Pemvidutide (ALT-801), a Balanced (1:1) GLP-1/Glucagon Dual Receptor Agonist, Induces Rapid and Marked Weight Loss without the Need for Dose Titration in People with Overweight/Obesity

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Presenter Disclosures

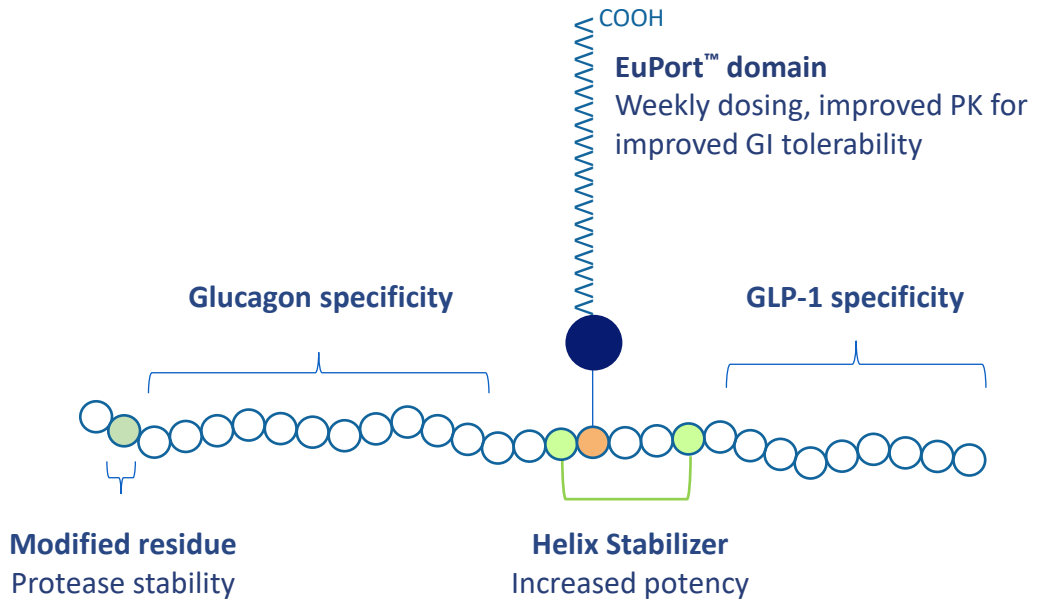
Samuel Klein has a sponsored research agreement with Janssen Pharmaceuticals Inc., serves on scientific advisory board for Altimmune, Inc. and as a consultant for B2M Medical

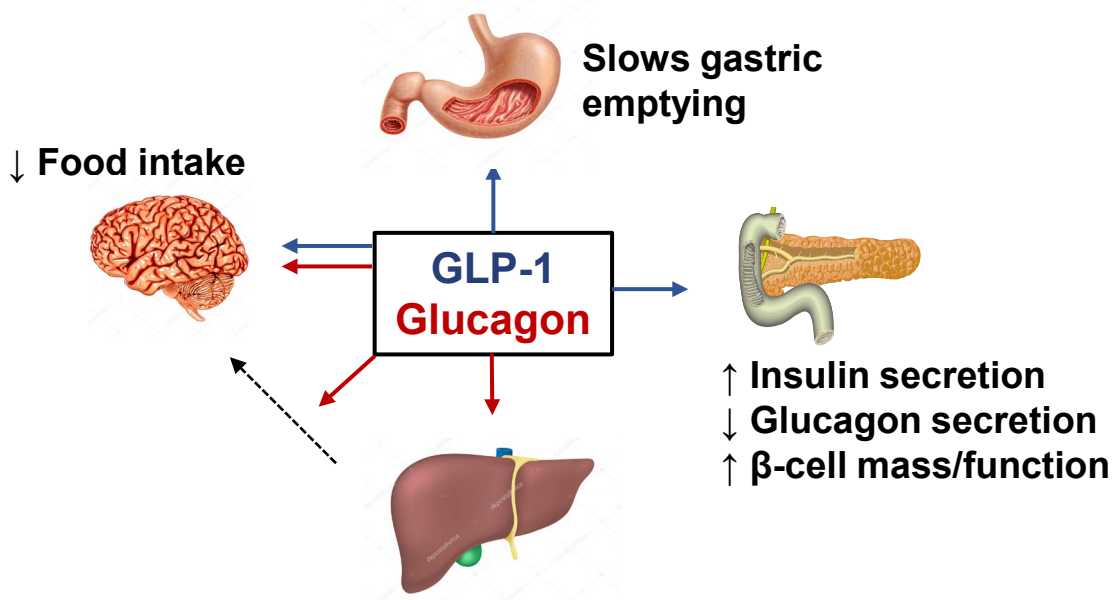
John J. Nestor is a consultant to Altimmune, Inc.

M. Scott Harris, Jacques D. Payne, Staci M. Steele, Robert Casper, Anvar Suyundikov, Vyjayanthi Krishnan, M. Scot Roberts, and Sarah K. Browne 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 Trial Design

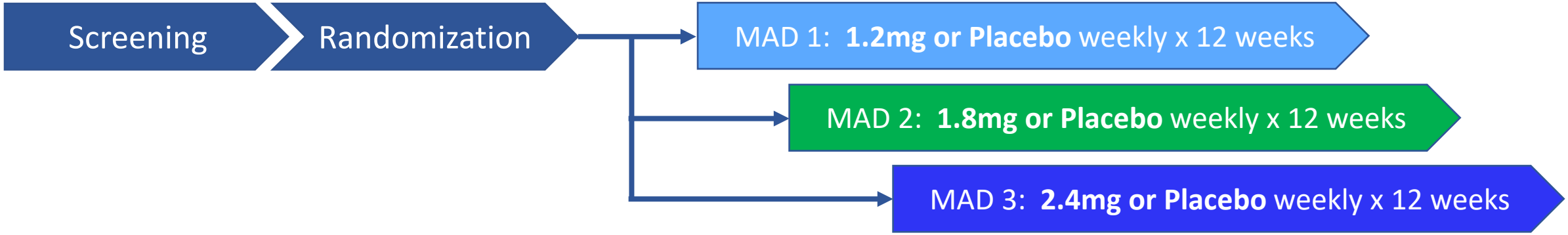
12-week, randomized, placebo-controlled, multiple ascending dose (MAD) study pemvidutide (ALT-801) in 34 subjects with overweight/obesity on:

- **Safety & tolerability (cardiometabolic outcomes)**
- **Pharmacokinetics**

4:1 randomization (pemvidutide: placebo), with placebos pooled

No caloric restriction or lifestyle intervention

No dose titration



Characteristics of Study Participants

Characteristic		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%)
Blood pressure, mm Hg	systolic, mean (SD)	123.4 (12.4)	118.1 (9.8)	123.9 (11.5)	117.2 (12.3)
	diastolic, mean (SD)	76.0 (8.0)	73.3 (7.4)	76.5 (9.3)	72.4 (9.4)
Heart rate, bpm	mean (SD)	75.0 (11.9)	60.3 (9.1)	78.9 (5.7)	70.2 (14.3)
Fasting glucose, mg/dL	mean (SD)	86.4 (4.5)	88.2 (5.0)	86.4 (8.6)	86.4 (5.6)
Fasting insulin, mU/L	mean (SD)	11.4 (5.2)	9.9 (9.8)	12.3 (7.3)	11.1 (5.5)
HbA1c, %	mean (SD)	5.3 (0.1)	5.5 (0.2)	5.3 (0.2)	5.3 (0.2)
HOMA-IR	mean (SD)	2.5 (1.2)	2.4 (2.5)	3.1 (1.8)	2.4 (1.7)
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)

Pemvidutide Phase 1 – Study Disposition

No withdrawals for adverse events (without titration)

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

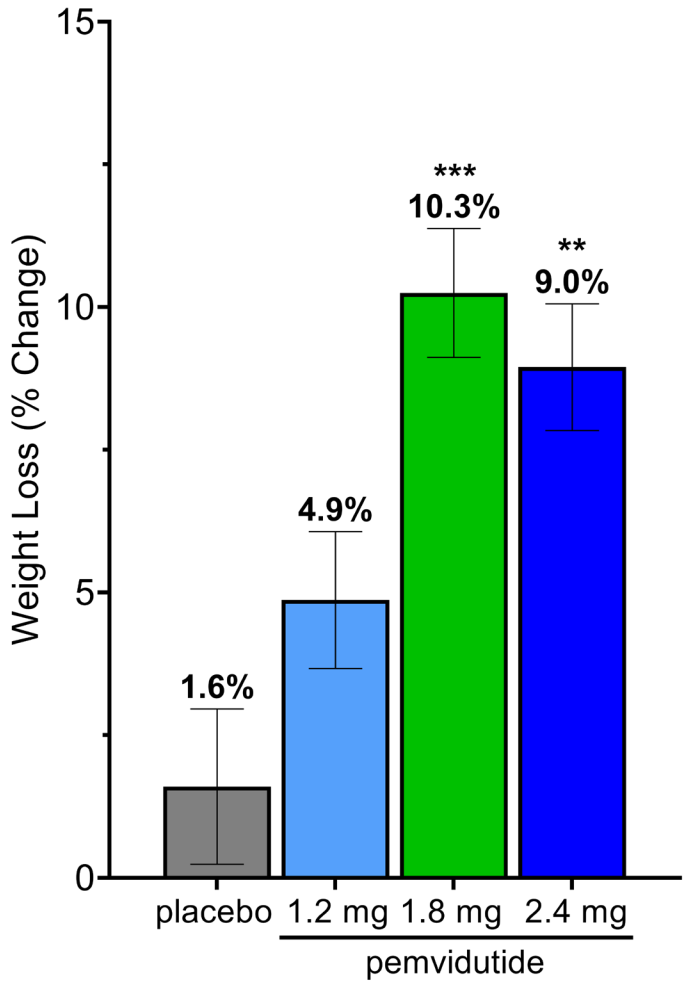
Pemvidutide PK Profile

Long half-life supports weekly dosing

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

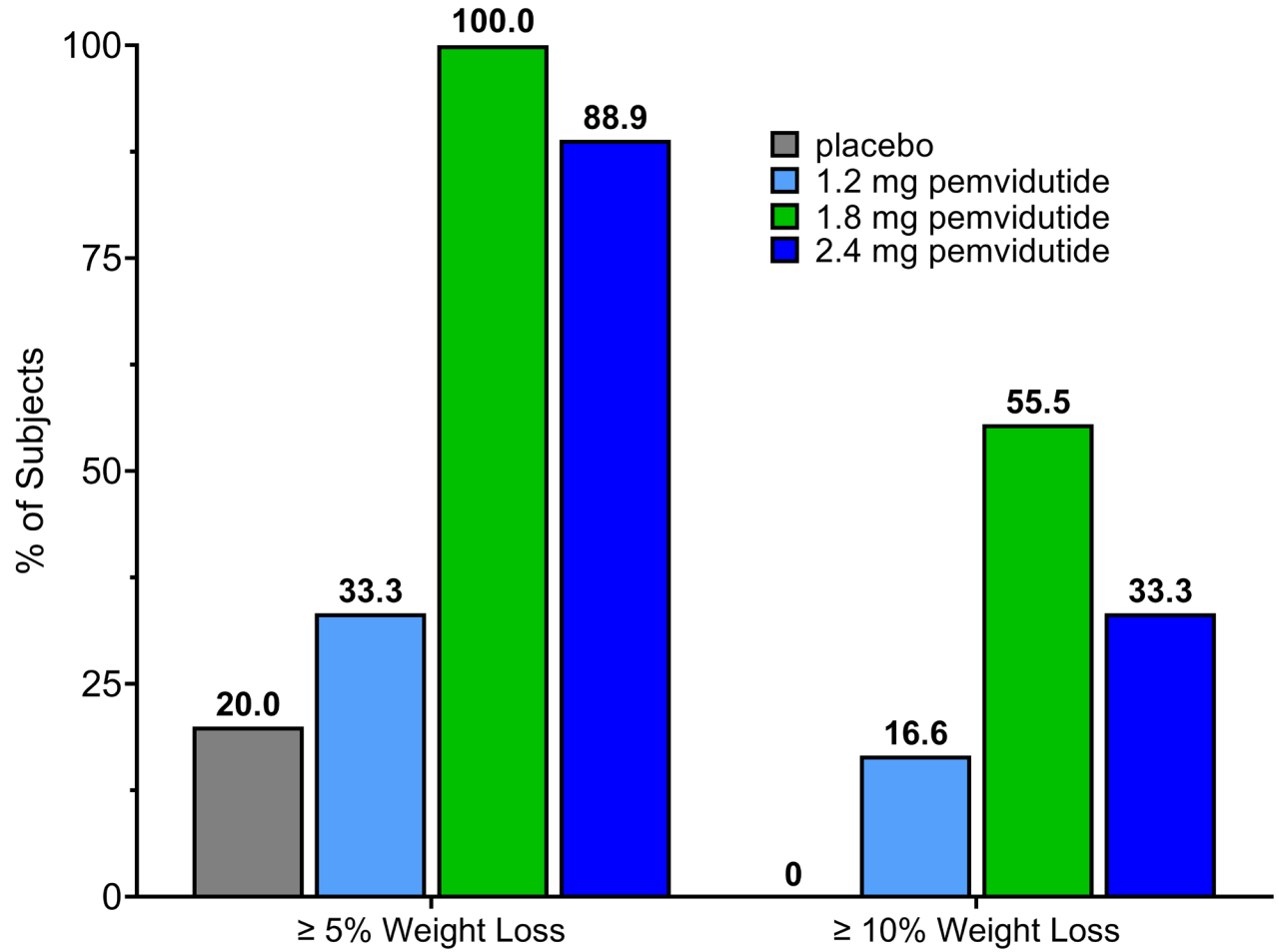
PK PARAMETER	ALT-801 1.8 mg SC
Peak concentration (C_{max})	27.1 nmol/L
Area under curve (AUC) $_{0\text{-}168}$	3400 nmol•hr
Half-life ($t_{1/2}$)	110 hrs
Time to peak concentration (T_{max})	70 hrs

Weight Loss At Week 12

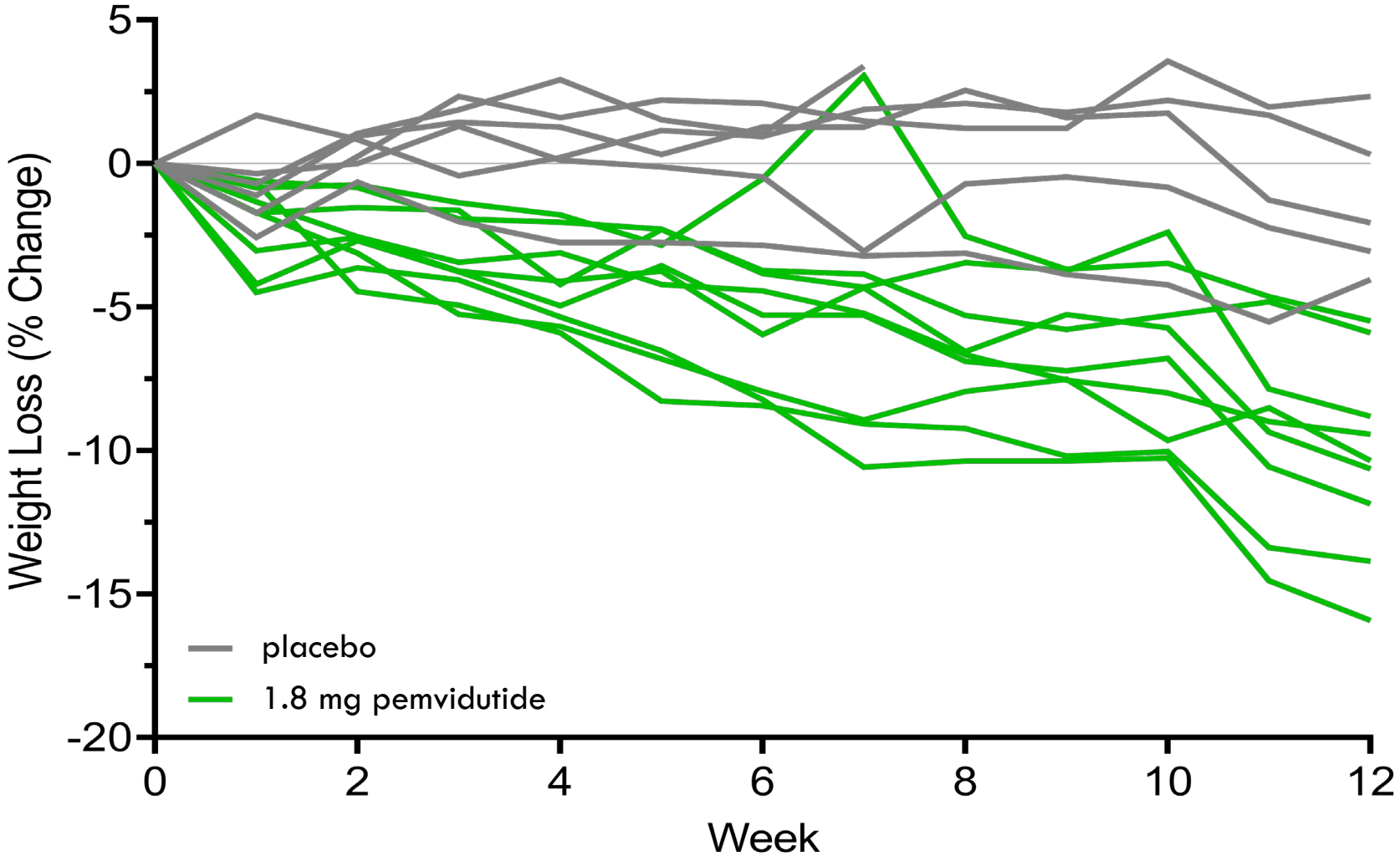


Mean ± SEM

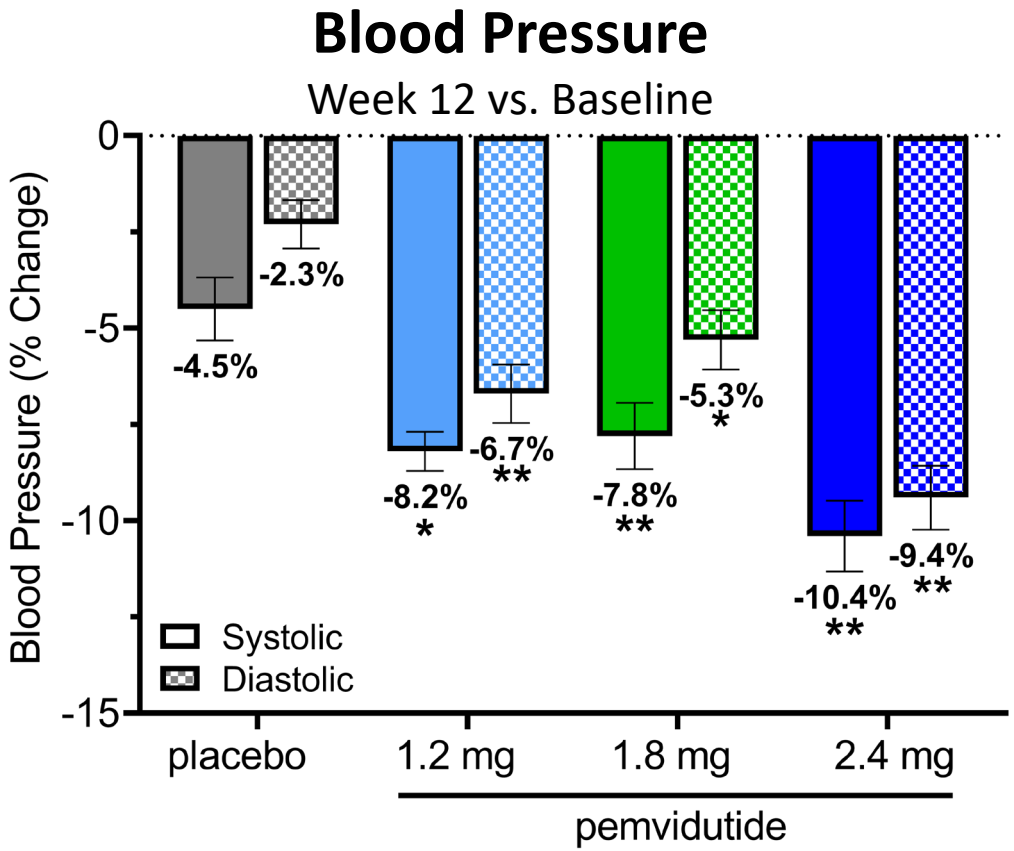
** p < 0.01, *** p < 0.001 vs. placebo

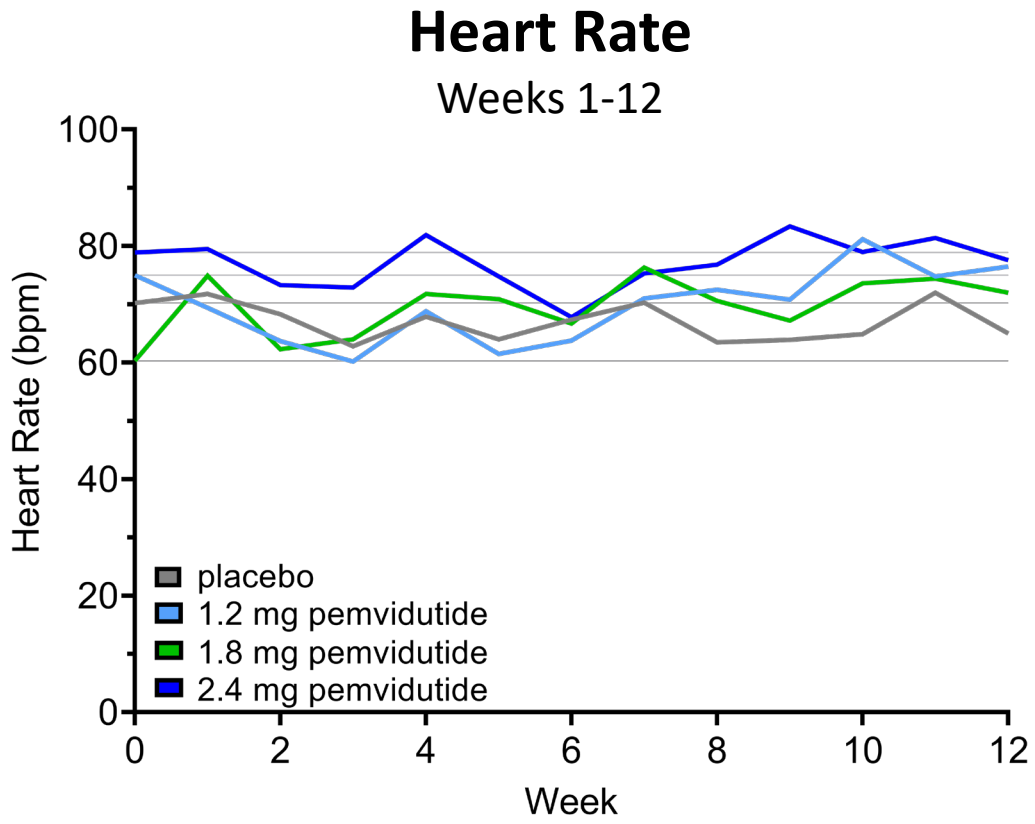


Weight Loss over 12 weeks



Blood Pressure and Heart Rate

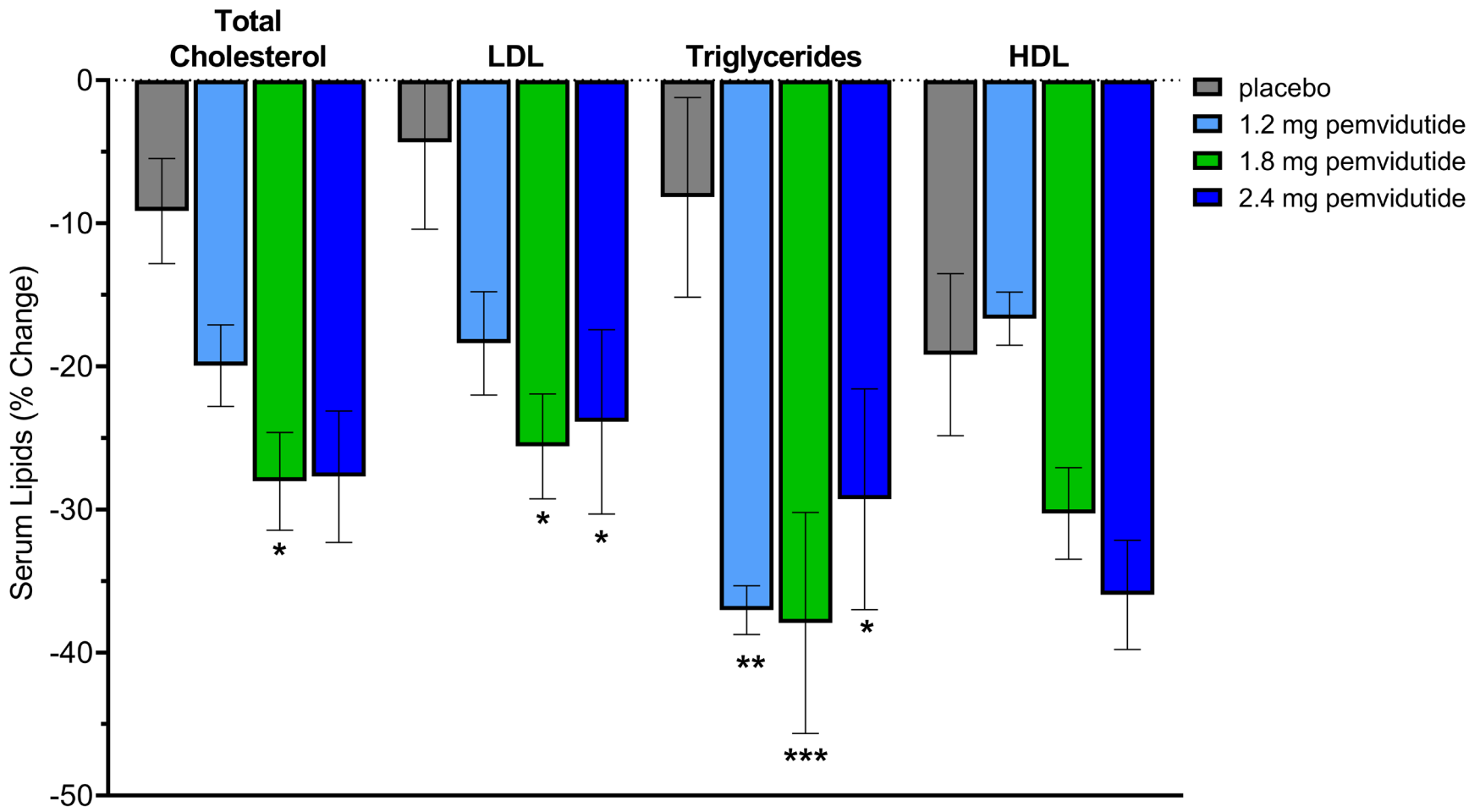




Mean ± SEM

* $p < 0.001$, ** $p < 0.0001$ vs. placebo

Changes in Serum Lipids at Week 12



Mean ± SEM

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

Safety Overview

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 and Conclusions

Weight loss

- 10.3% mean weight loss achieved at 1.8 mg dose at 12 weeks
- No decline in rate of weight loss at 12 weeks suggests weight loss will continue after 12 weeks

Other measures

- Robust improvements in blood pressure and plasma lipids

Safety and tolerability

- No dose titration
- No serious or severe AEs and no AE-related study discontinuations
- Glucose homeostasis maintained (fasting blood glucose, insulin and HbA1c)
- No changes in heart rate