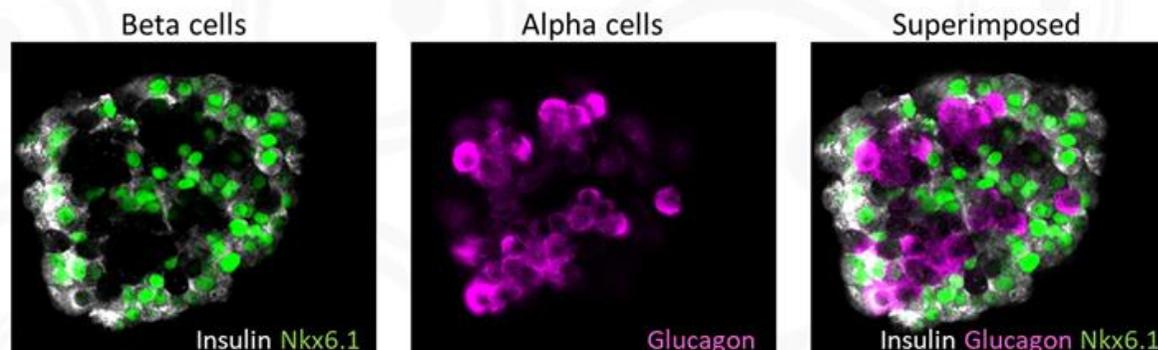
Proliferating beta cells plotted as fraction of total beta cells



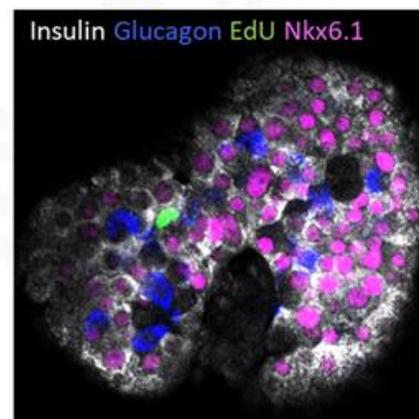
Data represent mean \pm SEM of 1 donor with n = 9-12 technical replicates.
One-way ANOVA with Dunnett's post hoc test rel. to DMSO control. *p < 0.05, **p < 0.01, ***p < 0.001

Application of Advanced Confocal Microscopy to Study the Impact of Therapeutics on Human Beta Cell Health and Function

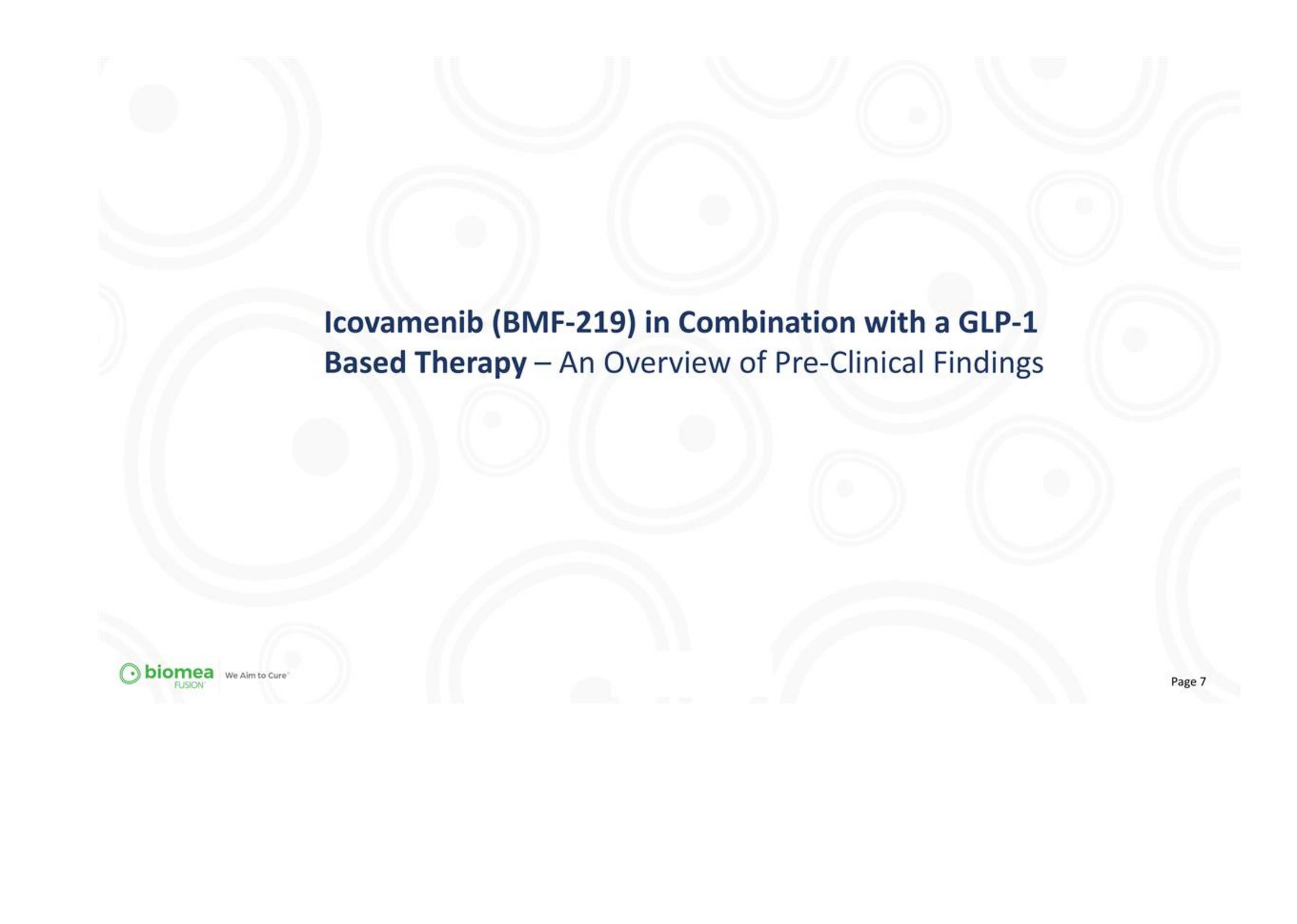
- An optical cross-section through an intact human islet, showing distribution of alpha and beta cells.



- Imaging tools aid in studying physiological events within the islet cells and the effects of drug treatment, e.g. quantifying compound treatment induced effects on beta cell proliferation in whole human islets.

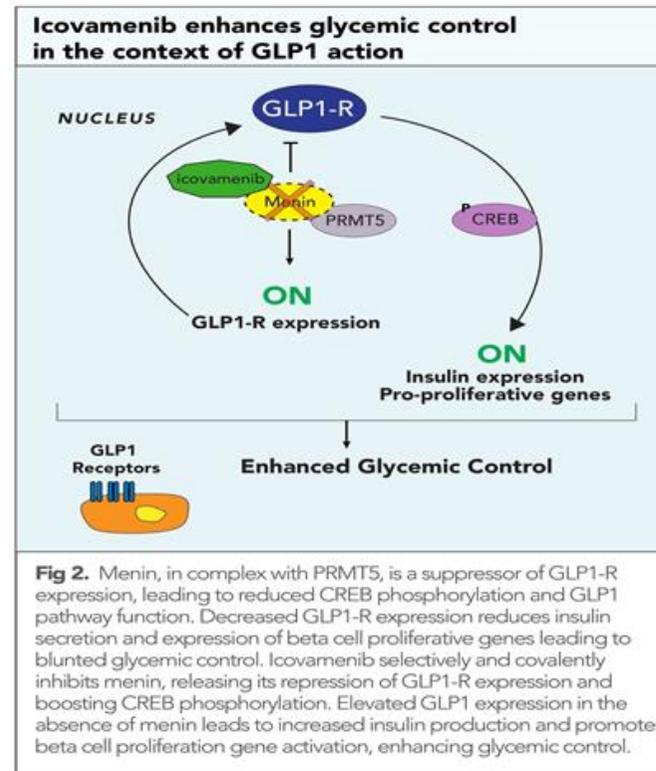
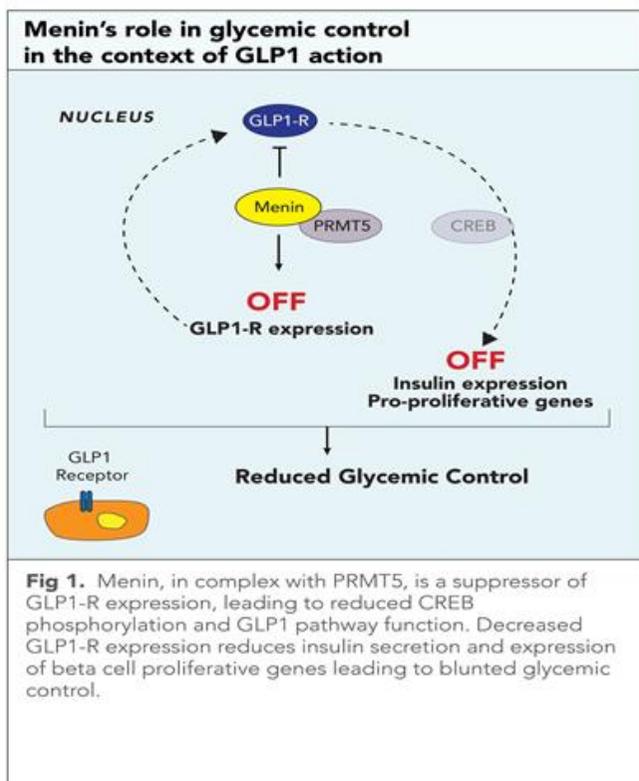


EdU positive = Proliferating cell

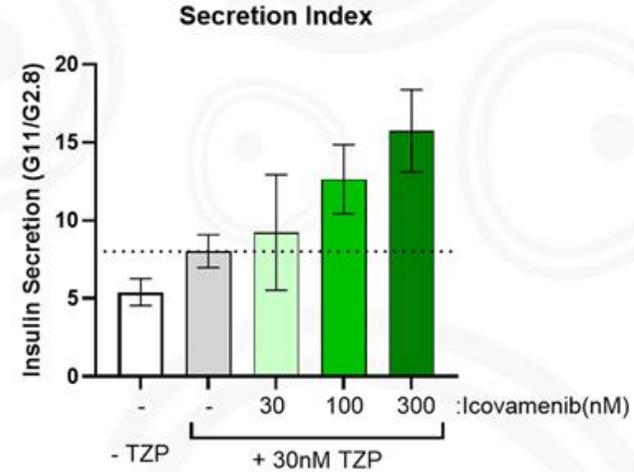
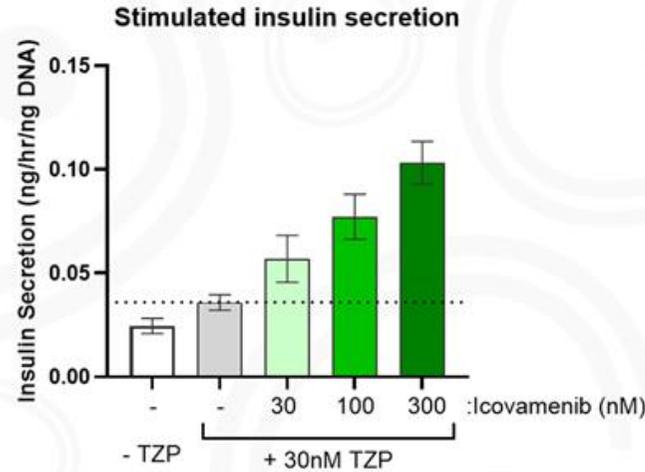
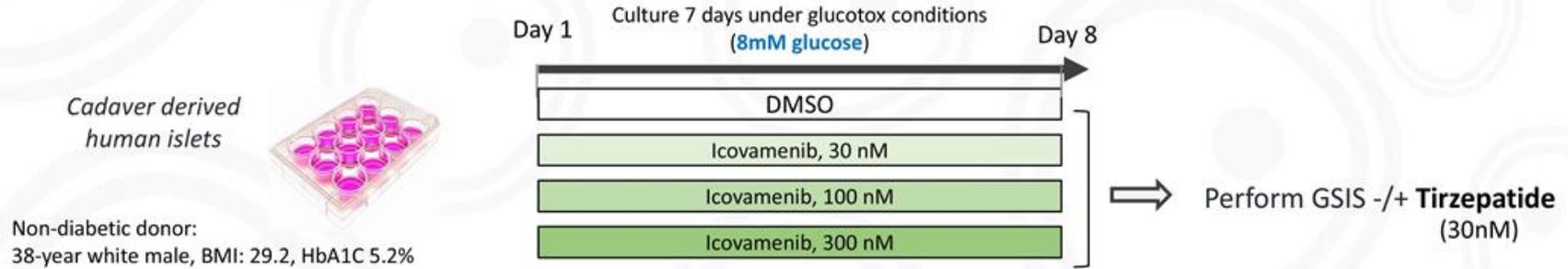
The background of the slide features a repeating pattern of stylized, light gray circular and arc-like shapes, resembling biological cells or molecular structures, scattered across the white background.

Icovamenib (BMF-219) in Combination with a GLP-1 Based Therapy – An Overview of Pre-Clinical Findings

Menin Suppresses GLP-1 Receptor Transcript Levels



Combination Treatment: icovamenib Enhanced Responsiveness of Islets to GLP-1/GIP Dual Receptor Agonist - Tirzepatide

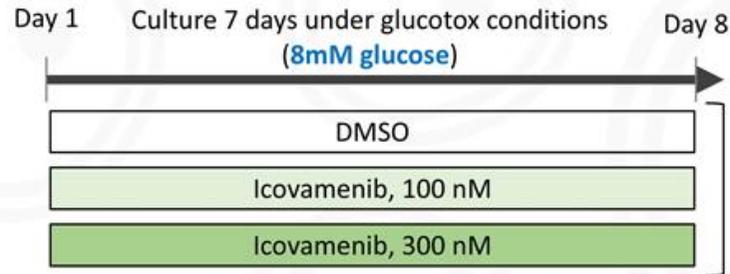


Combination Treatment: icovamenib Enhanced Responsiveness of Islets to GLP-1 Receptor Agonist - Semaglutide

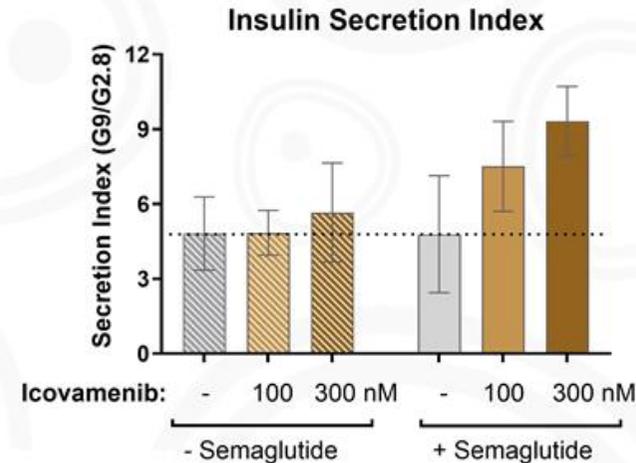
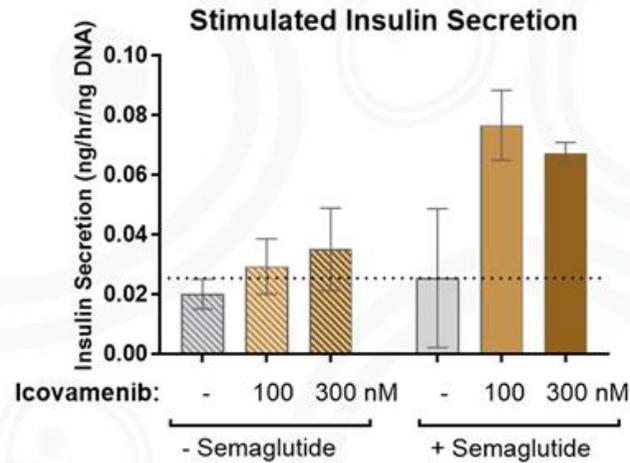
Cadaver derived human islets



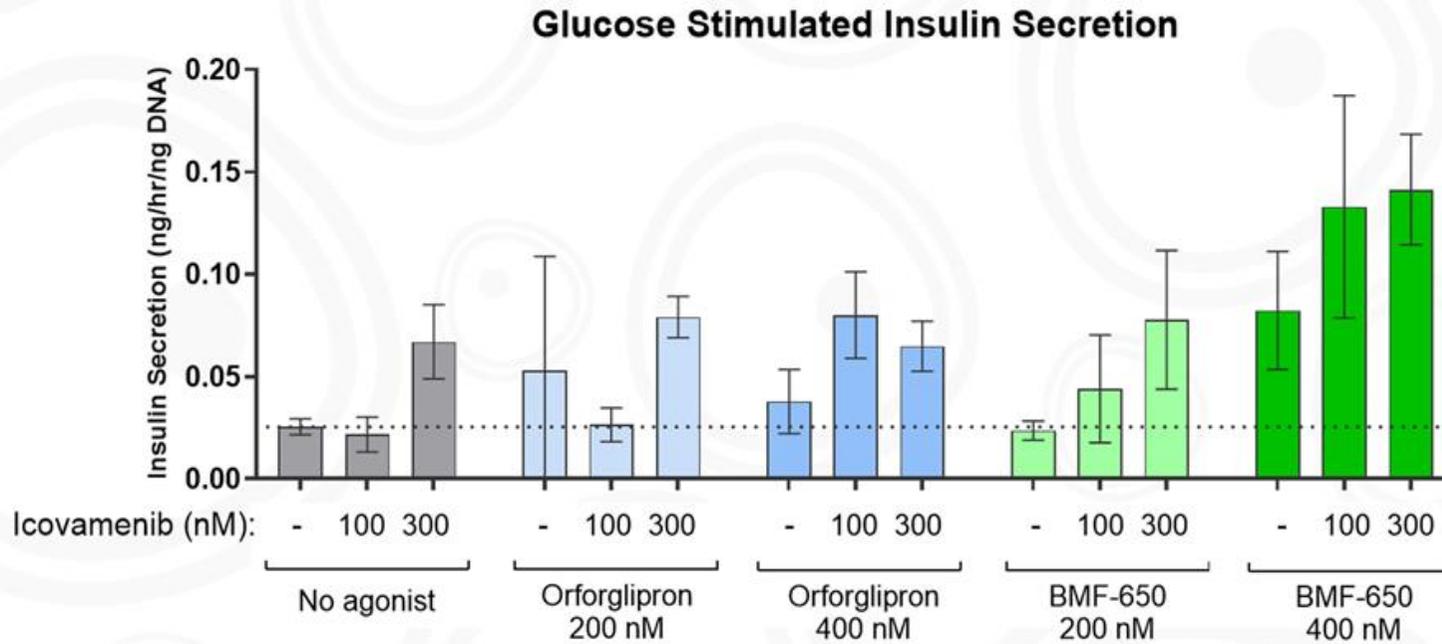
Non-diabetic donor:
41-year Hispanic male, BMI: 27.8, HbA1c 5.3%



Perform GSIS +/- **Semaglutide** (200nM)



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



New Treatment Potential in Diabetes and for Obesity

Combining Covalent Binding Menin Inhibitor 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's clinical development:

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

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

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

Attributes of Biomea’s GLP-1 Receptor Agonist Development Candidate:

- Less PK variability
- Greater bioavailability
- Greater protein binding
- Less side effects

Why a greater “Therapeutic Window”?

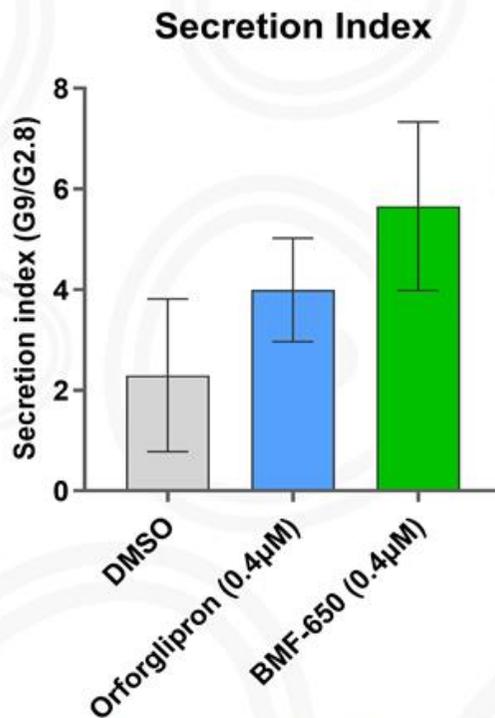
Only 3 of 10 patients in the real-world setting are staying on a GLP-1 based therapy after 12 months

BMF-650 Showed Favorable In Vitro On-Target Activity and Off-Target Selectivity

| | GLP-1 human EC ₅₀ | β-arrestin1 EC ₅₀ | β-arrestin2 EC ₅₀ |
|--------------|---------------------------------|---------------------------------|---------------------------------|
| BMF-650 | < 5 nM | > 10 μM | > 10 μM |
| orforglipron | < 5 nM | > 10 μM | > 10 μM |

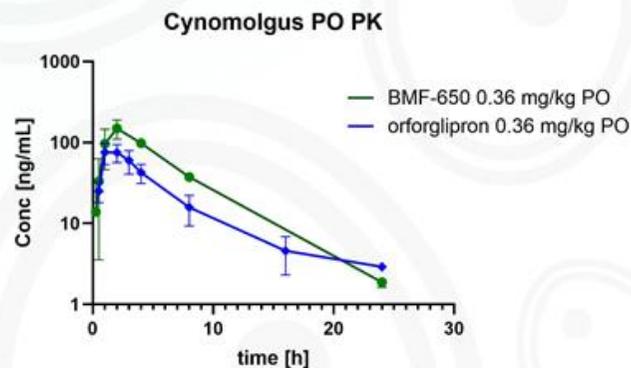
- Good potency on-target
- No off-target concerns from counter-screening assays

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

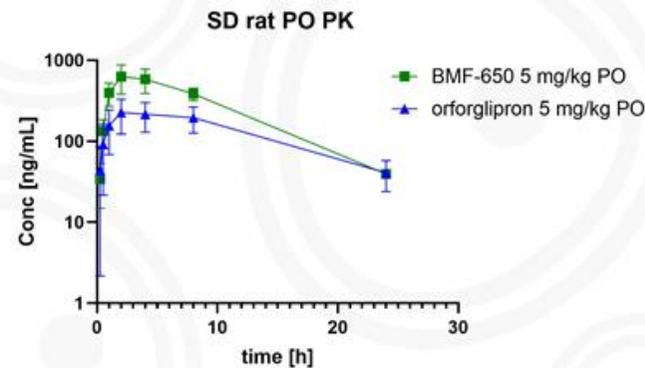


BMF-650 demonstrated improved insulin secretion vs orforglipron

Pharmacokinetics of BMF-650 Showed Very Good Non-Human Primate and Rodent Bioavailability with Low Inter-Individual Variability



| Compound | cynomolgus PO | T _{1/2} (h) | %F |
|--------------|---------------|----------------------|------|
| BMF-650 | 0.36 mg/kg | 3.66 | 54.0 |
| orforglipton | 0.36 mg/kg | 3.70 | 29.4 |



| Compound | rat PO | T _{1/2} (h) | %F |
|--------------|---------|----------------------|------|
| BMF-650 | 5 mg/kg | 5.14 | 32.6 |
| orforglipton | 5 mg/kg | 7.44 | 11.2 |

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

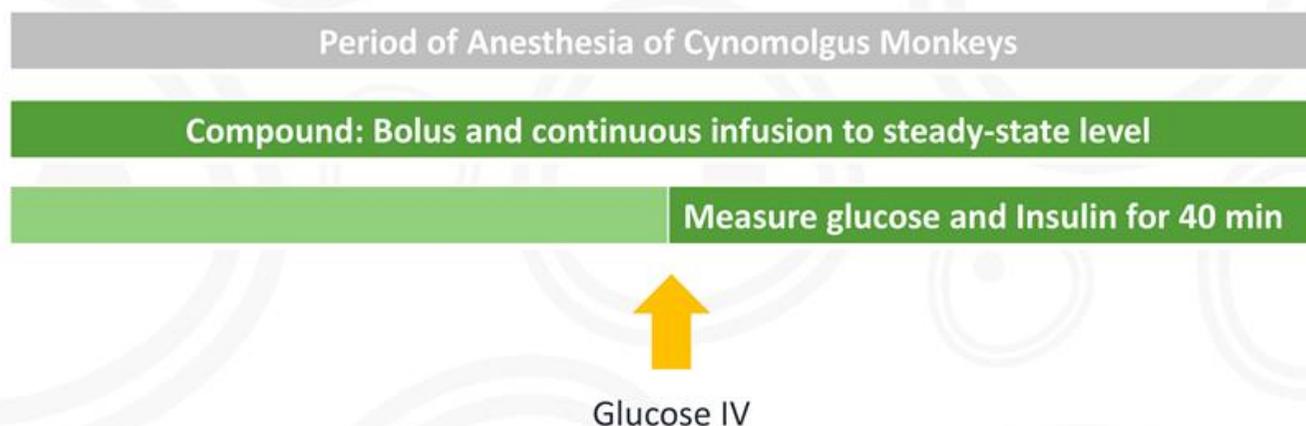
Dosages Used in Cynomolgus Monkeys are Species Dependent and Specific to Properties of Compounds

| | 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 |

Primary Evaluation of Preclinical Activity

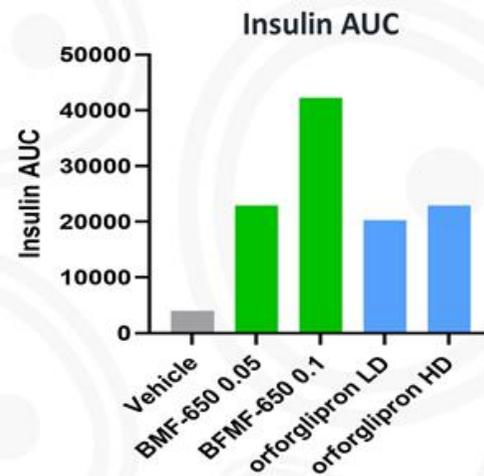
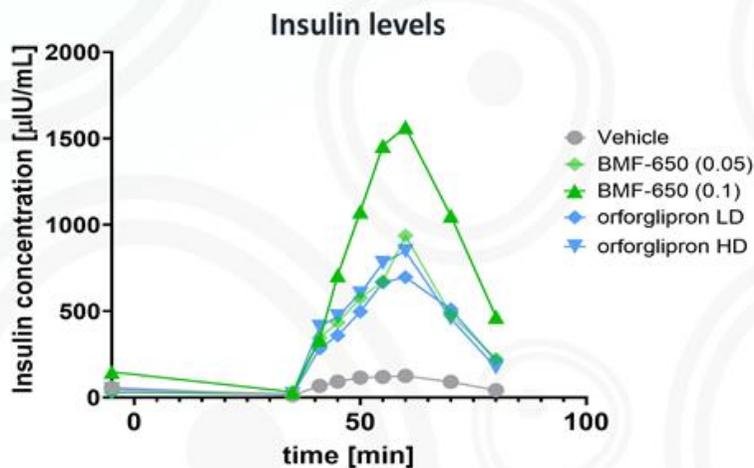
Set up of Intravenous Glucose Tolerance Test in Cynomolgus Monkeys

Cynomolgus monkeys (n=4) were anesthetized. Compounds were administered via IV route. Glucose was infused. Blood Glucose and Insulin levels were measured during the following 40 minutes window.



Study designed to capture both glucose lowering and insulin release properties

BMF-650 Potentiated Glucose-Stimulated Insulin Secretion in Cynomolgus Monkeys



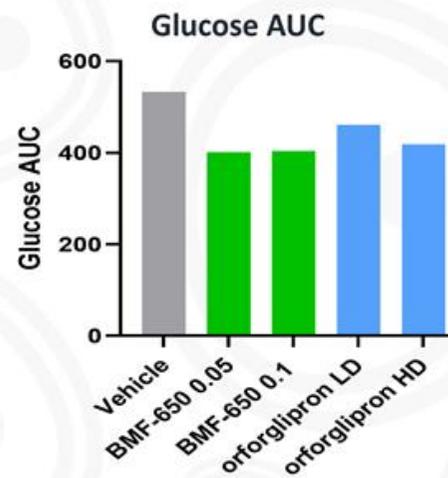
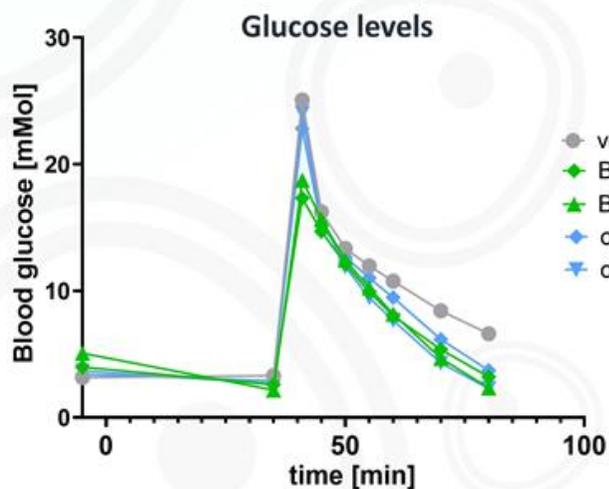
| | Vehicle | BMF-650 0.05mg/kg | BMF-650 0.1 mg/kg | orforglipron Low dose (lit)* | orforglipron High dose (lit)* |
|------------------------|---------|----------------------|----------------------|---------------------------------|----------------------------------|
| AUC Mean (N=4) | 4021 | 22930 | 42262 | 20304 | 22922 |
| Insulin improvement | 0 | 470% | 951% | 405% | 470% |

High and low dosing levels for orforglipron based on publications: 0.0018 and 0.0054 mg/kg

*PNAS November 24, 2020. vol. 117 no. 47 29959-29967

High levels of insulin release observed with small molecule GLP-1 R agonists

BMF-650 Potentiated Blood Glucose Reduction in Cynomolgus Monkeys



| | Vehicle | BMF-650 0.05mg/kg | BMF-650 0.1mg/kg | orforglipron Low dose (lit)* | orforglipron high dose (lit)* |
|------------------|---------|----------------------|---------------------|---------------------------------|----------------------------------|
| AUC Mean (N=4) | 533 | 401 | 404 | 461 | 418 |
| Glucose lowering | 0 | -25% | -24% | -14% | -22% |

High and low dosing levels for orforglipron based on publications: 0.0018 and 0.0054 mg/kg

*PNAS November 24, 2020. vol. 117 no. 47 29959-29967

Good glucose control observed with small molecule GLP-1 R agonists

Primary Evaluation of Preclinical Activity

Set up of Appetite Suppression Test in Cynomolgus Monkeys

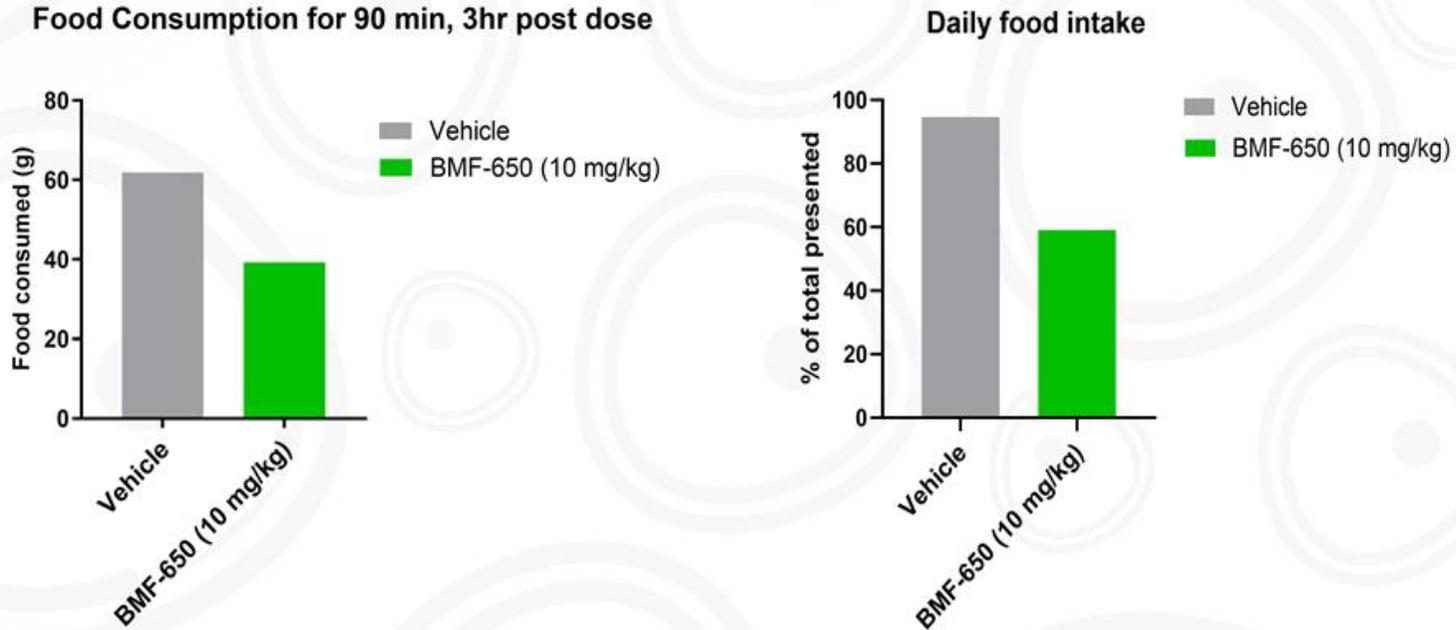
- Fasted monkeys (n=4) were dosed orally (PO) with compound. Food was presented starting at 3 hours post dose. Recorded food intake for time window 3 hours to 4.5 hours and the whole day.
- Design of study as multiday of active drug and multiday of washout



Study designed to capture both peak and daily food intake reduction.

BMF-650 Appetite Suppression in Cynomolgus Monkeys

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

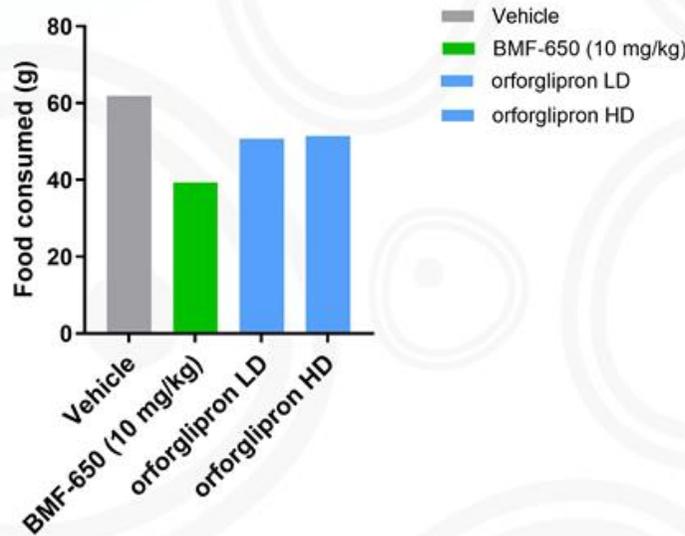


Food consumption tested daily in cynomolgus monkeys (n=4)
BMF-650 demonstrated good appetite suppression over 6 days

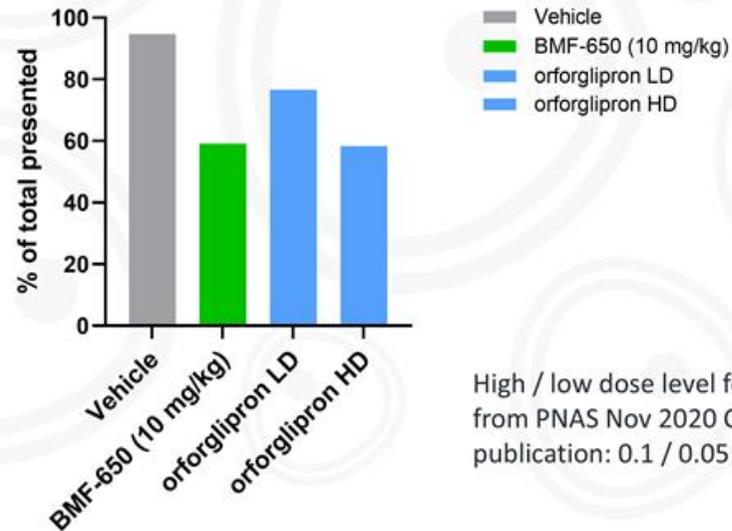
BMF-650 Appetite Suppression in Cynomolgus Monkeys Compares Well to Orforglipron

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

Projected Timeline for BMF-650 with IND Filing Anticipated in 2H 2025



Program was placed on a timeline targeting IND submission in 2H 2025
Development plan for obesity and type 2 diabetes

THANK YOU



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