Pemvidutide (ALT-801), a novel GLP-1/glucagon dual receptor agonist, achieves rapid and potent reductions in body weight and liver fat: Results of a placebo-controlled, double-blind, first-in-human (FIH) clinical trial

Stephen A. Harrison[1], John Nestor[2], Sarah K. Browne[3], Jacques D. Payne[3], Staci M. Steele[3], Robert Casper[3], Anvar Suyundikov[3], Vyjayanthi Krishnan[3], M. Scot Roberts[3], M. Scott Harris[3]

[1] Pinnacle Research, San Antonio, TX, USA; [2] Spitfire Pharma, South San Francisco, CA, USA; [3] Altimmune, Inc., Gaithersburg, MD, USA

Presenter Disclosures

Stephen Harrison

- Scientific advisor or consultant to: Akero, Alentis, Altimmune, Arrowhead, Axcella, BMS, Echosens, Galectin, Gilead, Hepion, Hepagene, HistoIndex, Intercept, Madrigal, Medpace, Metacrine, NGM Bio, Northsea, Novartis, Novo Nordisk, PathAI, Perspectum, Poxel, Sagimet, Terns, Viking
- Stock options: Akero, Cirius, Galectin, Genfit, Hepion, HistoIndex, Metacrine, NGM Bio, Northsea
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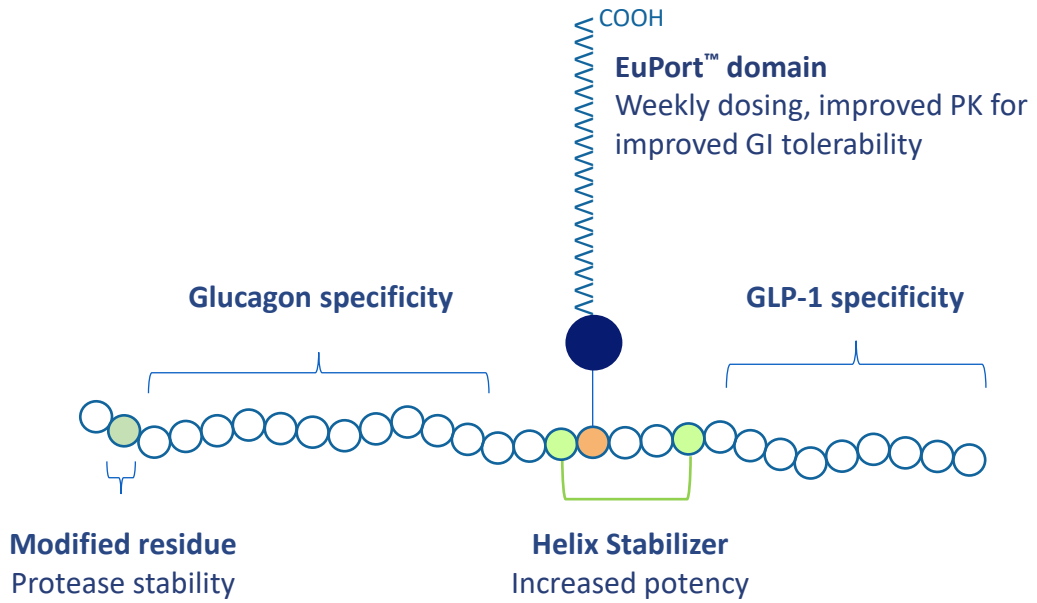
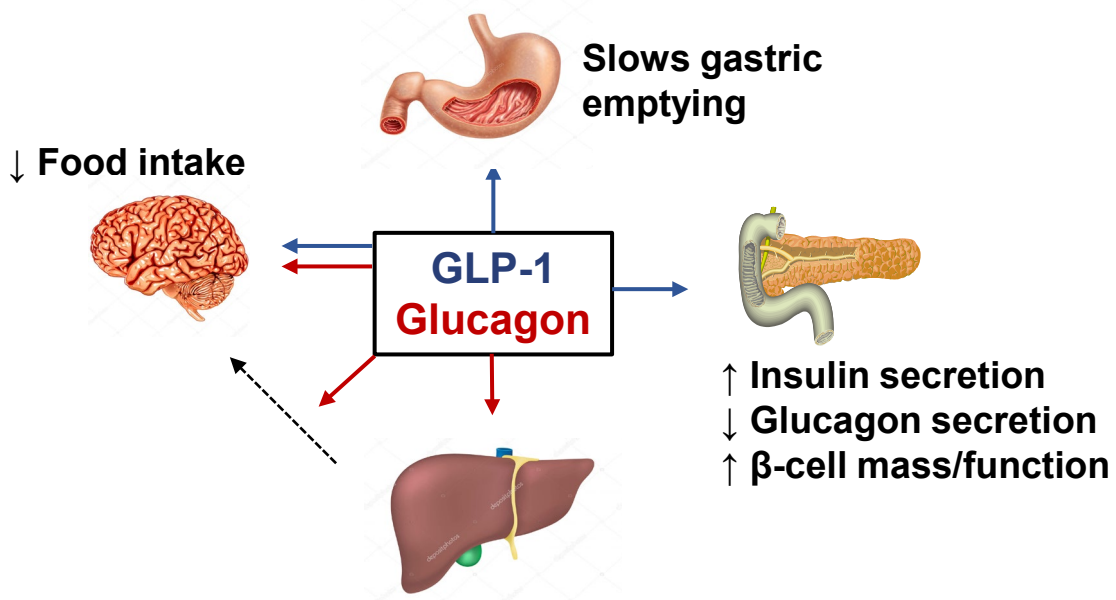
John J. Nestor is a consultant to Altimmune, Inc.

Sarah K. Browne, Jacques D. Payne, Staci M. Steele, Robert Casper, Anvar Suyundikov, Vyjayanthi Krishnan, M. Scot Roberts, and M. Scott Harris are employees of Altimmune, Inc.

Pemvidutide (ALT-801)

Balanced (1:1) GLP-1:glucagon dual receptor agonist





↑ Glucose, FGF21, bile acid production
↑ TG lipolysis, Fatty acid oxidation, ketogenesis
↓ Hepatic *de novo* lipogenesis
↑ LDL receptor activity (↓plasma LDL-C)
↑ Energy expenditure (hepatic, brain: SNS, FGF21, BA-FXR)

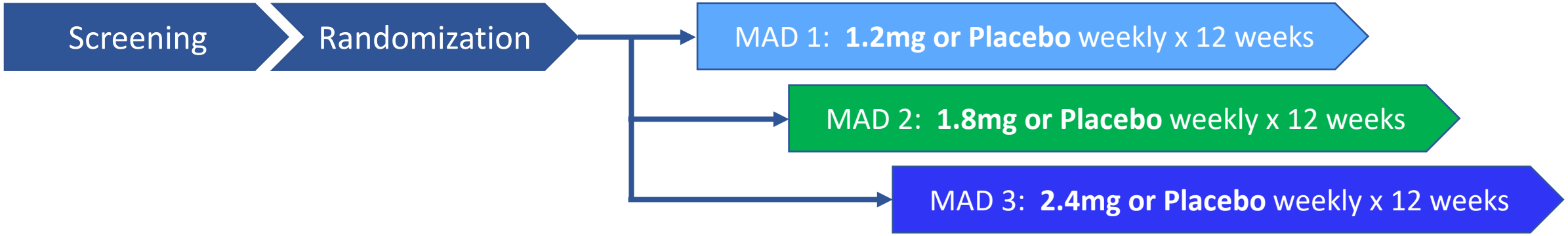
Pemvidutide Phase 1 SAD/MAD Trial Design

SAD/MAD Design

Randomized, double-blind placebo-controlled study
70 subjects with overweight/obesity (BMI 25 - 40 kg/m^2)

Multiple ascending dose (MAD) phase (n = 34)

4:1 randomization (pemvidutide: placebo), with placebos pooled
No caloric restriction or lifestyle intervention
No dose titration
Endpoints included pharmacokinetics, biologic activity and safety



Characteristics of Study Participants (MAD Phase)

Baseline Characteristics		Treatment			
		1.2 mg (n=7)	1.8 mg (n=9)	2.4 mg (n=11)	Pooled placebo (n=7)
Age, years	mean (SD)	27.7 (11)	32.0 (11)	31.4 (12)	35.3 (12)
BMI, kg/m^2	mean (SD)	30.0 (4)	30.1 (4)	31.8 (3)	31.0 (4)
Sex	female, n (%)	1 (14%)	4 (44%)	7 (64%)	4 (57%)
HbA1c, %	mean (SD)	5.3 (0.1)	5.5 (0.2)	5.3 (0.2)	5.3 (0.2)
Total cholesterol, mg/dL	mean (SD)	207.7 (46)	216.1 (33)	190.2 (42)	187.3 (42)
LDL cholesterol, mg/dL	mean (SD)	134.2 (33)	146.1 (28)	123.0 (33)	109.9 (34)
Triglycerides, mg/dL	mean (SD)	159.3 (81)	114.1 (57)	112.6 (54)	117.6 (24)
HDL cholesterol, mg/dL	mean (SD)	42.5 (5.1)	46.8 (7.1)	44.3 (10.0)	44.7 (8.1)

Study Disposition (MAD Phase)

No withdrawals for adverse events

Characteristic		Treatment			
		1.2 mg	1.8 mg	2.4 mg	Pooled placebo
Safety population[1]	n (%)	7 (100%)	9 (100%)	11 (91.7%)	7 (100%)
Completed study	n (%)	6 (86%)	9 (100%)	9 (82%)	5 (71%)
Early withdrawal	n (%)	1 (14%)	0 (0%)	2 (18%)	2 (29%)
Lost to follow-up	n (%)	0 (0%)	0 (0%)	0 (0%)	1 (14%)
Withdrawal of consent	n (%)	1 (14%)	0 (0%)	2 (18%)	1 (14%)
Due to adverse event	n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

[1] Subjects who were randomized, dosed and had one or more post-dose assessments

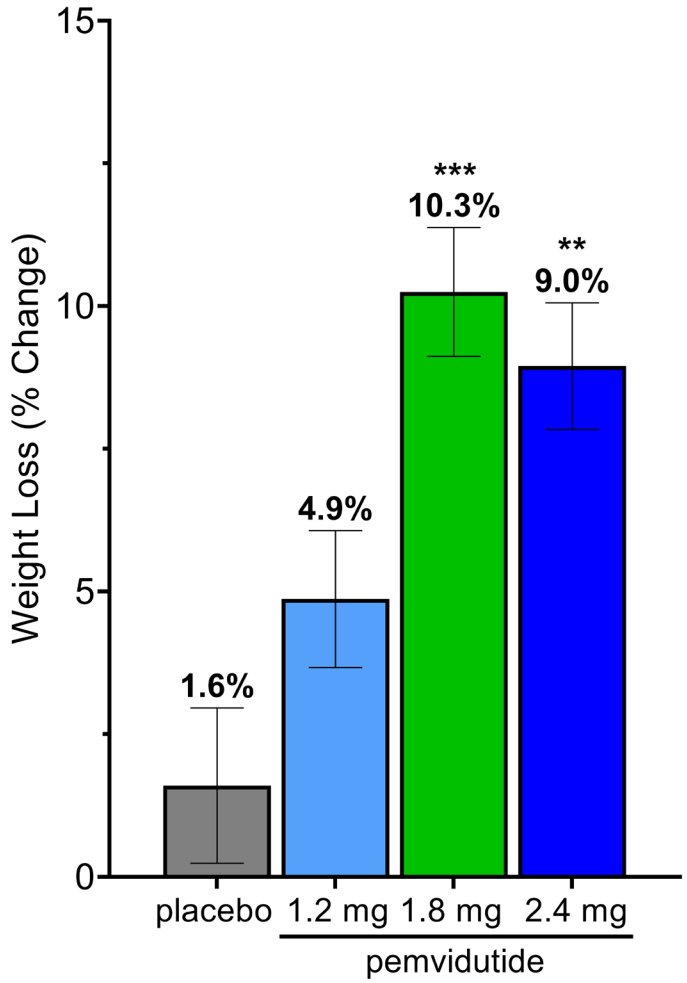
Pemvidutide PK Profile

Long half-life supports weekly dosing

Lower C_{max} and delayed T_{max} may enhance tolerability

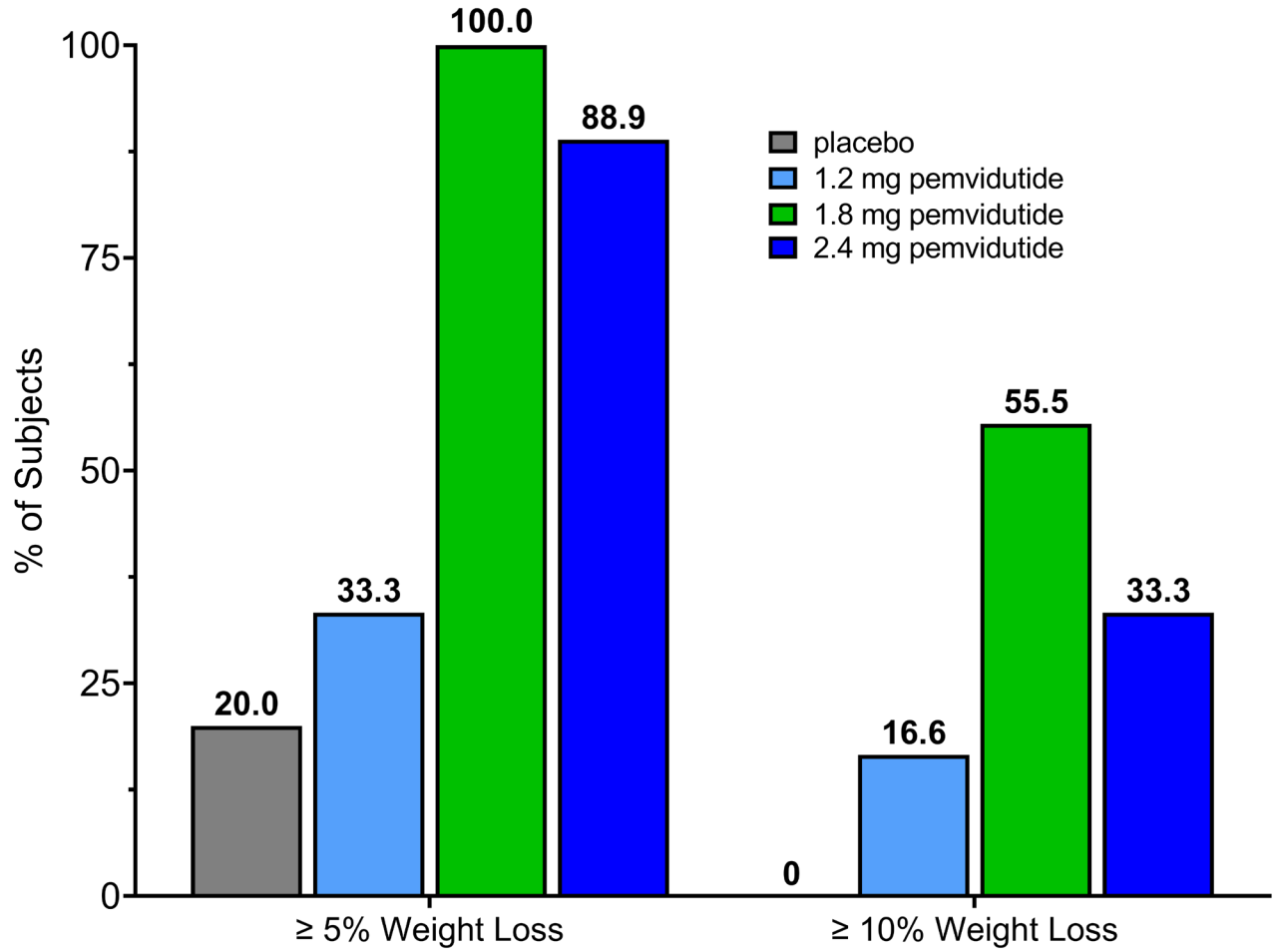
PK PARAMETER	ALT-801 1.8 mg SC
Peak concentration (C_{max})	27.1 nmol/L
Area under curve (AUC) $_{0\text{-}168}$	3400 nmol•hr
Half-life ($t_{1/2}$)	110 hrs
Time to peak concentration (T_{max})	70 hrs

Weight Loss at Week 12 – Group Responses

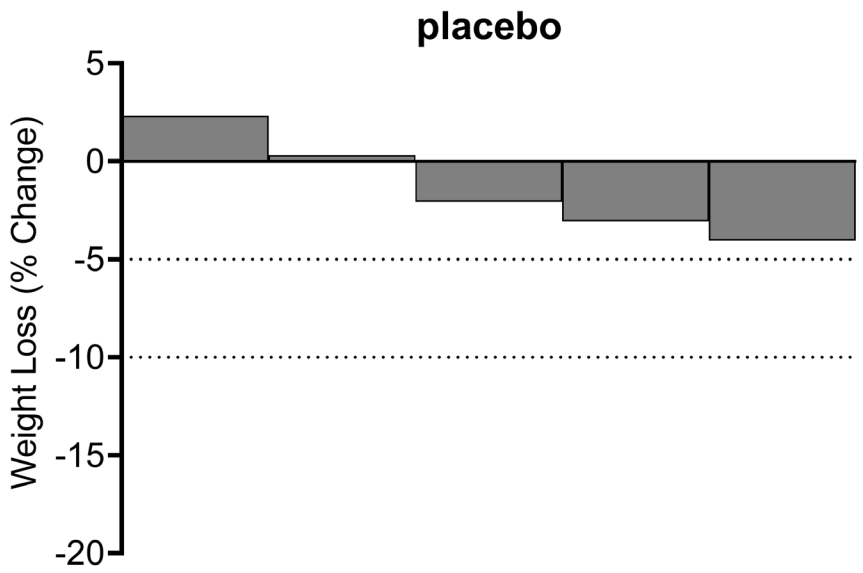


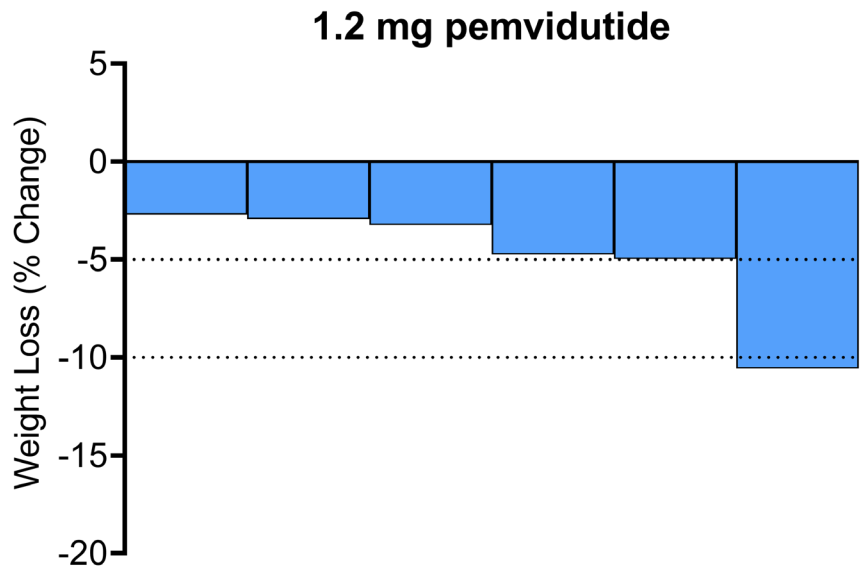
Mean ± SEM

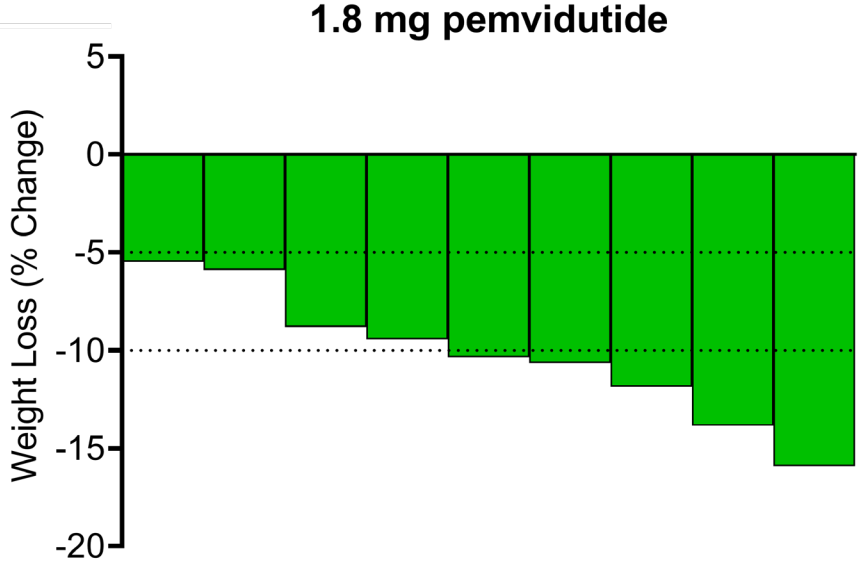
** p < 0.01, *** p < 0.001 vs. placebo

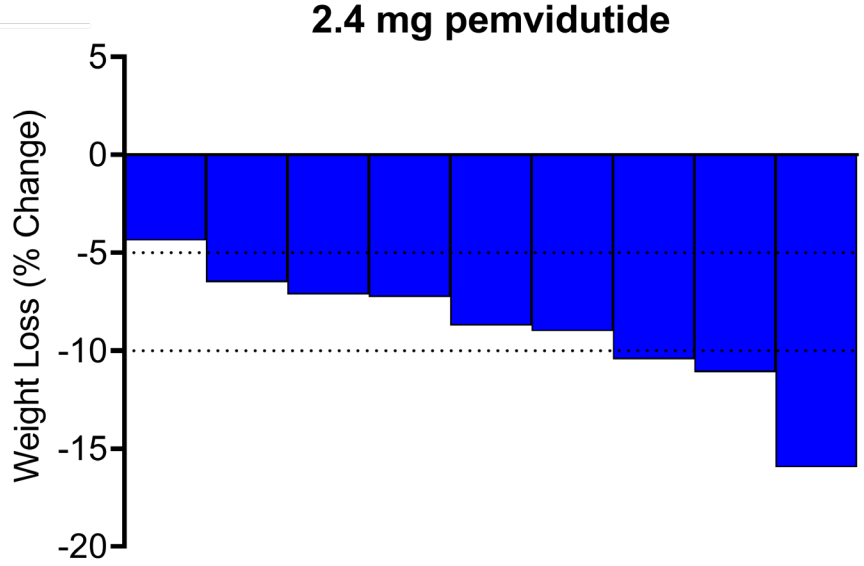


Weight Loss at Week 12 – Individual Responses

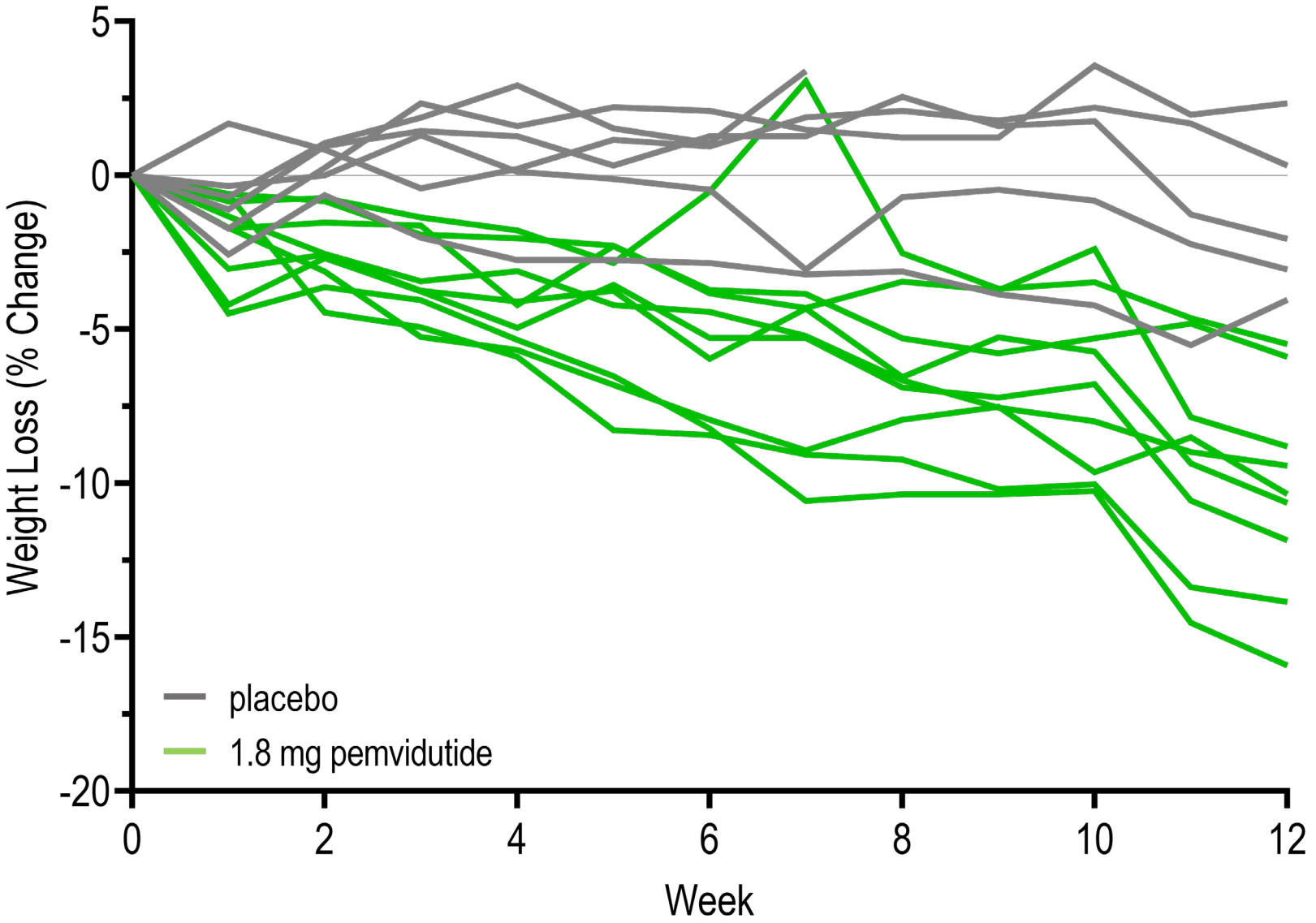




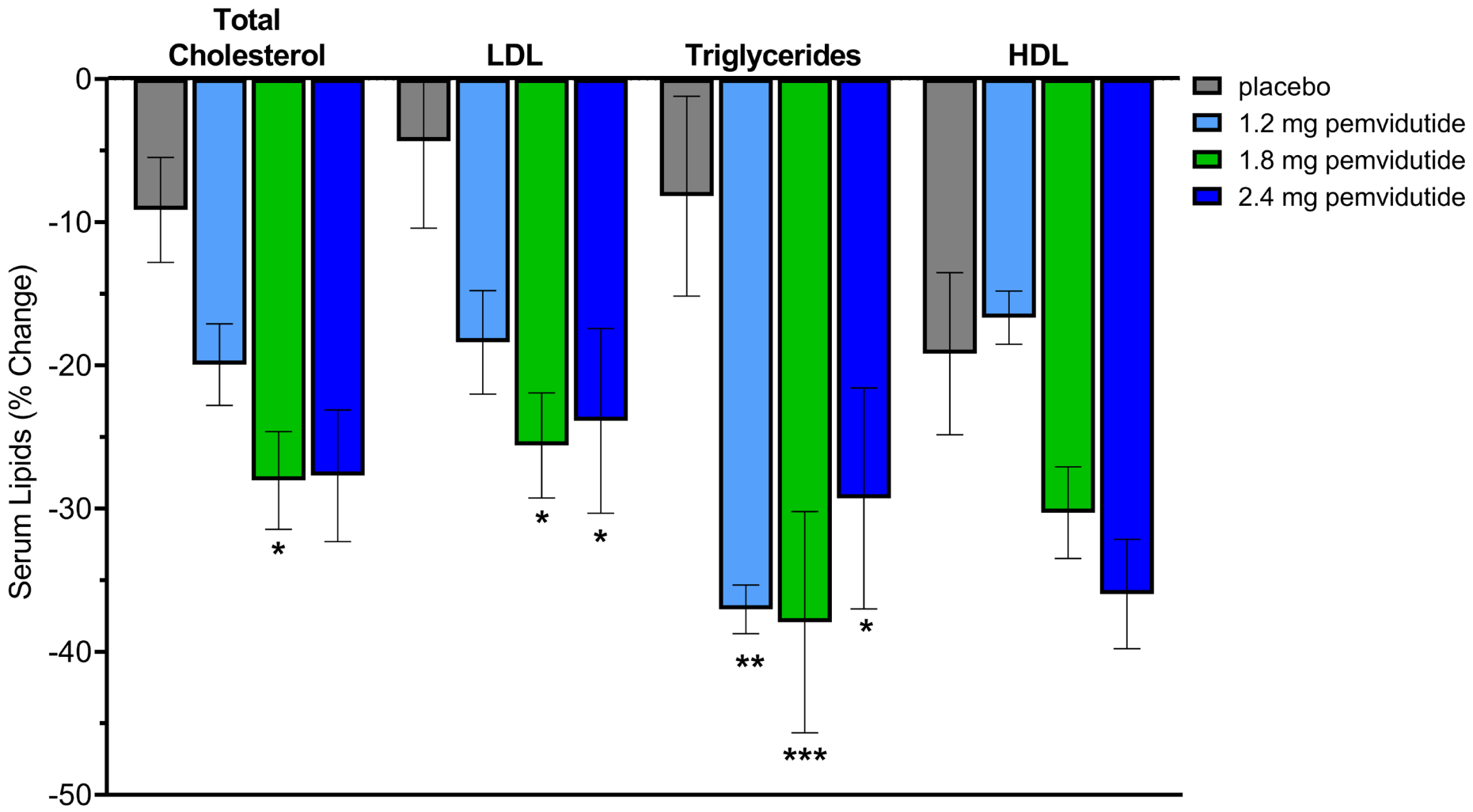




No Decline in Rate of Weight Loss at 12 weeks



Changes in Serum Lipids at Week 12

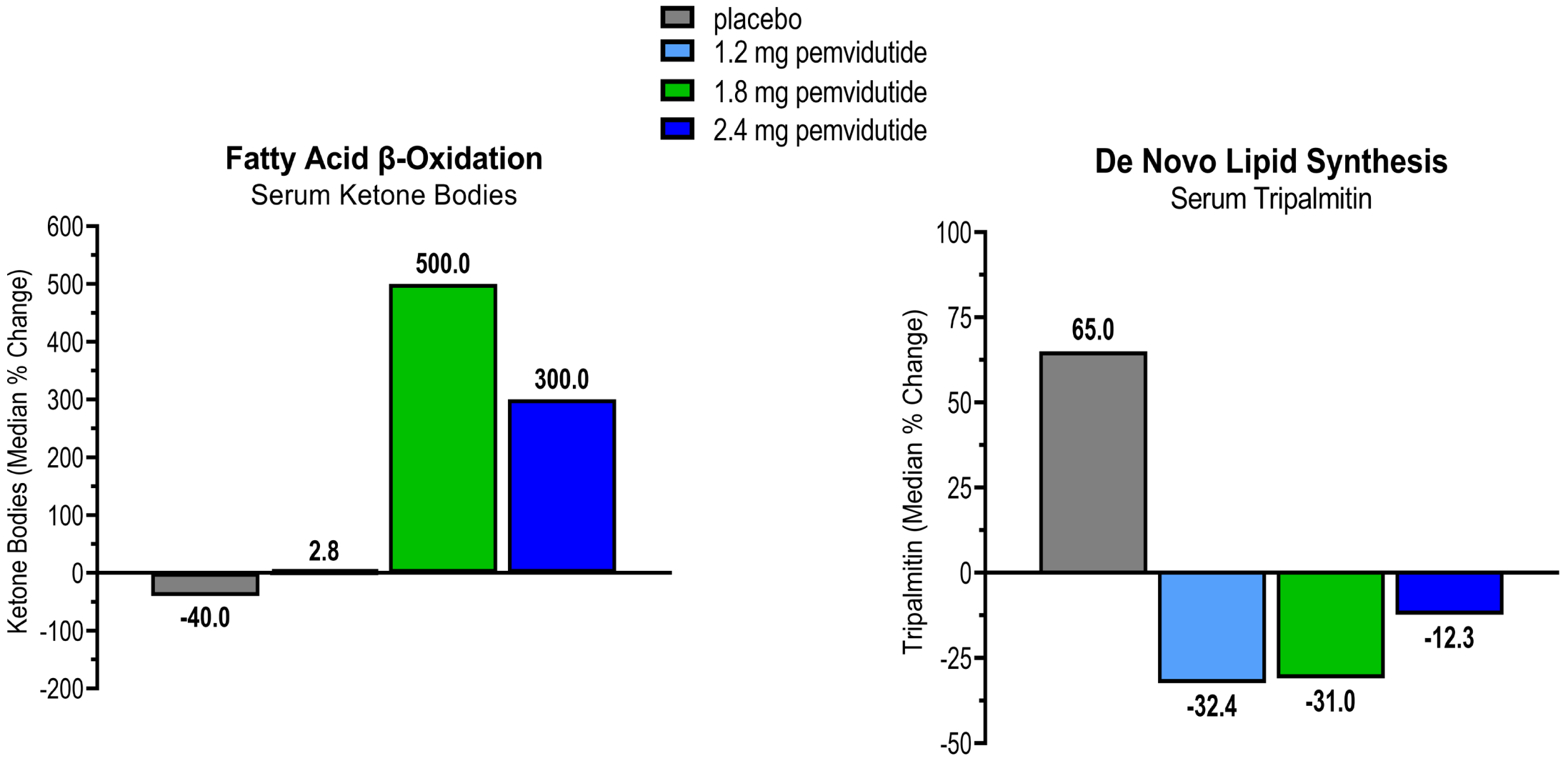


Mean ± SEM

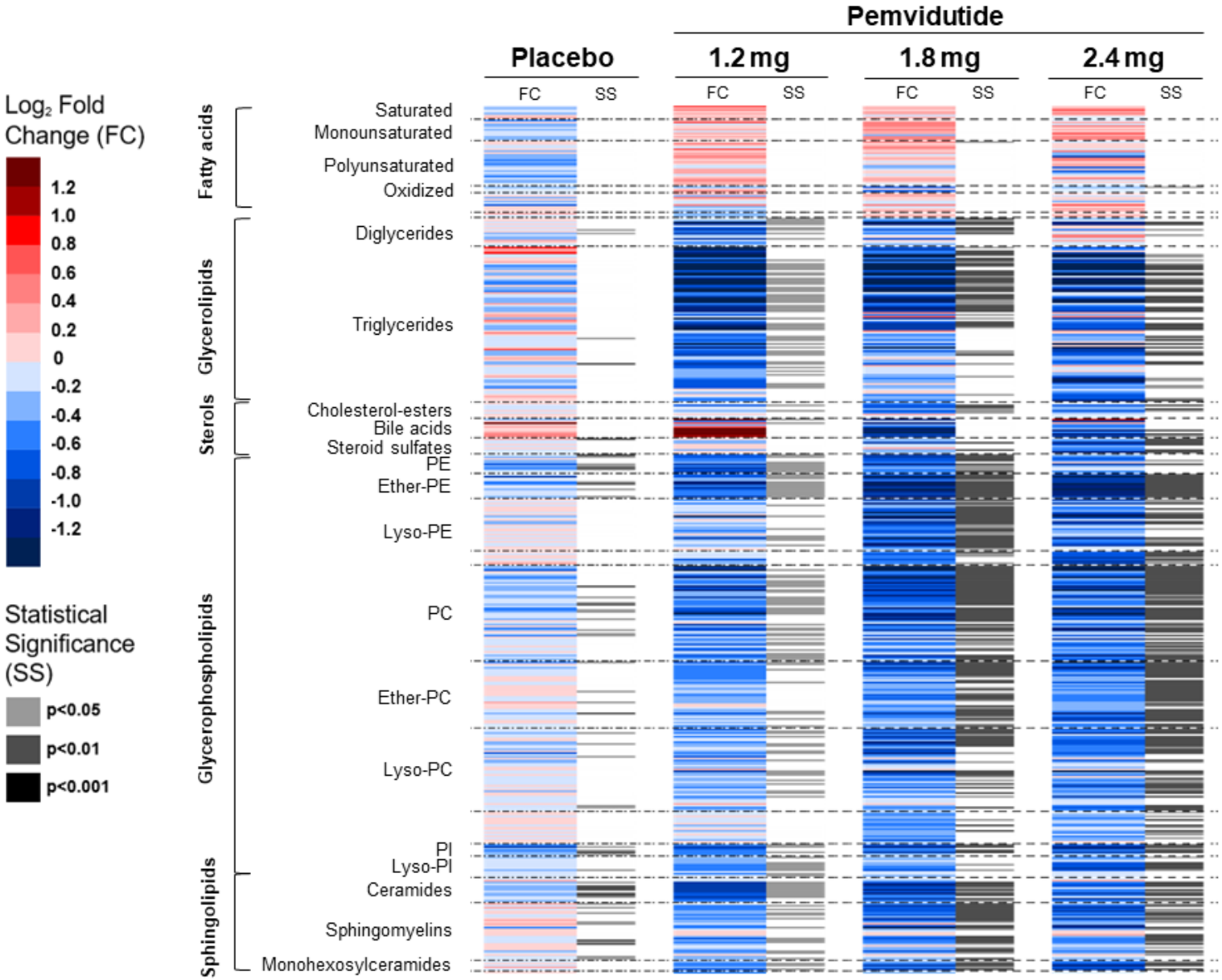
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. placebo

Effects on Lipid Metabolism

Increased lipid oxidation and decreased lipid synthesis



Robust Decreases in Lipids Implicated in NASH Inflammation



Reduction of Liver Fat to Below Limit of Detection (LOD) by Week 6

Greater than 90% reduction at 1.8 mg and 2.4 mg

Individual Subjects with MRI-PDFF ≥ 5% at Baseline

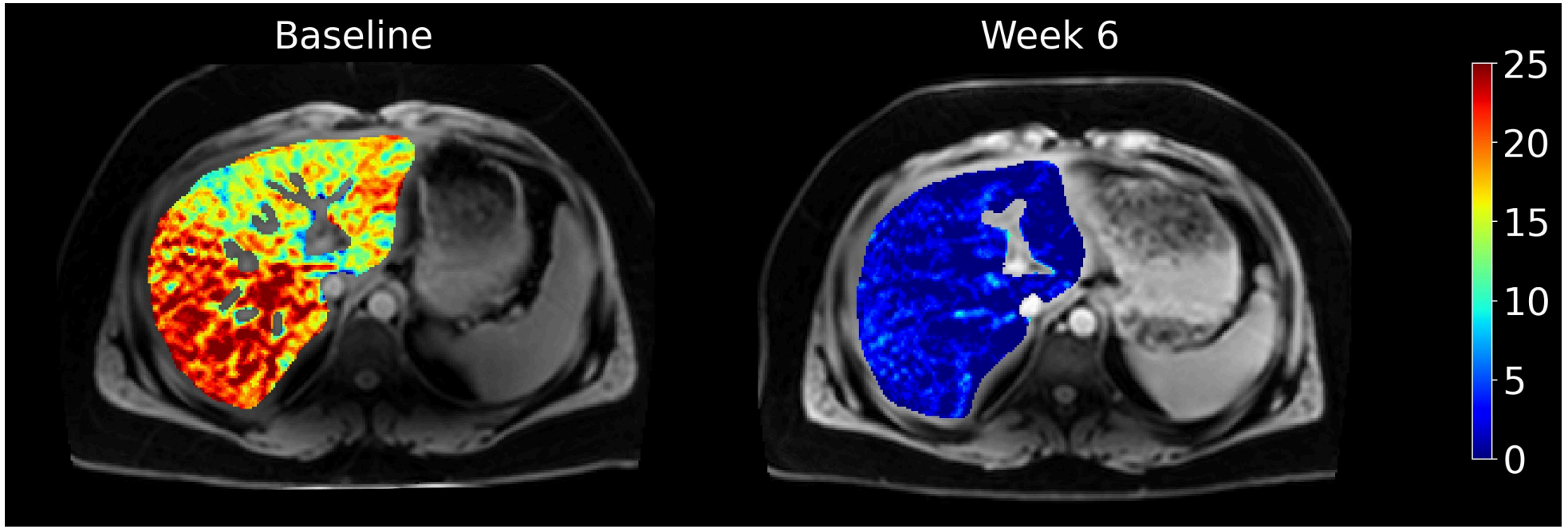
Treatment Group	MRI-PDFF (%)			
	Baseline	Week 6	Relative Δ at Week 6	
			Individual	Mean
Placebo	5.2	3.7	28.8	28.8
Pemvidutide 1.2 mg	19.1	14.0	26.7	48.2
	11.2	3.4	69.6	
Pemvidutide 1.8 mg	12.4	**< LOD**	94.0	**94.0**
Pemvidutide 2.4 mg	17.0	**< LOD**	95.6	**91.9**
	5.5	**< LOD**	86.4	
	7.0	**< LOD**	89.3	
	19.5	**< LOD**	96.2	

For calculation of absolute and relative Δ, values < LOD is set at 0.75%

Robust Reduction of Liver Fat Content by MRI-PDFF

From 19.5% to below limit of detection (LOD) by Week 6

Subject at 2.4 mg dose



19.5%

Below LOD

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Safety Overview (MAD Phase)

No serious AEs, severe AEs or AEs leading to treatment discontinuation

Characteristic		Treatment			
		1.2 mg (n = 7)	1.8 mg (n = 9)	2.4 mg (n = 12)	Pooled placebo (n = 7)
Serious or severe AEs	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
AEs leading to treatment discontinuation	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
Nausea					
Mild	n (%)	1 (14.3%)	5 (55.6%)	5 (45.5%)	1 (14.3%)
Moderate	n (%)	1 (14.3%)	1 (11.1%)	5 (45.5%)	0 (0.0%)
Vomiting					
Mild	n (%)	1 (14.3%)	1 (11.1%)	5 (45.5%)	1 (14.3%)
Moderate	n (%)	0 (0.0%)	1 (11.1%)	3 (27.3%)	0 (0.0%)
Diarrhea					
Mild	n (%)	0 (0.0%)	0 (0.0%)	2 (18.2%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation					
Mild	n (%)	0 (0.0%)	1 (11.1%)	2 (18.2%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	1 (11.1%)	1 (9.1%)	0 (0.0%)
Hyperglycemia	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

One subject receiving pemvidutide 1.8 mg and one receiving placebo experienced 3-5x ALT elevations with subsequent resolution

Summary

Weight loss

- 10.3% mean weight loss achieved at 1.8 mg dose at 12 weeks
- The trajectory suggests that the rate of weight loss will continue beyond 12 weeks

Lipids

- Reduction of liver fat content to below LOD, equivalent to a greater than 90% decrease
- Robust improvements in lipids species associated with NASH and CV disease

Safety and tolerability

- No dose titration
- No serious or severe AEs and no AE-related study discontinuations

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Conclusions and Next Steps

- Pemvidutide represents a promising new agent for the treatment of obesity and NASH
- Upcoming data:
  - NAFLD and obesity trial
    - 72 subjects with obesity or overweight plus baseline MRI-PDFF ≥ 10%, with endpoints of liver fat reduction and weight loss
    - Data readouts expected Q3 2022 (after 12 weeks of treatment) and Q4 2022 (after 24 weeks of treatment)
  - Phase 2 MOMENTUM obesity trial
    - 320 subjects with obesity or overweight with at least one obesity complication
    - Interim analysis at 24 weeks of treatment expected at end of 2022

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