



**GLP-131 Phase 1 Study
of BMF-650 in Otherwise
Healthy Overweight
or Obese Adult Participants**

Week 4 Topline Results

October 13, 2026

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Agenda

Opening Remarks

Ramses Erdtmann

Co-Founder, Chief Operating Officer & President, Biomea Fusion

Design Hypothesis for BMF-650

Thorsten Kirschberg, PhD

Executive VP, Research, Biomea Fusion

GLP-131 Topline Results

Juan Pablo Frías, MD

Co-Chair of the Scientific Advisory Board, Biomea Fusion

Executive Summary

Mick Hitchcock, PhD

Interim Chief Executive Officer & Board Member, Biomea Fusion

Q & A

Ramses Erdtmann

Co-Founder, Chief Operating Officer & President, Biomea Fusion

Opening Remarks

A large and growing market with a meaningful persistence challenge

GLP-1 therapies have transformed obesity treatment, but broad adoption and long-term persistence remain distinct opportunities

100M+

U.S. adults living
with obesity

~40% of the U.S. adult population

~1B

Adults globally projected
to live with obesity by 2030

A chronic disease with substantial
cardiometabolic consequences

~11M

Unique U.S. patients using
GLP-1 based therapies across
indications

As of Q2 2025, highlighting rapid
adoption of the class

Treatment tolerability seems to prevent long-term persistence

~65%

Of patients without T2D discontinued use within one

Large U.S. real-world cohort of >125,000 adults with overweight or obesity

Sources: CDC/NCHS, U.S. adult obesity prevalence (Aug 2021–Aug 2023; updated Feb 2026); World Obesity Atlas 2025; IQVIA, “Obesity Deep Dive” (Sep 2025); Rodriguez et al., JAMA Network Open (2025).

Opportunities for a next-generation GLP-1 Receptor Agonist

More tolerable therapy

Reduce adverse events that can limit treatment

Easier and quicker titration

Reach the targeted dose quicker and with fewer dose increases to achieve simplified administration and early adherence

Persistent weight management

Support continuation of treatment with convenient dosing and manageable tolerability

Thorsten Kirschberg, PhD

Executive VP, Research, Biomea Fusion

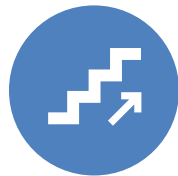
Design Hypothesis for BMF-650

A potential differentiated oral next-generation GLP-1 receptor agonist designed to separate GI adverse effects from weight loss



Oral administration

Convenience without injections



One-step titration

Faster path to maintenance dose and efficacy



Designed for improved GI tolerability

Potential for better tolerability and adherence



Built for persistent use

Intended for continued use

BMF-650 was designed to reduce on-target agonism to achieve long-term tolerability

Compound	GLP-1 human EC ₅₀	β-arrestin EC ₅₀
BMF-650	2.6 nM	> 10 μM
orforglipron	0.1 nM	> 10 μM

BMF-650 is designed as a biased small molecule GLP-1 receptor agonist, to selectively engage GLP-1 signaling

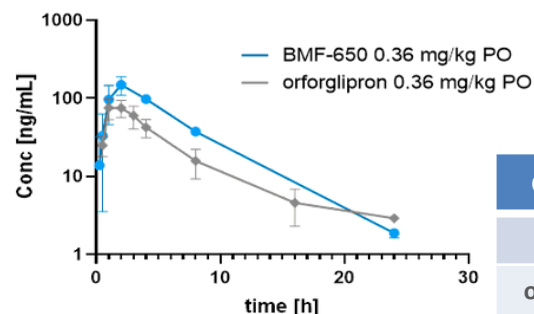
Designed with reduced on-target potency to achieve less concentrated agonism

No off-target activity of concern identified in the counter-screening panels

Wang X, et al. ObesityWeek® 2025; Poster 085.

Pharmacokinetics showed enhanced preclinical bioavailability signals with low variability

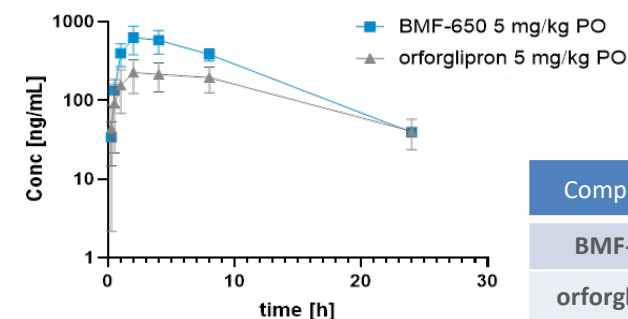
CYNOMOLGUS MONKEY PO PK DATA



BMF-650 showed approx. 2-fold greater oral bioavailability in comparison to orforglipron

Compound	cyno PO	%F
BMF-650	0.36 mg/kg	54.0
orforglipron	0.36 mg/kg	29.4

SPRAGUE-DAWLEY RAT PO PK DATA



BMF-650 showed approx. 3-fold greater oral bioavailability in comparison to orforglipron

Compound	rat PO	%F
BMF-650	5 mg/kg	32.6
orforglipron	5 mg/kg	11.2

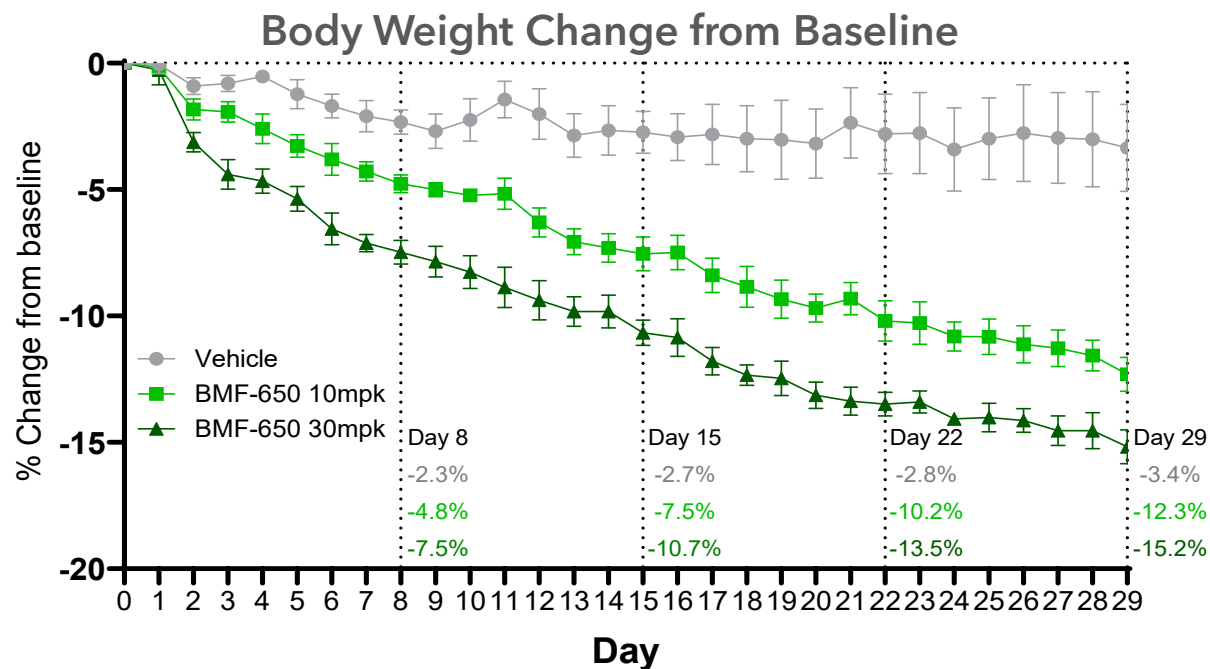
Wang X, et al. ObesityWeek® 2025; Poster 085.

Favorable PK observed across species with high oral bioavailability and long exposure



BMF-650 demonstrated robust, dose-dependent weight loss in obese monkeys with low rates of emesis

BMF-650 up to ~15% body weight reduction after 28 days



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

Week	Emesis (Vomiting)
1	18.2%*
2	7.0%
3	5.6%
4	1.4%

*One monkey (#3) in the low-dose cohort accounted for 12 of the 23 total events. % calculated for 70 dosing events/week

With 280 active dosing occurrences, there were a total of 23 emesis events (8.2%) balanced across both dosing cohorts.

A next-generation oral small-molecule GLP-1 RA with a differentiated profile designed to separate GI effects from weight loss

Broader intestinal absorption

Intended to reduce localized concentration peaks within the GI tract, and to promote better tolerated absorption across a broader intestinal surface and time window

Improved oral bioavailability

Intended to achieve systemic exposure with less unabsorbed drug

Gradual, sustained systemic exposure

Designed to limit peak-to-trough fluctuations to avoid uneven systemic GLP-1 receptor stimulation

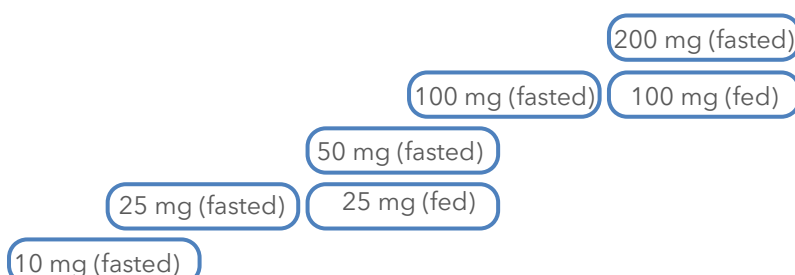
Juan Pablo Frías, MD

Co-Chair of the Scientific Advisory Board, Biomea Fusion

GLP-131 Phase 1 Topline Results

GLP-131: Phase 1 study design

Randomized, double-blind, placebo-controlled study evaluating safety, tolerability, and weight reduction with BMF-650 in overweight or obese participants

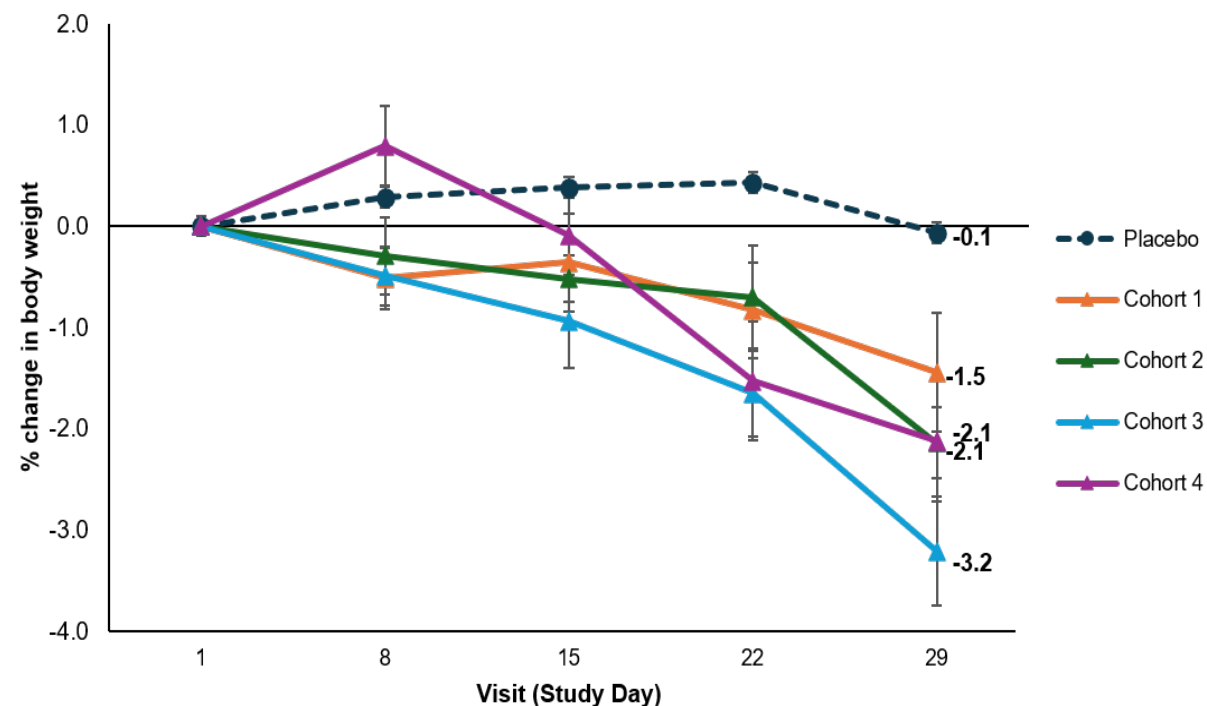
Single Ascending Dose (SAD) Phase 1a		Multiple Ascending Dose (MAD) Phase 1b								
Primary & Secondary Objectives	Safety and tolerability, PK, PD, and food effect	Safety and tolerability, and efficacy (weight-loss)								
Eligibility	Healthy overweight or obese participants (BMI 25.0–40.0 kg/m²)	Healthy obese participants (BMI 30.0–45.0 kg/m²)								
Design	N=40 5 cohorts x    BMF-650 active drug  placebo	N=40 4 cohorts x  COHORT Wk 1 → Wk 2 → Wk 3 → Wk 4 <table><tr><td>4</td><td>75 mg → 200 mg → 400 mg → 400 mg</td></tr><tr><td>3</td><td>75 mg → 150 mg → 300 mg → 300 mg</td></tr><tr><td>2</td><td>50 mg → 100 mg → 200 mg → 200 mg</td></tr><tr><td>1</td><td>10 mg → 25 mg → 50 mg → 100 mg</td></tr></table>	4	75 mg → 200 mg → 400 mg → 400 mg	3	75 mg → 150 mg → 300 mg → 300 mg	2	50 mg → 100 mg → 200 mg → 200 mg	1	10 mg → 25 mg → 50 mg → 100 mg
4	75 mg → 200 mg → 400 mg → 400 mg									
3	75 mg → 150 mg → 300 mg → 300 mg									
2	50 mg → 100 mg → 200 mg → 200 mg									
1	10 mg → 25 mg → 50 mg → 100 mg									

Baseline Demographics & Characteristics

Doses for Weeks 1-4	Active BMF-650				MAD Cohorts 1-4 Total (N=32)	Pooled Placebo (N=8)
	Cohort 1 10/25/50/100 mg (N=8)	Cohort 2 50/100/200/200 mg (N=8)	Cohort 3 75/150/300/300 mg (N=8)	Cohort 4 75/200/400/400 mg (N=8)		
Sex, female, n (%)	6 (75)	6 (75)	3 (38)	4 (50)	19 (59)	4 (50)
Age, years, mean	49.5	45.6	49.9	42.3	46.8	40.3
Weight, kg, mean	97.0	109.1	96.1	97.6	100.0	111.1
BMI, kg/m ² , mean	34.8	36.2	31.9	34.4	34.3	35.9

Clinical efficacy - weight reduction

	Mean percentage change in body weight from baseline at Day 29
Pooled Placebo (n=8)	-0.1%
Cohort 1 (n=8) (10/25/50/100 mg)	-1.5%
Cohort 2 (n=8) (50/100/200/200 mg)	-2.1%
Cohort 3 (n=8) (75/150/300/300 mg)	-3.2%
Cohort 4 (n=8) (75/200/400/400 mg)	-2.1%



Data are mean ± SE

Analysis of weekly weight reduction

	Pooled PLACEBO n=8	Cohort 1 10 → 25 → 50 → 100	Cohort 2 50 → 100 → 200 → 200	Cohort 3 75 → 150 → 300 → 300	Cohort 4 75 → 200 → 400 → 400
Week 1	+0.33 kg	10 mg -0.47 kg	50 mg -0.41 kg	75 mg -0.45 kg	75 mg +0.76 kg
Week 2	+0.06 kg	25 mg +0.12 kg	100 mg -0.20 kg	150 mg -0.39 kg	200 mg -0.83 kg
Week 3	+0.12 kg	50 mg -0.48 kg	200 mg -0.23 kg	300 mg -0.70 kg	400 mg -1.37 kg
Week 4	-0.82 kg	100 mg -0.63 kg	200 mg -1.57 kg	300 mg -1.47 kg	400 mg -0.63 kg
TOTAL Weight Loss	-0.10 kg	-1.46 kg	-2.41 kg	-3.01 kg	-2.07 kg

14 of 16 weekly dosing cohorts showed incremental weekly absolute weight reduction.

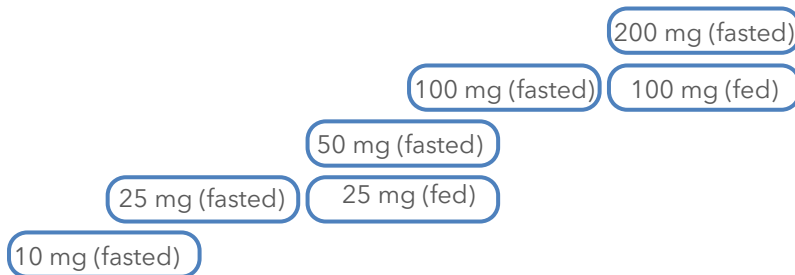
The average weight loss per week when dosed at 200 mg or higher dose was **0.97 kg / week.**

Placebo achieved a **0.1 kg** weight reduction after 4 weeks. Dose Cohort 3 showed a weight reduction of **3.0 kg after 4 weeks.**

PK results from Week 1 in Cohort 4 raised suspicion that patients were possibly not taking the drug, so a Cohort 5 was initiated under confinement.

GLP-131: Phase 1 study design + dose cohort 5

Randomized, double-blind, placebo-controlled study, evaluating safety, tolerability, and weight reduction with BMF-650 in overweight or obese participants

Single Ascending Dose (SAD) Phase 1a		Multiple Ascending Dose (MAD) Phase 1b												
Primary & Secondary Objectives	Safety and tolerability, PK, PD and food effect	Safety and tolerability, and efficacy (weight-loss)												
Eligibility	Healthy overweight or obese participants (BMI 25.0–40.0 kg/m²)	Healthy obese participants (BMI 30.0–45.0 kg/m²) Cohort 5 conducted under confinement to evaluate one-step titration regimen												
Design	N=40 5 cohorts x   Legend:  BMF-650 active drug  placebo	N=50 5 cohorts x  <table><tr><th>COHORT</th><th>Wk 1 → Wk 2 → Wk 3 → Wk 4</th></tr><tr><td>5</td><td>200 mg → 400 mg → 400 mg → 400 mg</td></tr><tr><td>4</td><td>75 mg → 200 mg → 400 mg → 400 mg</td></tr><tr><td>3</td><td>75 mg → 150 mg → 300 mg → 300 mg</td></tr><tr><td>2</td><td>50 mg → 100 mg → 200 mg → 200 mg</td></tr><tr><td>1</td><td>10 mg → 25 mg → 50 mg → 100 mg</td></tr></table>	COHORT	Wk 1 → Wk 2 → Wk 3 → Wk 4	5	200 mg → 400 mg → 400 mg → 400 mg	4	75 mg → 200 mg → 400 mg → 400 mg	3	75 mg → 150 mg → 300 mg → 300 mg	2	50 mg → 100 mg → 200 mg → 200 mg	1	10 mg → 25 mg → 50 mg → 100 mg
COHORT	Wk 1 → Wk 2 → Wk 3 → Wk 4													
5	200 mg → 400 mg → 400 mg → 400 mg													
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3	75 mg → 150 mg → 300 mg → 300 mg													
2	50 mg → 100 mg → 200 mg → 200 mg													
1	10 mg → 25 mg → 50 mg → 100 mg													

Baseline demographics & characteristics + dose cohort 5

Doses for Weeks 1-4	Active BMF-650					MAD BMF-650 Total (N=40)	Pooled Placebo (N=10)
	Cohort 1 10/25/50/100 mg (N=8)	Cohort 2 50/100/200/200 mg (N=8)	Cohort 3 75/150/300/300 mg (N=8)	Cohort 4 75/200/400/400 mg (N=8)	Cohort 5 200/400/400/400 mg (N=8)		
Sex, female, n (%)	6 (75)	6 (75)	3 (38)	4 (50)	5 (63)	24 (60)	5 (50)
Age, years, mean	49.5	45.6	49.9	42.3	41.6	45.8	37.4
Weight, kg, mean	97.0	109.1	96.1	97.6	102.1	100.4	107.2
BMI, kg/m ² , mean	34.8	36.2	31.9	34.4	34.0	34.3	35.3

Analysis of weekly weight reduction

Cohort 5 in-patient
confinement

	Pooled PLACEBO n=8	Cohort 1 10 → 25 → 50 → 100	Cohort 2 50 → 100 → 200 → 200	Cohort 3 75 → 150 → 300 → 300	Cohort 4 75 → 200 → 400 → 400	Cohort 5 200 → 400 → 400 → 400
Week 1	+0.33 kg	10 mg -0.47 kg	50 mg -0.41 kg	75 mg -0.45 kg	75 mg +0.76 kg	200 mg -1.72 kg
Week 2	+0.06 kg	25 mg +0.12 kg	100 mg -0.20 kg	150 mg -0.39 kg	200 mg -0.83 kg	400 mg -1.38 kg
Week 3	+0.12 kg	50 mg -0.48 kg	200 mg -0.23 kg	300 mg -0.70 kg	400 mg -1.37 kg	400 mg -1.39 kg
Week 4	-0.82 kg	100 mg -0.63 kg	200 mg -1.57 kg	300 mg -1.47 kg	400 mg -0.63 kg	400 mg -1.71 kg
TOTAL Weight Los	-0.10 kg	-1.46 kg	-2.41 kg	-3.01 kg	-2.07 kg	-6.20 kg

Cohort 5 used confinement to monitor dosing adherence, with 200 mg once daily for one week, then 400 mg once daily for three weeks.

Mean weight loss with BMF-650 was **1.55 kg/week**, and similar weight loss with placebo (n=2).

All participants were provided 2,100 kcal/day. The 2 placebo participants consumed approximately 33% of the presented food, complicating interpretation of weight loss under confinement.

Primary Endpoint: Overall Treatment-Emergent Adverse Events (TEAEs)

	Active BMF-650					MAD BMF-650 Total (N=40)	Pooled Placebo (N=10)
	Cohort 1 10/25/50/100 mg (N=8)	Cohort 2 50/100/200/200 mg (N=8)	Cohort 3 75/150/300/300 mg (N=8)	Cohort 4 75/200/400/400 mg (N=8)	Cohort 5 200/400/400/400 mg (N=8)		
Doses for Weeks 1-4							
Participants, n(%)							
Any TEAE	6 (75.0)	4 (50.0)	5 (62.5)	6 (75.0)	7 (87.5)	28 (70.0)	4 (40.0)
Mild (Grade 1)	3 (37.5)	3 (37.5)	4 (50.0)	5 (62.5)	5 (62.5)	20 (50.0)	4 (40.0)
Moderate (Grade 2)	3 (37.5)	1 (12.5)	1 (12.5)	1 (12.5)	2 (25.0)	8 (20.0)	0

0	Severe TEAE (Grade 3)	0	Serious TEAE	0	TEAE-leading to dose modification	0	TEAE-leading to study discontinuation
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All TEAEs were mild or moderate and there were no dose modifications or discontinuations related to BMF-650.
TEAEs were not associated with dose escalation, dosing cohort, or time at a given dose.

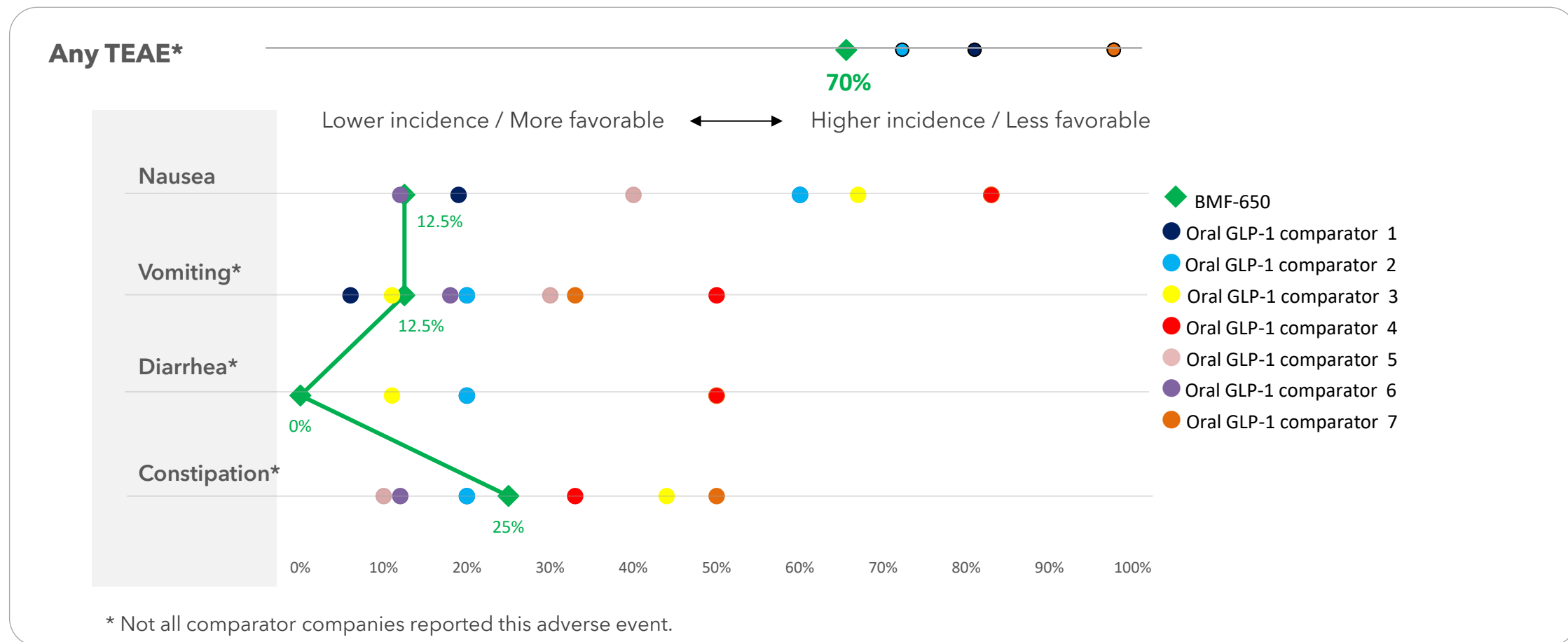
Select Gastrointestinal TEAEs

Doses for Weeks 1-4 Participants, n (%)	Active BMF-650					MAD BMF-650 Total (N=40)	Pooled Placebo (N=10)
	Cohort 1 10/25/50/100 mg (N=8)	Cohort 2 50/100/200/200 mg (N=8)	Cohort 3 75/150/300/300 mg (N=8)	Cohort 4 75/200/400/400 mg (N=8)	Cohort 5 200/400/400/400 mg (N=8)		
Nausea	0	3 (37.5)	1 (12.5)	2 (25.0)	1 (12.5)	7 (17.5)	0
Constipation	0	1 (12.5)	1 (12.5)	0	2 (25.0)	4 (10.0)	1 (10.0)
Vomiting	1 (12.5)	0	1 (12.5)	0	1 (12.5)	3 (7.5)	0
Diarrhea	0	1 (12.5)	1 (12.5)	0	0	2 (5.0)	1 (10.0)

The select GI-related TEAEs were all Grade 1 AEs in the highest dose level cohort.

BMF-650 at highest dose level vs late-stage oral GLP-1 Phase 1 disclosures

Select GI tolerability



Class-like changes in liver enzymes, fasting glucose and heart rate

Doses for Weeks 1-4	Active BMF-650					MAD BMF-650 Total (N=40)	Pooled Placebo (N=10)
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5		
	10/25/50/100 mg (N=8)	50/100/200/200 mg (N=8)	75/150/300/300 mg (N=8)	75/200/400/400 mg (N=8)	200/400/400/400 mg (N=8)		
Alanine aminotransferase (ALT), U/L	-1.6	-1.4	-7.4	-9.9	-9.4	-5.9	-6.1
Aspartate aminotransferase (AST), U/L	-1.9	-1.7	-2.8	-3.7	-3.8	-2.8	-2.9
Fasting glucose, mg/dL	-7.1	-5.9	-7.2	-14.7	-11.4	-9.2	-3.5
Heart rate, beats/min	0.6	8.1	10.4	3.7	9.0	6.4	0.8

Data shown represents mean change from baseline to Day 28

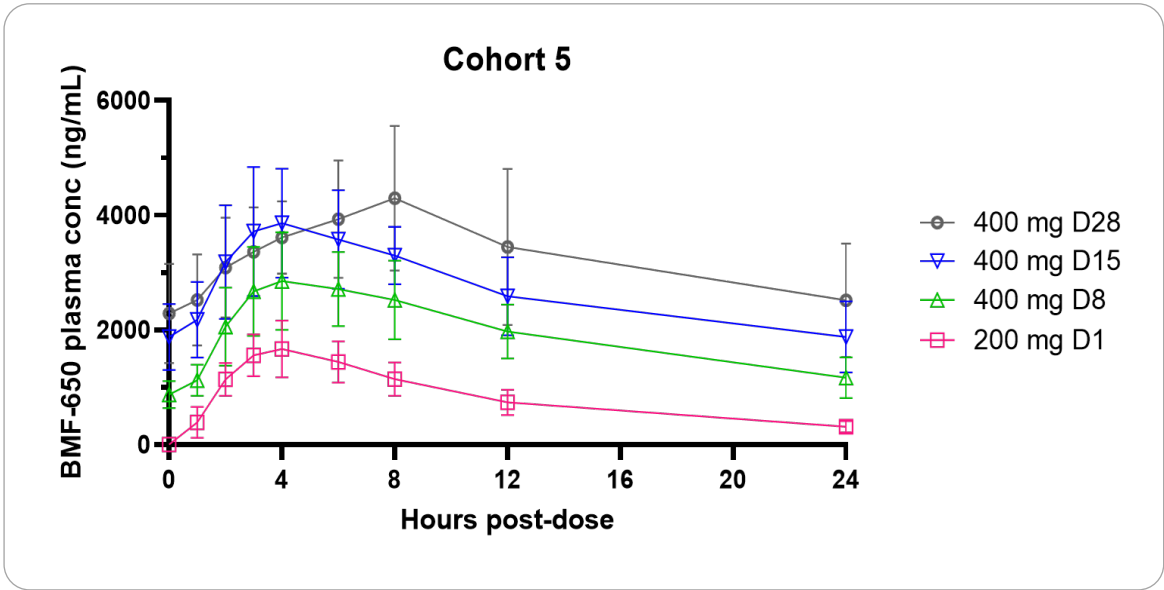
No adverse events involving ALT/AST elevations or heart rate were reported
Reductions in fasting glucose were observed for all doses of BMF-650

BMF-650 delivered target exposure with low peak to trough ratio in human PK

Selected PK parameters for Cohort 5 Day 28

	Cohort 5 Day 28
C _{max} (peak plasma concentration)	4400 ng/mL (± 26.4%)
C _{min} (trough plasma concentration)	2520 ng/mL (± 39.4%)
Peak to trough ratio	1.7
AUC _{0-24hrs}	79000 hr*ng/mL (± 31.8%)

* Preliminary PK analysis (mean).



* Preliminary PK analysis (mean).

Human PK for BMF-650 aligned well with nonclinical predictions and showed low peak/trough ratio
Observed human PK exposure matched favorable monkey exposure in the respective weight-loss study

Phase 1 findings provide support for the BMF-650 design hypothesis

Rapid one-step titration to 400 mg is well tolerated

BMF-650 reached the target dose of 400 mg QD via a single titration step design post week 1, supporting a potentially simple and practical dosing paradigm

Sustained and meaningful weight reduction observed at higher dose regimens

Cohort 5 demonstrated mean weight loss at 400 mg across consecutive weeks (−1.4, −1.4 and −1.7 kg/week), reaching 6.1% at week 4, with no evidence of attenuation over the observed treatment period

Encouraging GI tolerability profile

No serious TEAEs, no TEAE-related dose modifications and no TEAE-related study discontinuations occurred across active MAD cohorts, supporting longer-duration evaluation

Next Steps: Advancing BMF-650 development while optimizing the clinical profile

Clinical Findings

- Highest dose achieved with only a single titration step while maintaining favorable tolerability
- Weight loss as expected in line with other GLP-1 agents
- Overall, generally well tolerated with no exposure-related safety signals

BMF-650 Next Steps

- Initiate longer-term toxicology studies to support Phase 2 dosing
- Advance Phase 2 development planning incl. a “no-titration” regimen at 400 mg QD

Mick Hitchcock, PhD

Interim Chief Executive Officer & Board Member, Biomea Fusion

Executive Summary

Q & A