PHASE 2, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF PEMVIDUTIDE, A GLP-1/GLUCAGON DUAL RECEPTOR AGONIST, IN SUBJECTS WITH OVERWEIGHT OR OBESITY: A 24-WEEK INTERIM ANALYSIS

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Disclosures

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Other: ERX Pharmaceuticals, Intellihealth, Jamieson Wellness

US PREVALENCE AND SIGNIFICANCE OF OBESITY COMORBIDITIES

19-23% T2DM[1,7]

41-45% Sleep Apnea[8,9]

45-55% Hypertension[1,7]

58-75% NAFLD[3,4,5]

30-36% NASH[3,4,6]

66-70% Dyslipidemia[1,2]

Most significant comorbidities are dyslipidemia, NAFLD/NASH, and hypertension

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5) Le, Michael, et. al. (2022) 2019 Global NAFLD Prevalence: A Systematic Review and Meta-analysis. Clinical Gastroenterology and Hepatology 2022;20:2809–2817
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8) Romero-Corral, Abel, et. al. (2010) Interactions Between Obesity and Obstructive Sleep Apnea. Chest 137(3): 711-719.
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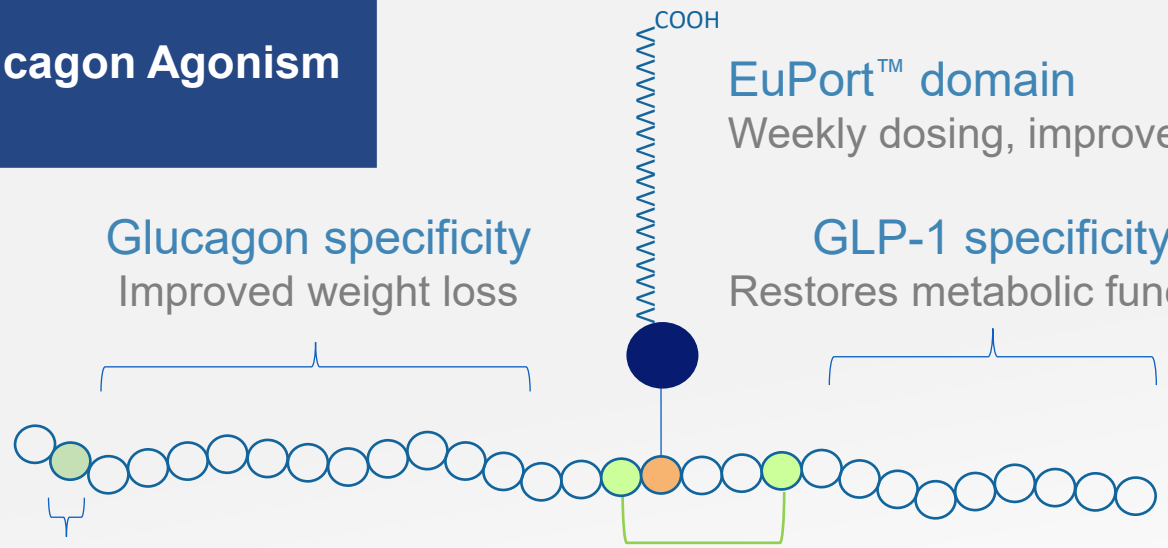
PEMVIDUTIDE: RATIONALLY DESIGNED AND HIGHLY DIFFERENTIATED

EUPORT™ DOMAIN PROVIDES PROLONGED SERUM HALF-LIFE AND DELAYED TIME TO PEAK CONCENTRATION

Pemvidutide:
Balanced GLP-1:Glucagon Agonism



[1]Nestor JJ et al, Peptide Science. 2021;113:e24221

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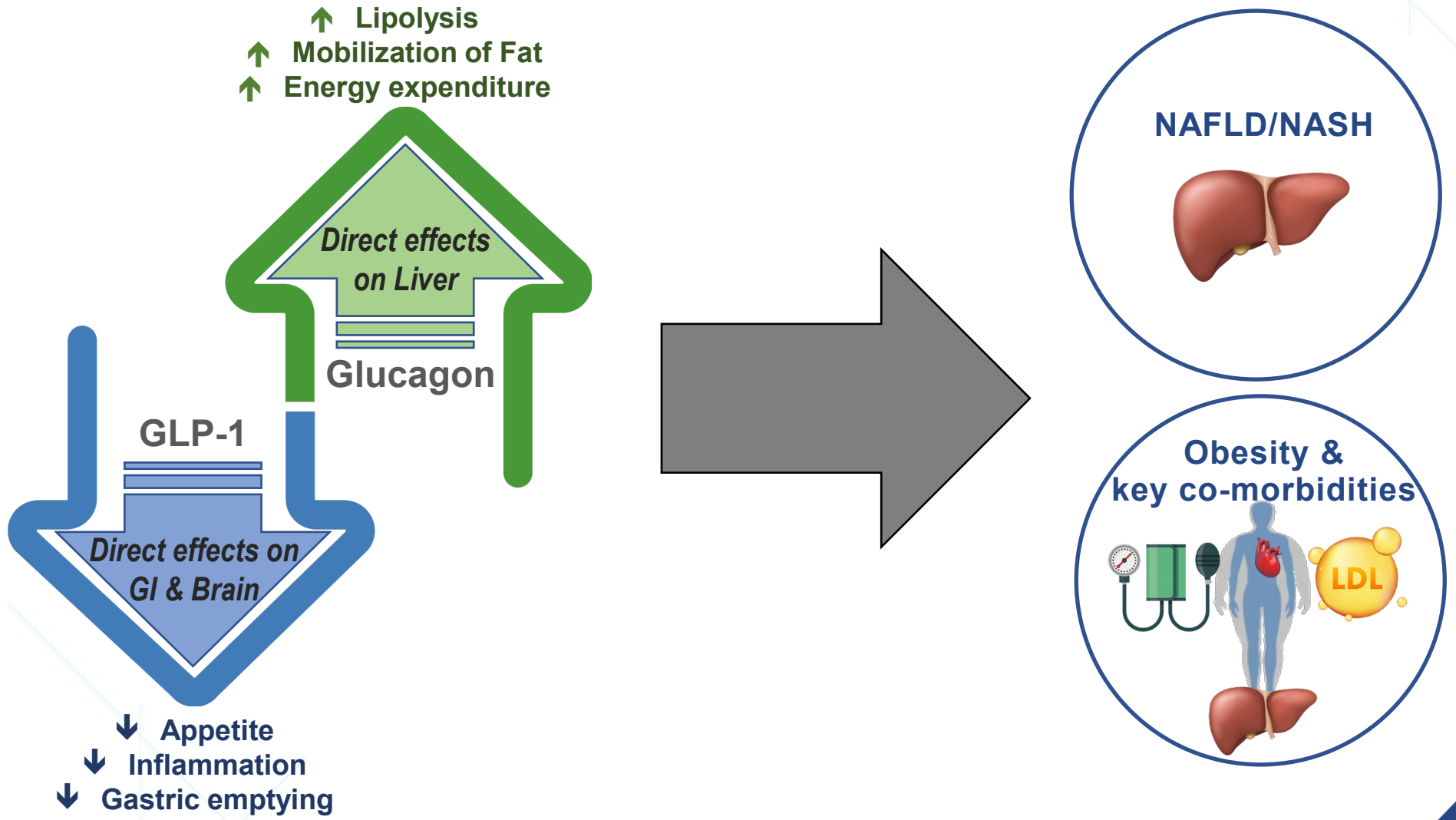
PEMVIDUTIDE: GLP-1/GLUCAGON DUAL RECEPTOR AGONIST

OPTIMIZED FOR TREATMENT OF NASH, OBESITY AND KEY CO-MORBIDITIES



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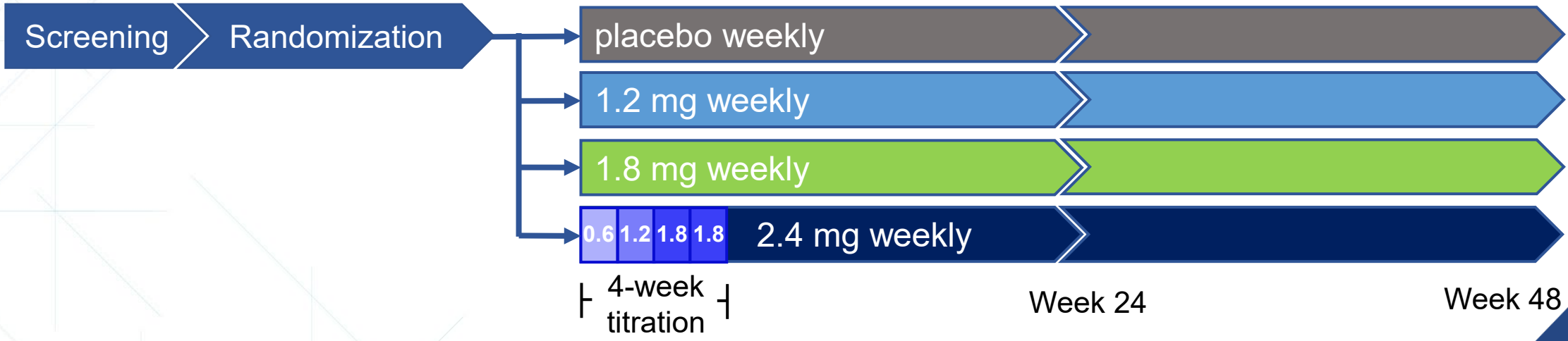
MOMENTUM OBESITY TRIAL DESIGN

- Phase 2, 48-week trial of pemvidutide in ~320 subjects with overweight or obesity
- Randomized 1:1:1:1 to 4 treatment arms, stratified by sex and baseline BMI, with standard lifestyle interventions
- Rapid (4 week) dose titration for 2.4 mg arm; dose reduction due to intolerability was not allowed
- A pre-specified 24-week interim analysis was performed on 160 subjects



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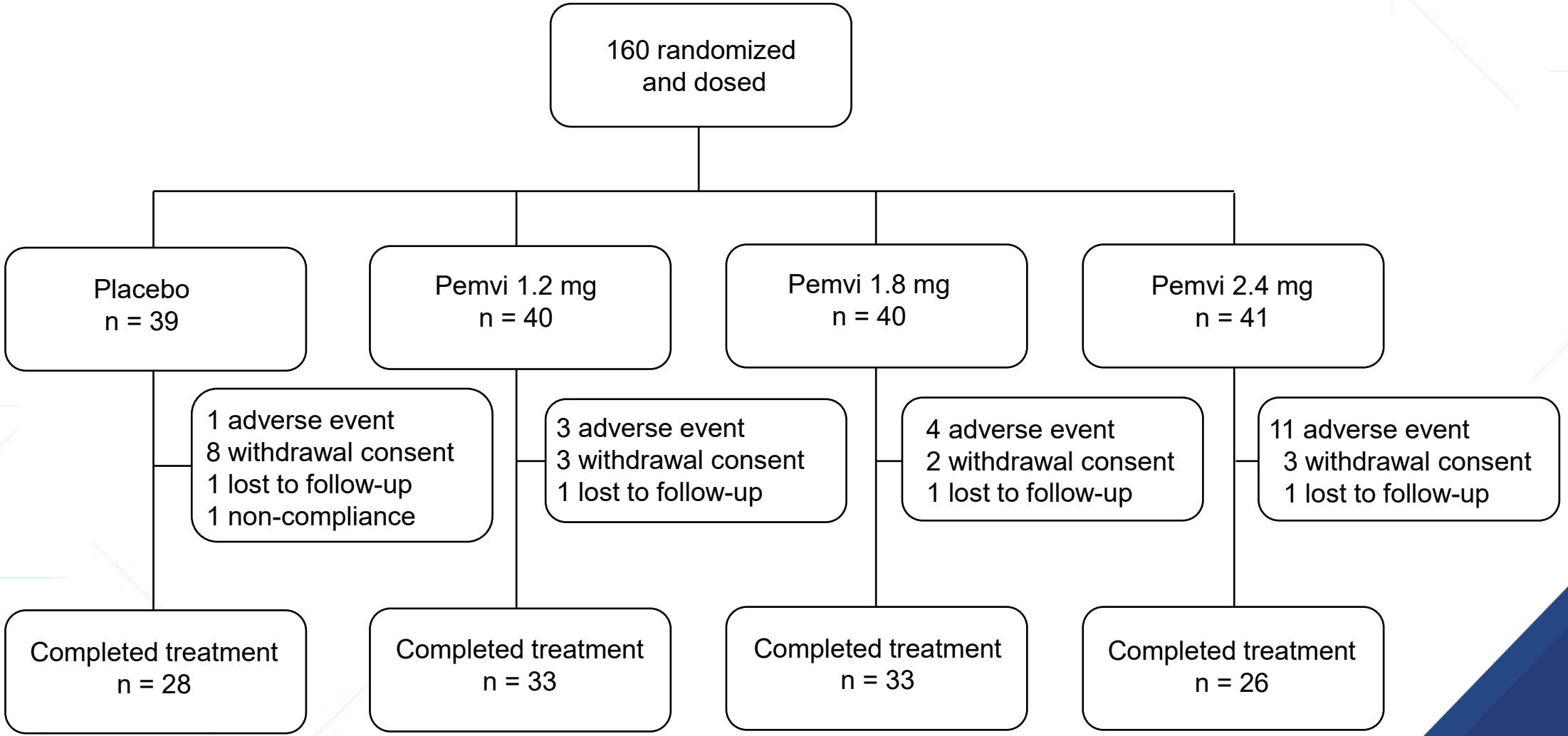
MOMENTUM KEY ELIGIBILITY CRITERIA

- **Men and women ages 18-75 years**
- **BMI ≥ 30 kg/m^2 or BMI ≥ 27 kg/m^2 with at least one obesity-related comorbidity**
  - History of cardiovascular disease
  - Hypertension
  - Dyslipidemia
  - Pre-diabetes
  - Obstructive sleep apnea
- **Non-diabetes: HbA1c ≤ 6.5% and fasting glucose ≤ 125 mg/dL**
- **At least one unsuccessful weight loss attempt**
- **25% of subjects were to be male**

SUBJECT DISPOSITION



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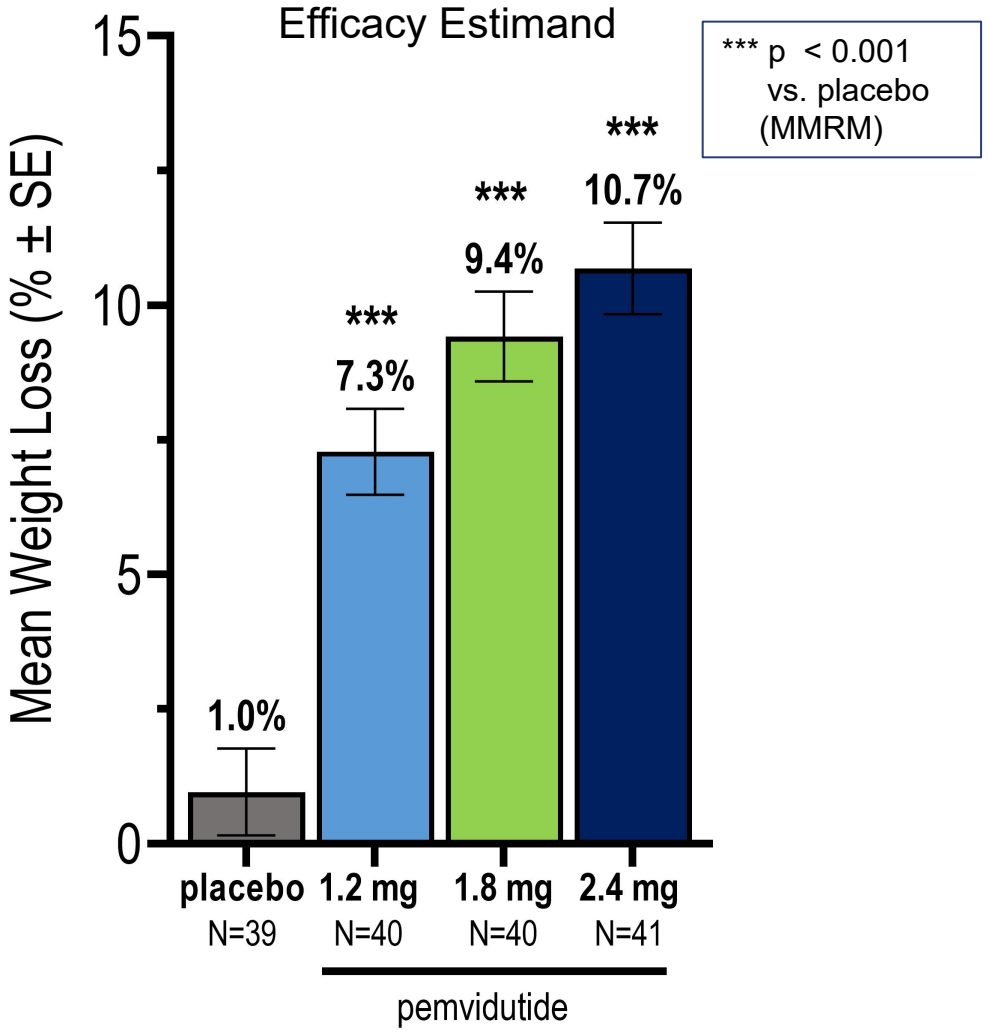
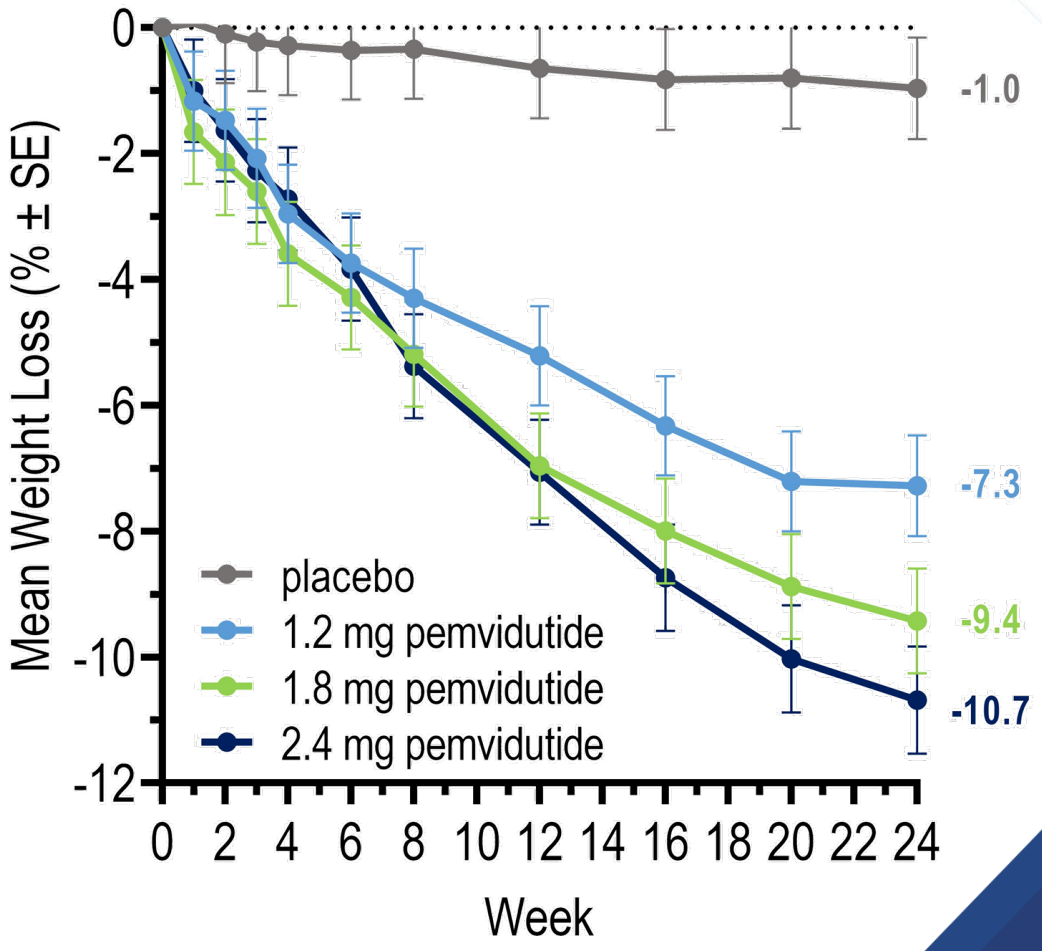
DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Characteristic		Treatment			
		Placebo (n = 39)	1.2 mg (n=40)	1.8 mg (n=40)	2.4 mg (n=41)
Age, years	Mean (SD)	46.7 (14.2)	46.5 (12.0)	49.5 (13.5)	48.2 (13.4)
Sex					
Male	n (%)	9 (23.1)	9 (22.5)	10 (25.0)	10 (24.4)
Female	n (%)	30 (76.9)	31 (77.5)	30 (75.0)	31 (75.6)
Race					
White	n (%)	31 (79.5)	36 (90.0)	35 (87.5)	34 (82.9)
Black or African American	n (%)	6 (15.4)	2 (5.0)	4 (10.0)	7 (17.1)
Asian	n (%)	2 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)
Other	n (%)	0 (0.0)	2 (5.0)	1 (2.5)	0 (0.0)
Body weight, kg	Mean (SD)	105.4 (24.8)	104.8 (24.0)	100.0 (20.4)	102.1 (17.7)
Body Mass Index, kg/m^2	Mean (SD)	37.8 (7.9)	37.1 (5.9)	36.0 (5.4)	36.0 (5.5)
Blood Pressure					
Systolic, mmHg	Mean (SD)	121.5 (13.0)	121.0 (12.2)	126.2 (12.6)	125.5 (13.7)
Diastolic, mmHg	Mean (SD)	75.4 (9.3)	77.4 (7.0)	79.2 (7.7)	80.3 (7.9)
Hemoglobin A1C, %	Mean (SD)	5.5 (0.4)	5.6 (0.3)	5.5 (0.4)	5.5 (0.4)
Fasting Serum Glucose, mg/dL	Mean (SD)	96.1 (9.8)	97.0 (12.2)	103.1 (12.1)	100.3 (12.9)

SIGNIFICANT WEIGHT LOSS THROUGH WEEK 24

INTERIM DATA DEMONSTRATES PROMISING WEIGHT LOSS TRENDS





MMRM, mixed model for repeated measures

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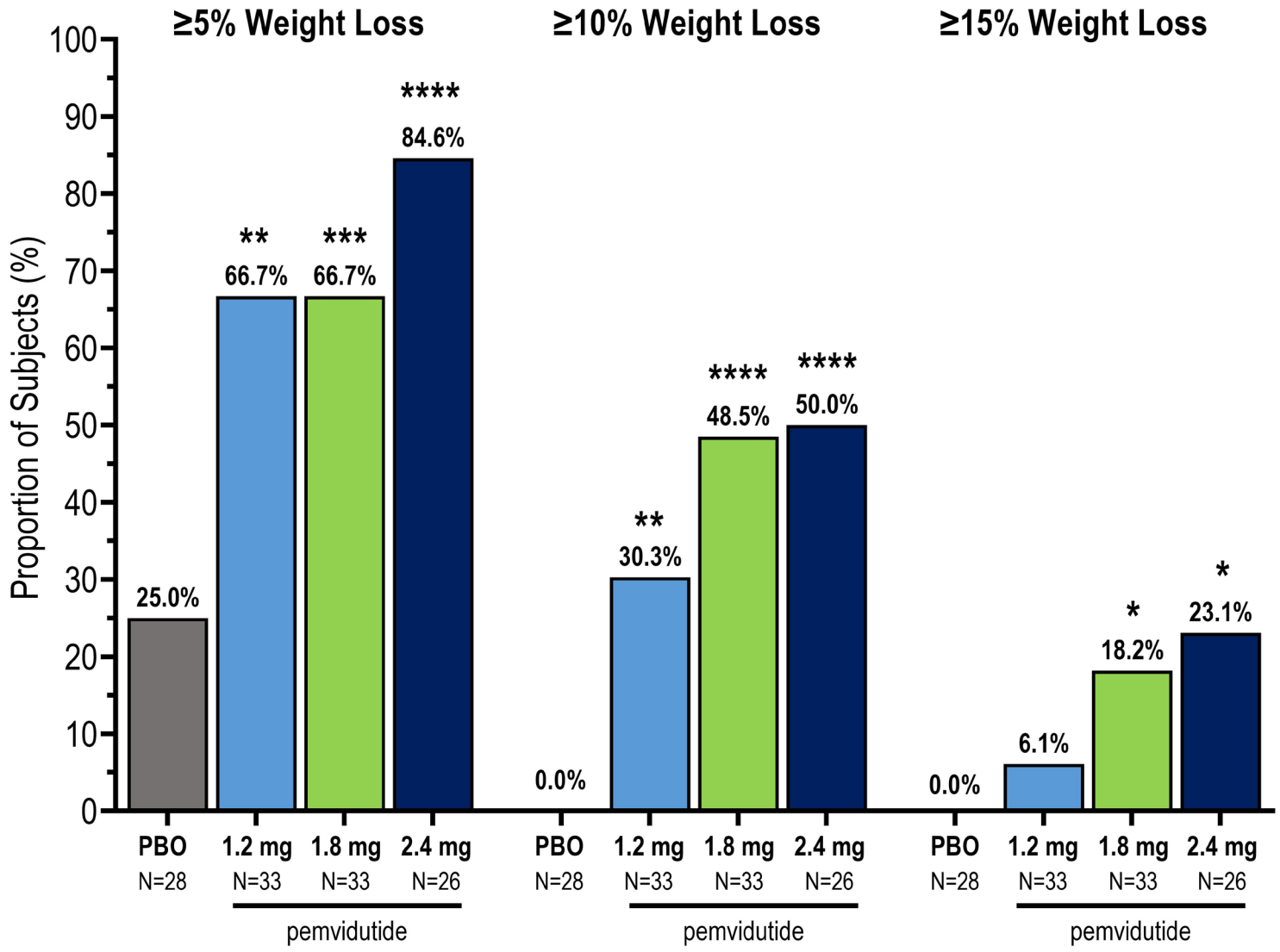
WEIGHT LOSS RESPONDER ANALYSIS

50% OF SUBJECTS LOST 10% BODY WEIGHT AT 24 WEEKS



* p < 0.05
** p < 0.005
*** p < 0.001
**** p < 0.0001
vs. placebo
(CMH)

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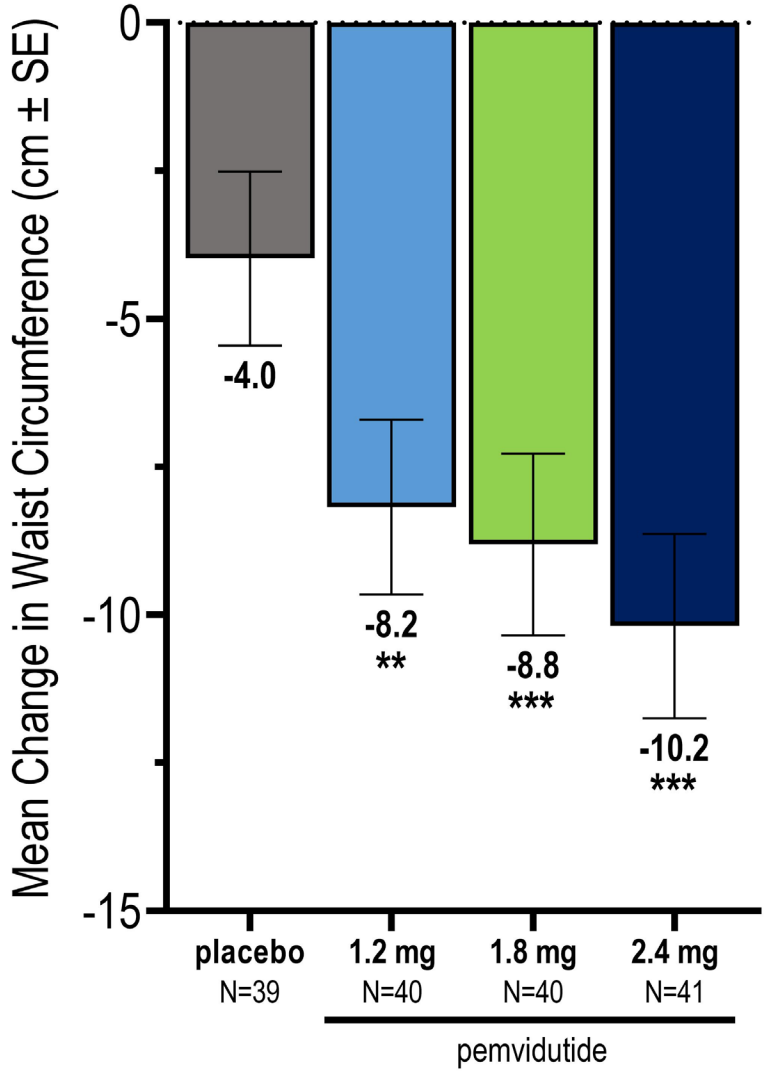
REDUCTIONS IN WAIST CIRCUMFERENCE

REDUCTIONS IN CENTRAL OBESITY – A MARKER FOR VISCERAL FAT



** p < 0.005
*** p < 0.001
vs. placebo
(MMRM)

MMRM, mixed model for repeated measures

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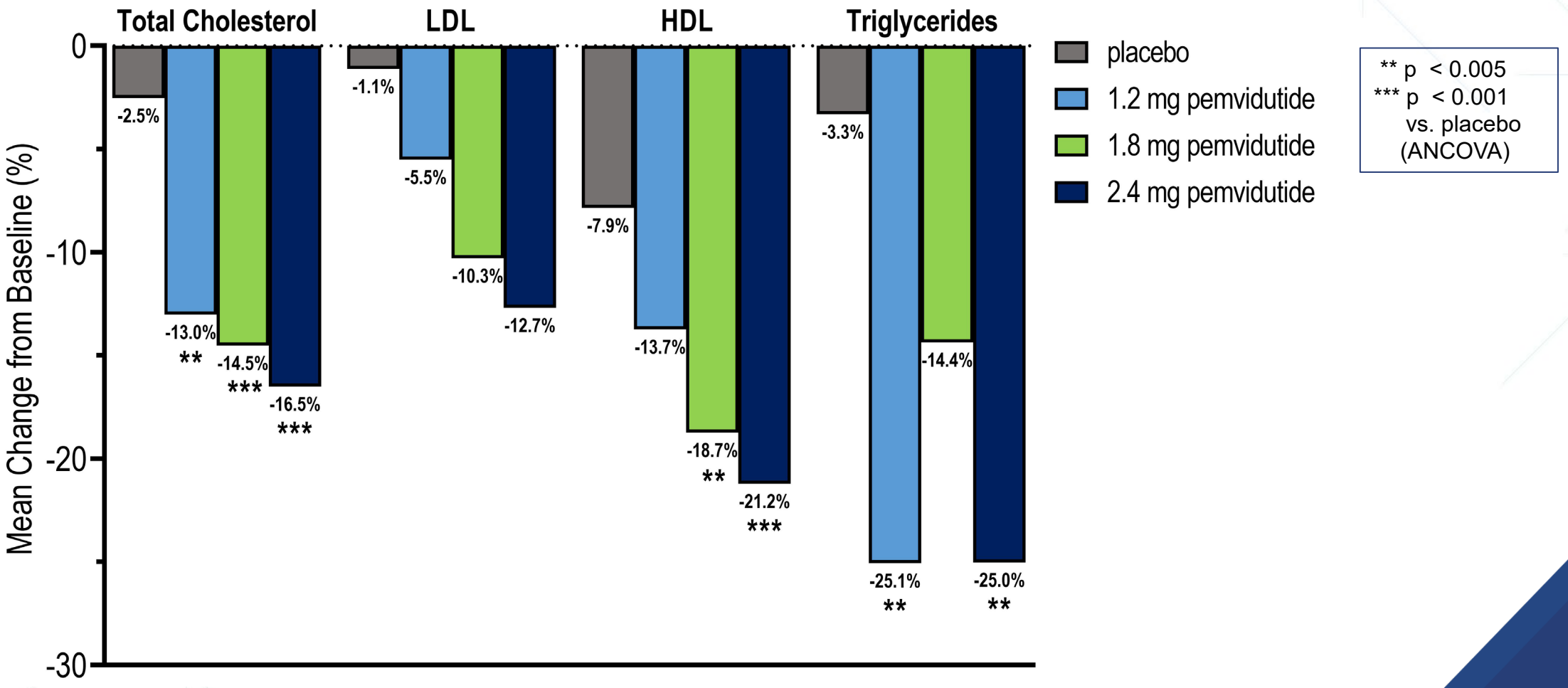
SIGNIFICANT REDUCTIONS IN SERUM LIPIDS AT WEEK 24



ANCOVA, analysis of covariance

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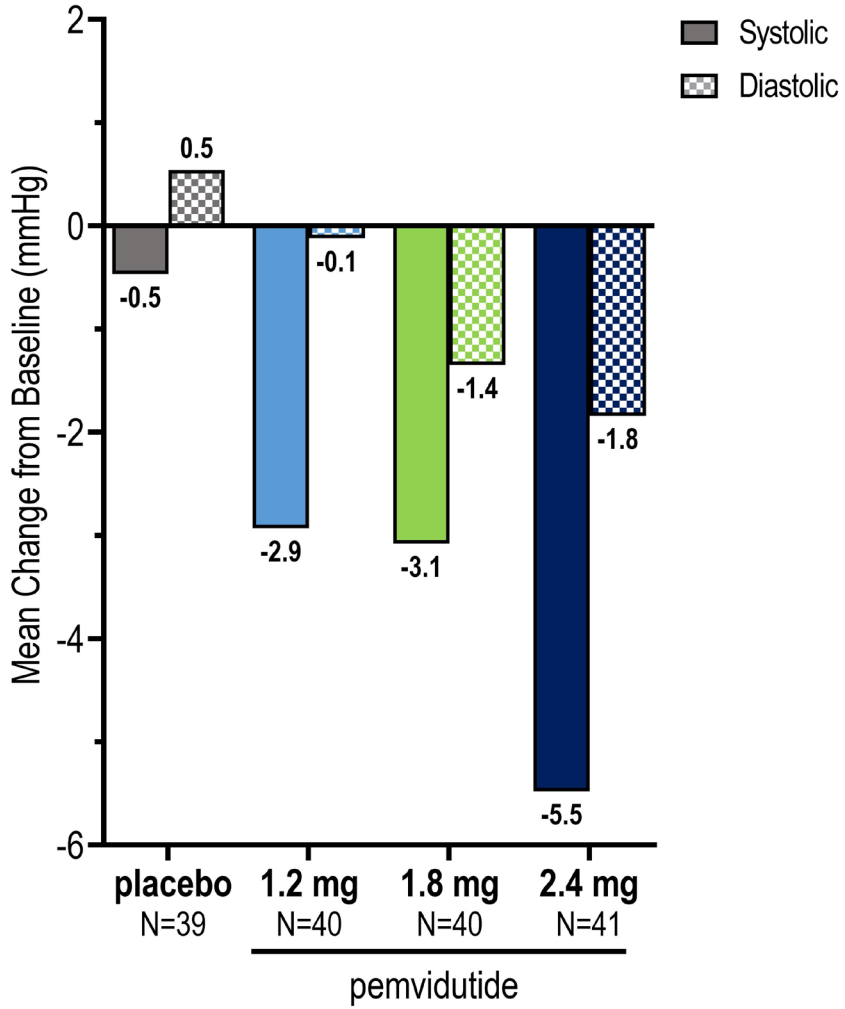
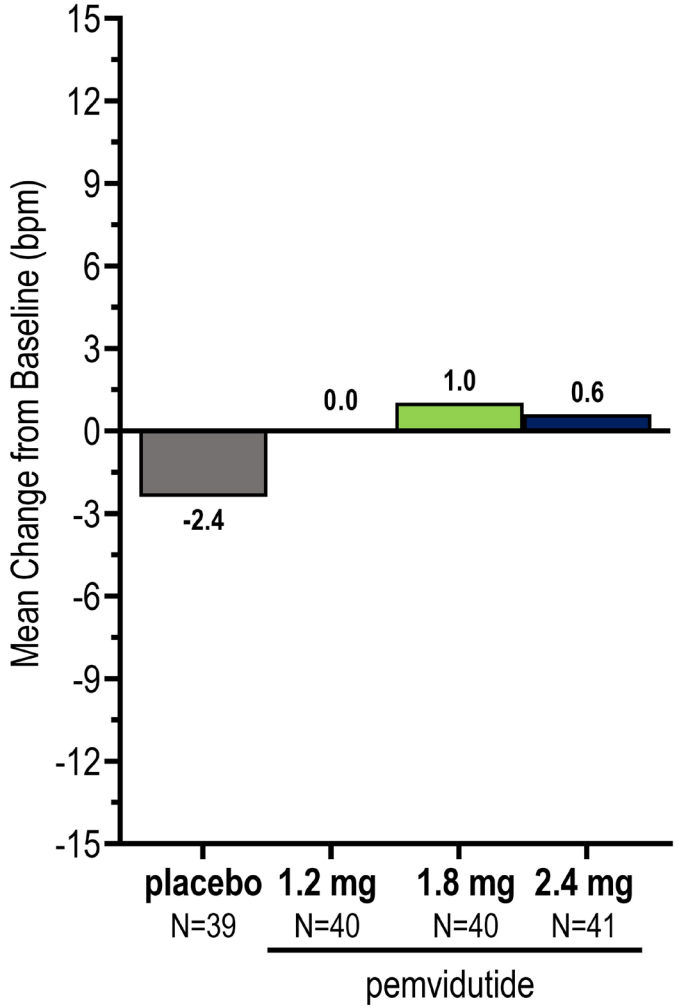
SAFETY OVERVIEW—AEs THROUGH WEEK 24

Characteristic		Treatment			
		Placebo (n = 39)	1.2 mg (n=40)	1.8 mg (n=40)	2.4 mg (n=41)
Serious adverse events	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)[1]
Severe adverse events	n (%)	1 (2.6%)	1 (2.5%)	1 (2.5%)	2 (4.9%)
Gastrointestinal AEs					
Nausea					
Mild	n (%)	2 (5.1%)	5 (12.5%)	9 (22.5%)	12 (29.3%)
Moderate	n (%)	0 (0.0%)	3 (7.5%)	13 (32.5%)	9 (22.0%)
Severe	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)
Vomiting					
Mild	n (%)	0 (0.0%)	0 (0.0%)	2 (5.0%)	5 (12.2%)
Moderate	n (%)	0 (0.0%)	2 (5.0%)	3 (7.5%)	4 (9.8%)
Severe	n (%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (2.4%)
Diarrhea					
Mild	n (%)	0 (0.0%)	3 (7.5%)	2 (5.0%)	4 (9.8%)
Moderate	n (%)	2 (5.1%)	0 (0.0%)	0 (0.0%)	2 (4.9%)
Constipation					
Mild	n (%)	0 (0.0%)	3 (7.5%)	1 (2.5%)	5 (12.2%)
Moderate	n (%)	2 (5.1%)	2 (5.0%)	1 (2.5%)	1 (2.4%)

[1]Rehydration for nausea and vomiting

IMPROVEMENTS IN BLOOD PRESSURE WITHOUT MEANINGFUL CHANGES IN HEART RATE THROUGH WEEK 24





MMRM, mixed model for repeated measures

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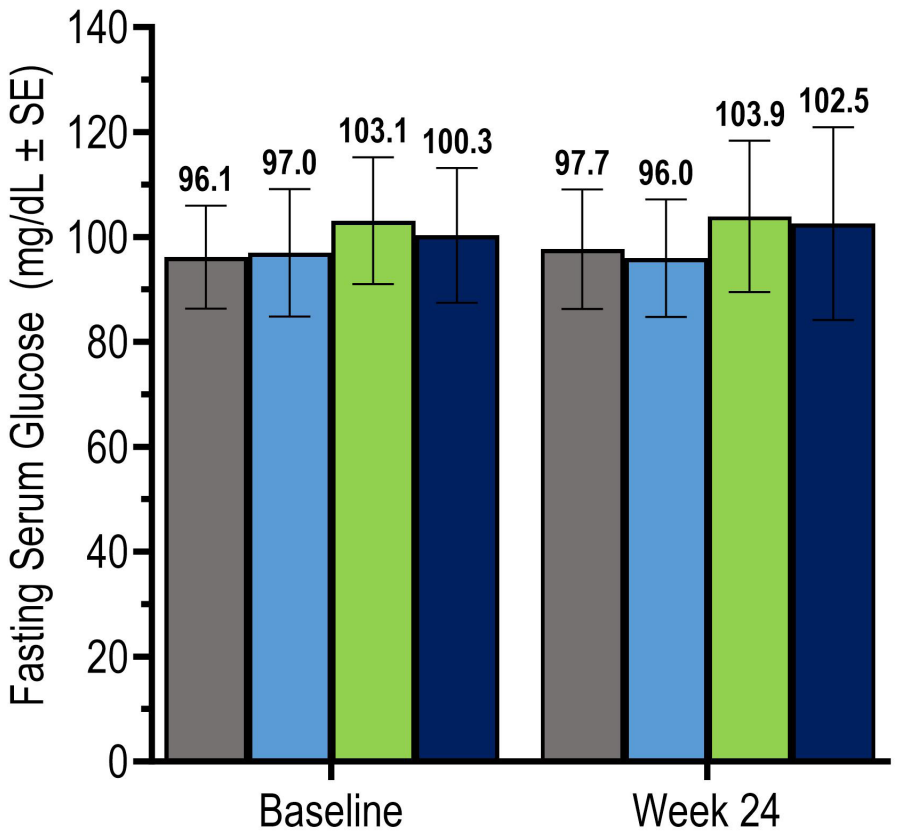
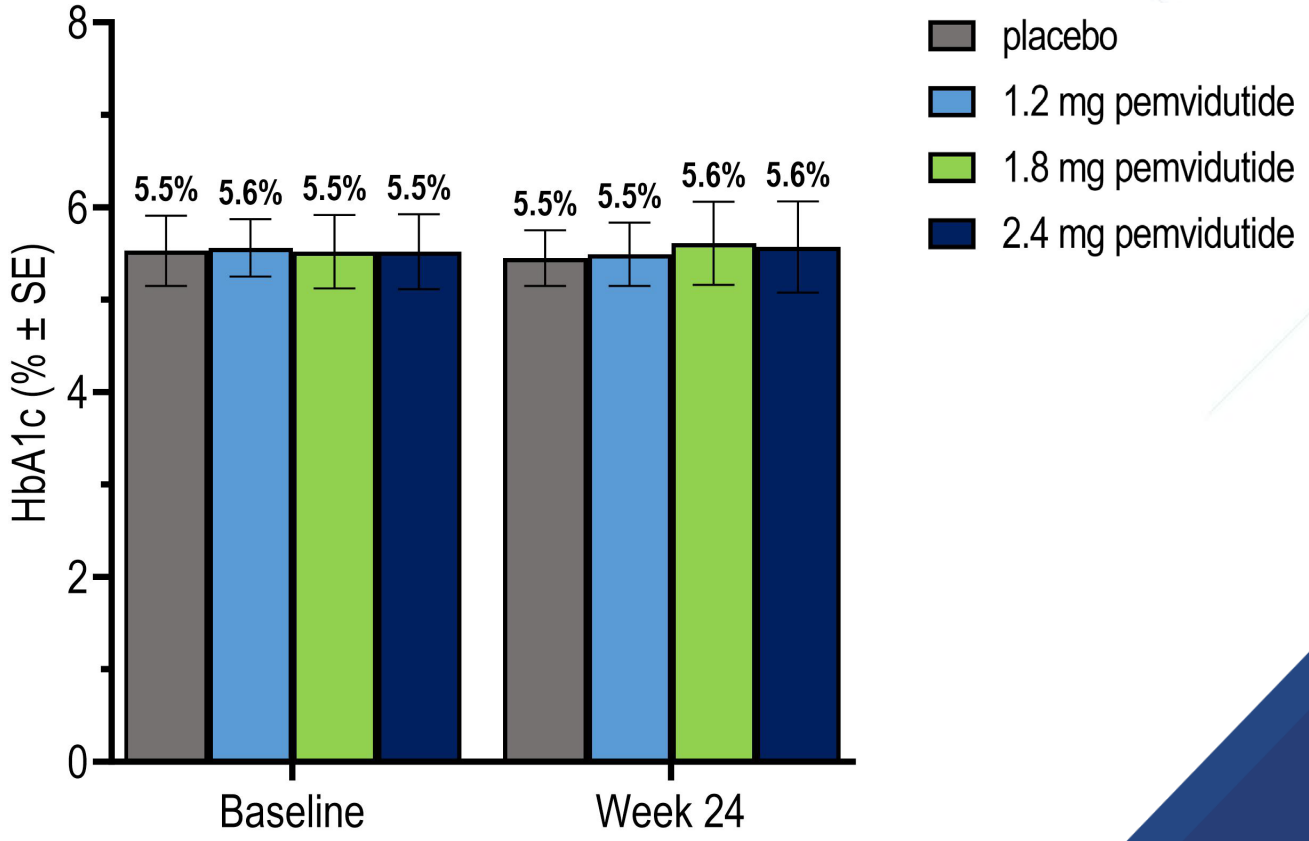
GLUCOSE HOMEOSTASIS MAINTAINED THROUGH WEEK 24





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SUMMARY AND CONCLUSIONS

OBESITY

- Up to 10.7% (9.7% placebo-adjusted) reduction in body weight in 24 weeks
- Significant reductions in LDL-C and triglyceride levels
- Significant reductions in blood pressure without changes in heart rate

SAFETY & TOLERABILITY

- Gastrointestinal adverse event rates similar to other incretin-based agents
- Administered with little to no dose-titration
- Tolerability can be enhanced by allowing dose reduction in future trials

FUTURE DIRECTIONS

- 48-wk results to be announced in Q4 2023