PEMVIDUTIDE, A GLP-1/GLUCAGON DUAL RECEPTOR AGONIST, IN SUBJECTS WITH OVERWEIGHT OR OBESITY: A 48-WEEK, PLACEBO-CONTROLLED, PHASE 2 TRIAL (MOMENTUM)

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DISCLOSURES

Grants/Consultancy: Allurion, Altimmune, Atria, Gelesis, Jamieson Wellness, Janssen Pharmaceuticals, Jazz Pharmaceuticals, Novo Nordisk, Pfizer, Optum, Eli Lilly, Senda Biosciences, Versanis. Grants; Allurion, AstraZeneca, Gelesis, Janssen Pharmaceuticals, Novo Nordisk, Eli Lilly.

Stock/Shareholding; Allurion, ERX Pharmaceuticals, Gelesis, Intellihealth, Jamieson Wellness, Myos Corp.

Other: ERX Pharmaceuticals, Intellihealth, Jamieson Wellness

US PREVALENCE AND SIGNIFICANCE OF OBESITY COMORBIDITIES

66-70% Dyslipidemia[1,2]

58-75% MASLD[3,4,5]
30-36% MASH[3,4,6]

45-55% Hypertension[1,7]

41-45% Sleep Apnea[8,9]

19-23% T2DM[1,7]

Most significant comorbidities are dyslipidemia, MASLD/MASH, and hypertension

1) Bays, Harold, et. al. (2013) Obesity, adiposity, and dyslipidemia: A consensus statement from the National Lipid Association. Journal of Clinical Lipidology 7(4):304–383.
2) Lim Y, Boster J. Obesity and Comorbid Conditions. [Updated 2023 Feb 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; https://www.ncbi.nlm.nih.gov/books/NBK574535/
3) Quek, Jingxuan, et. al. (2023) Global prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in the overweight and obese population:. The Lancet Gastroenterology & Hepatology 8(1):20-30.
4) Vernon, G, et. al. (2011) Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment Pharmacol Ther 34:274–285.
5) Le, Michael, et. al. (2022) 2019 Global NAFLD Prevalence: A Systematic Review and Meta-analysis. Clinical Gastroenterology and Hepatology 2022;20:2809–2817
6) Dufour, Jean-François, et. al. (2021) The global epidemiology of nonalcoholic steatohepatitis (NASH) and associated risk factors–A targeted literature review. Endocrine and Metabolic Science 3.
7) Pantalone KM, et al. Prevalence and recognition of obesity and its associated comorbidities. BMJ Open 2017;7:e017583. doi:10.1136/ bmjopen-2017-017583
8) Romero-Corral, Abel, et. al. (2010) Interactions Between Obesity and Obstructive Sleep Apnea. Chest 137(3): 711-719.
9) Garvey JF, Pengo MF, Drakatos P, Kent BD. Epidemiological aspects of obstructive sleep apnea. J Thorac Dis 2015;7(5):920-929.

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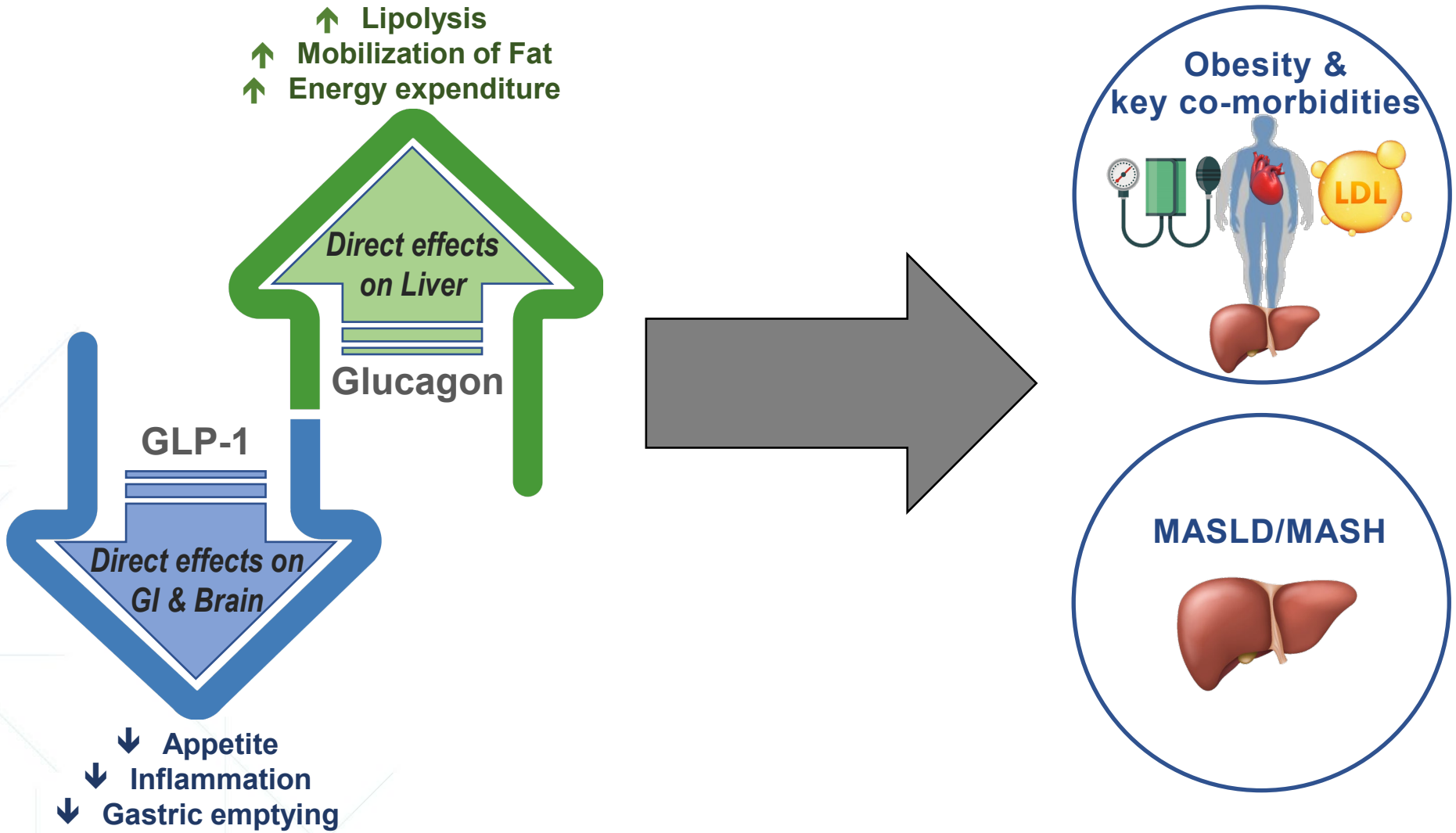
PEMVIDUTIDE MOA IS OPTIMIZED FOR OBESITY AND MASLD/MASH



[1]US Obesity Population: Hales CM et al. NCHS Data Brief. 2020 Feb;(360):1-8. PMID: 32487284.
[2]US MASH Population: Younossi ZM et all. Gut. 2020;(3):564-568. doi: 10.1136/gutjnl-2019-318813

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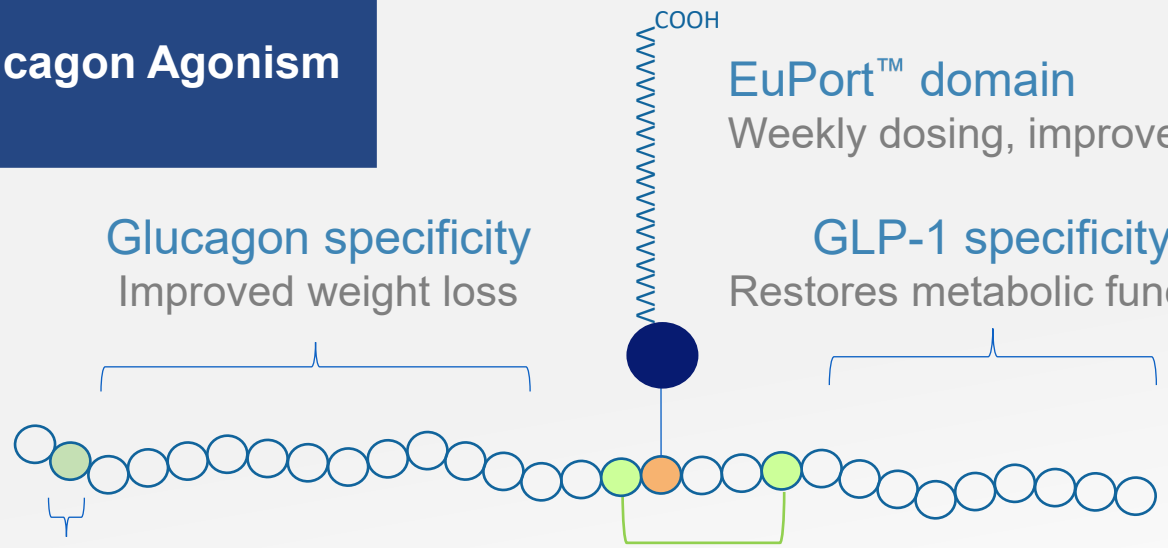
PEMVIDUTIDE: RATIONALLY DESIGNED AND HIGHLY DIFFERENTIATED

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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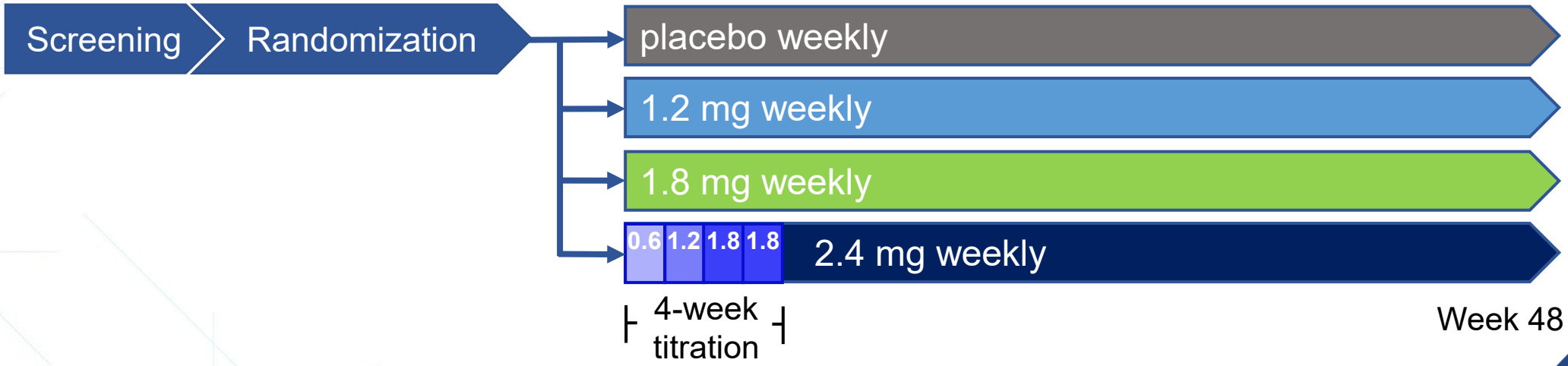
MOMENTUM OBESITY TRIAL DESIGN

- **Phase 2, 48-week trial of pemvidutide in 391 subjects with overweight or obesity**
- **Randomized 1:1:1:1 to 4 treatment arms, stratified by gender and baseline BMI, with standard lifestyle interventions**
- **No or rapid (4 week) dose titration; dose reduction for intolerability was not allowed**
- **Body composition MRIs were obtained in subset of subjects at baseline and week 48**



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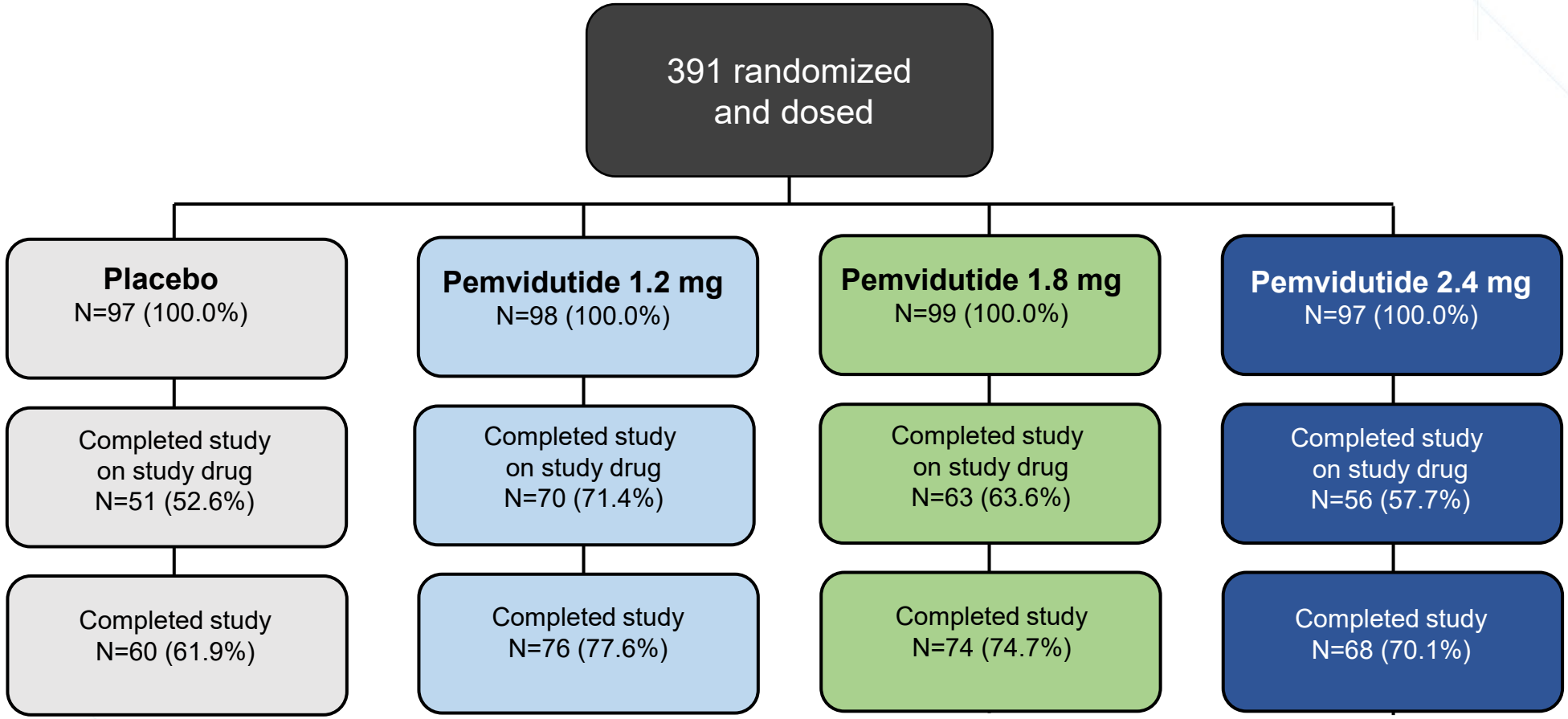
MOMENTUM KEY ELIGIBILITY CRITERIA

- **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**

DISPOSITION OF SUBJECTS



74.1% of subjects receiving pemvidutide completed the study

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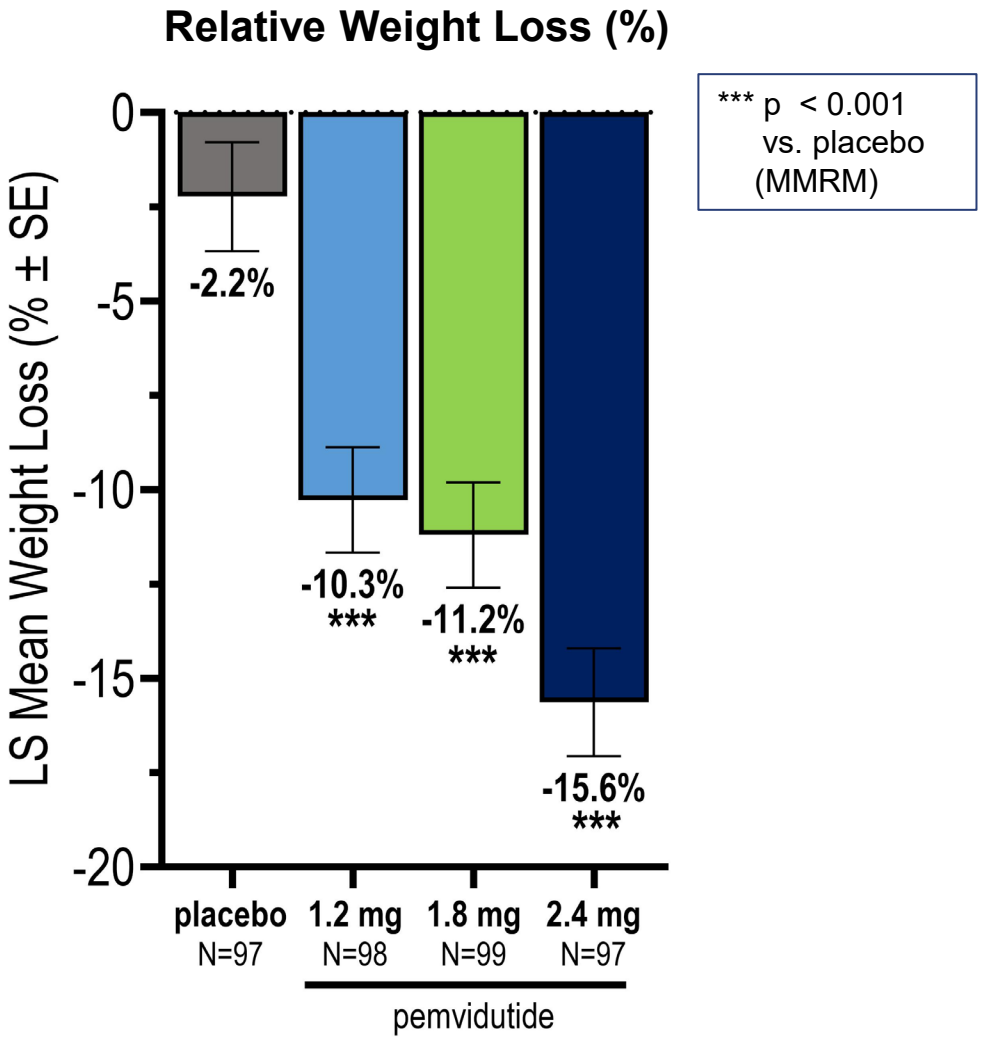
BASELINE CHARACTERISTICS OF SUBJECTS

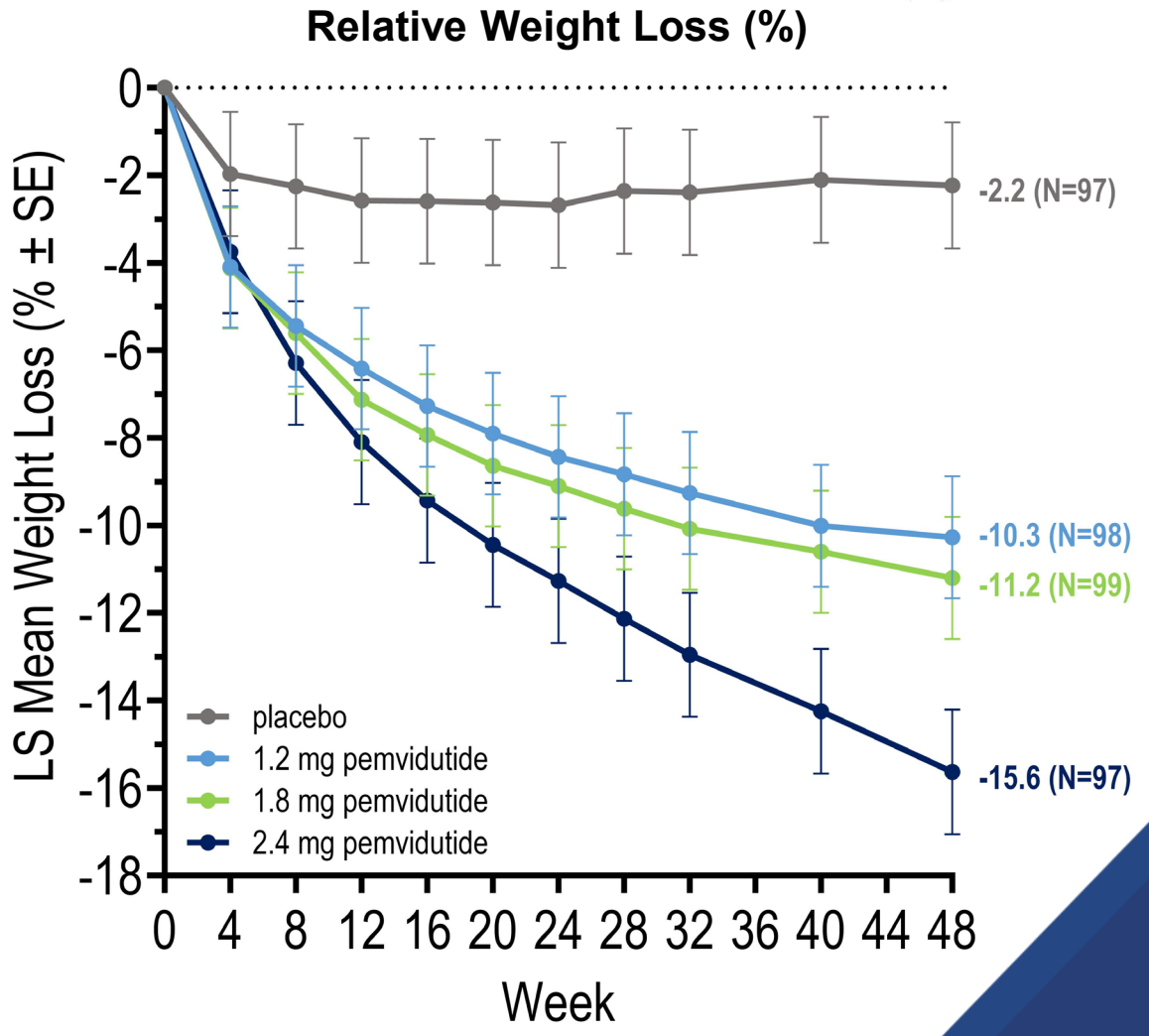
Characteristic		Treatment			
		Placebo (N=97)	1.2 mg (N=98)	1.8 mg (N=99)	2.4 mg (N=97)
Age, years	mean (SD)	50.3 (13.6)	49.6 (12.3)	50.1 (13.3)	48.5 (13.6)
Gender	female, N (%)	72 (74.2%)	75 (76.5%)	76 (76.8%)	74 (76.3%)
Race	White, N (%)	76 (78.4%)	86 (87.8%)	72 (72.7%)	77 (79.4%)
	African-American, N (%)	13 (13.4%)	8 (8.2%)	19 (19.2%)	16 (16.5%)
	Asian, N (%)	5 (5.2%)	1 (1.0%)	2 (2.0%)	0 (0.0%)
	Native or American Indian, N (%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)
	Other, N (%)	3 (3.1%)	3 (3.1%)	5 (5.1%)	4 (4.1%)
Ethnicity	Hispanic, N (%)	19 (19.6%)	19 (19.4%)	18 (18.2%)	24 (24.7%)
	not Hispanic, N (%)	78 (80.4%)	77 (78.6%)	79 (79.8%)	73 (75.3%)
	not reported, N (%)	0 (0.0%)	2 (2.0%)	2 (2.0%)	0 (0.0%)
BMI, kg/m^2	mean (SD)	37.8 (7.2)	37.4 (6.1)	37.4 (7.4)	37.1 (5.9)
Body weight, kg	mean (SD)	105.7 (22.5)	104.5 (22.7)	103.8 (23.8)	104.0 (19.7)
Blood pressure, mm Hg	systolic, mean (SD)	122.2 (12.8)	121.6 (12.9)	124.0 (12.8)	124.7 (13.0)
	diastolic, mean (SD)	76.4 (8.1)	77.9 (7.5)	78.2 (7.6)	80.0 (7.7)

Weight Loss of 15.6% Achieved at Week 48 on 2.4 mg

MEAN WEIGHT LOSS OF 32.2 LBS AND MAXIMAL WEIGHT LOSS OF 87.1 LBS



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



MMRM, mixed model for repeated measures

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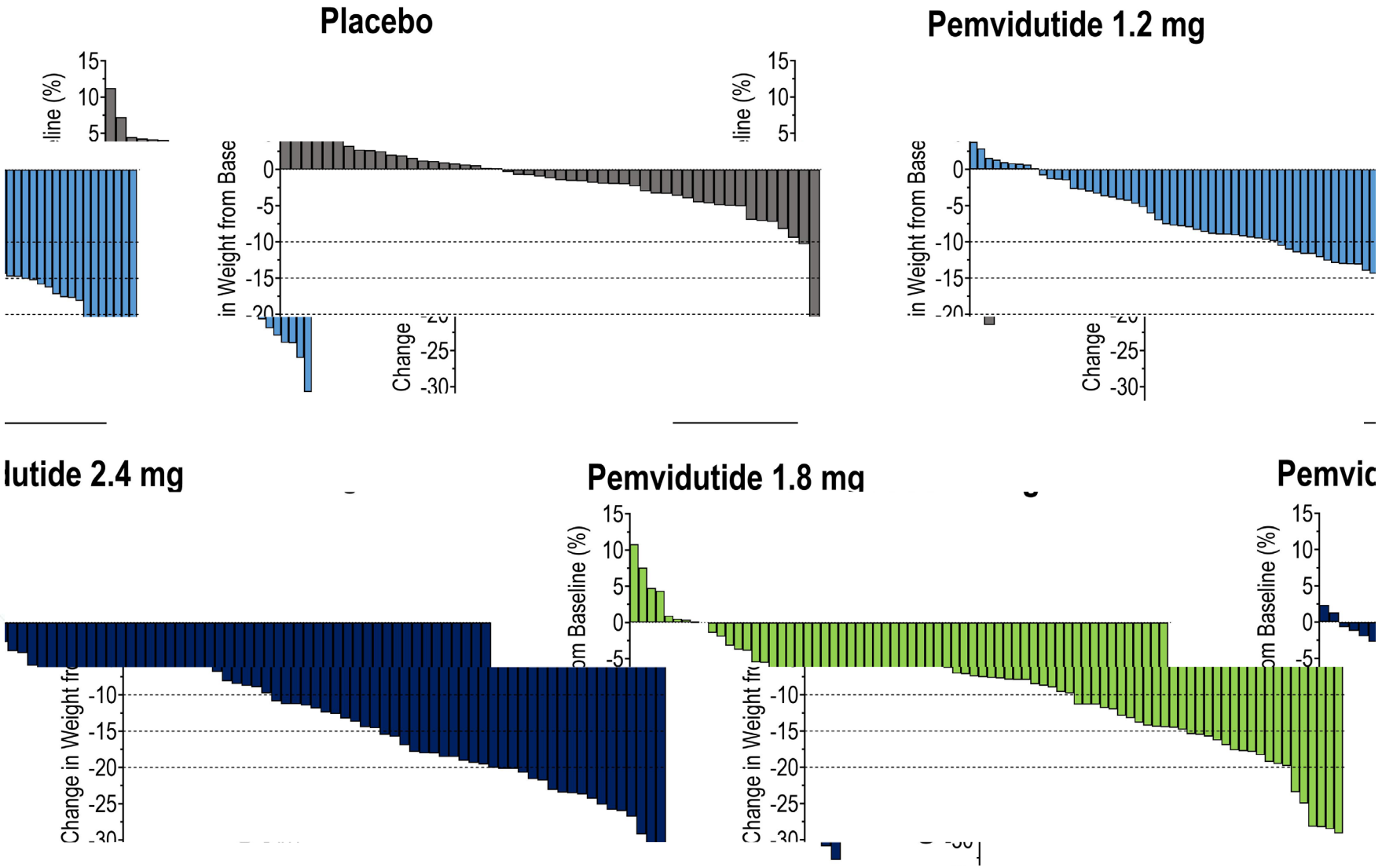
ROBUST WEIGHT LOSS AT ALL PEMVIDUTIDE DOSES

OVER 30% OF SUBJECTS LOST 20% OR MORE BODY WEIGHT ON 2.4 MG



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PRESERVATION OF LEAN MASS EMERGING AS KEY ATTRIBUTE OF CHRONIC WEIGHT MANAGEMENT

- **Lean mass loss of ~25% is an expected outcome of weight loss, however:**
  - Sarcopenia and loss of lean mass increase mortality[1]
  - Up to 19% of Americans have sarcopenic obesity[2]
- **Incretin therapy has been associated with up to 40% lean mass loss[3]**
- **Weight loss therapies that minimize loss of lean mass are needed**

1. Lee DH, Giovannucci EL. Body composition and mortality in the general population: A review of epidemiologic studies. Exp Biol Med (Maywood). 2018 Dec;243(17-18):1275-1285. doi: 10.1177/1535370218818161. Epub 2018 Dec 11. PMID: 30537867; PMCID: PMC6348595.
2. Gao Q, Mei F, Shang Y, Hu K, Chen F, Zhao, Ma B. lobal prevalence of sarcopenic obesity in older adults: A systematic review and meta-analysis. Epub 2021 Jun 21. 40(7):4633-4641. doi: 10.1016/j.clnu.2021.06.009.
3. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, McGowan BM, Rosenstock J, Tran MTD, Wadden TA, Wharton S, Yokote K, Zeuthen N, Kushner RF; STEP 1 Study Group. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021 Mar 18;384(11):989-1002. doi: 10.1056/NEJMoa2032183. Epub 2021 Feb 10. PMID: 33567185.

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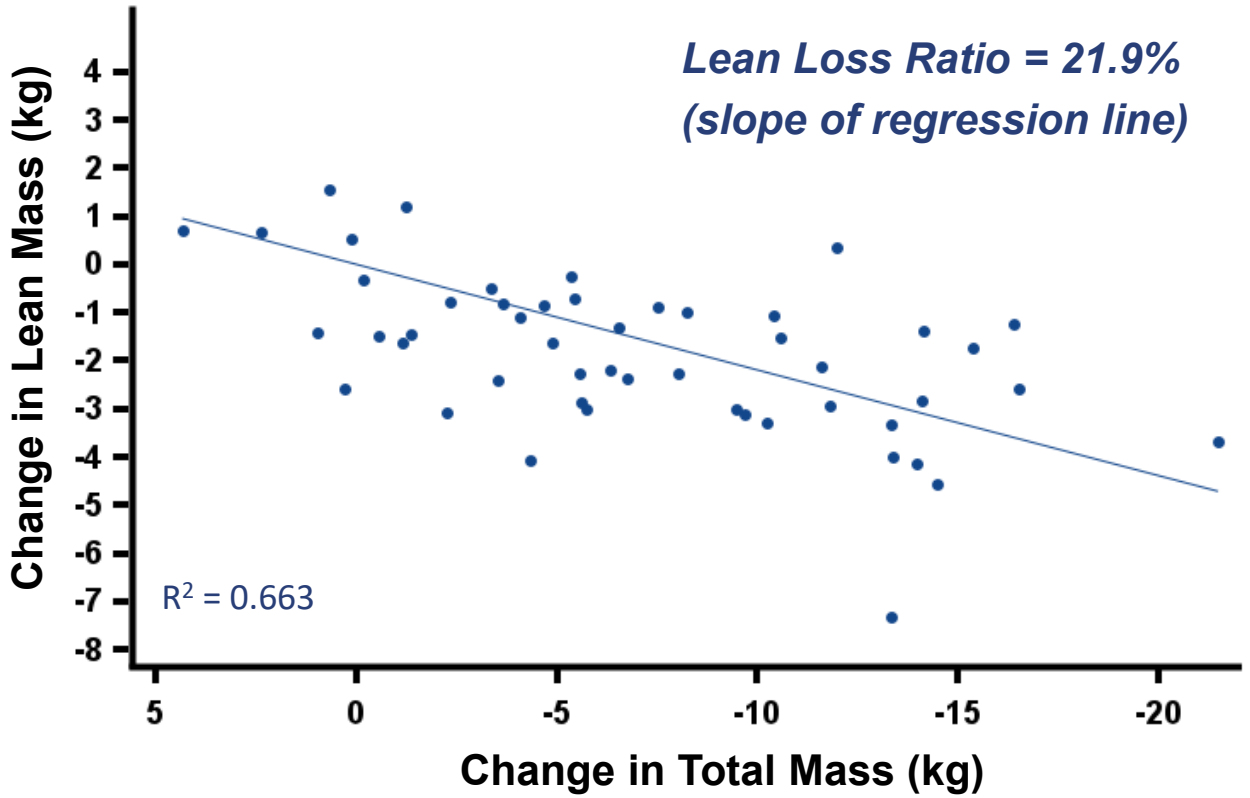
PEMVIDUTIDE– ONLY 21.9% OF WEIGHT LOSS FROM LEAN MASS

MRI-BASED BODY COMPOSITION ANALYSIS SUBSTANTIATES QUALITY OF WEIGHT LOSS WITH PEMVIDUTIDE TREATMENT

Regression Analysis of Change in Lean Mass vs. Change in Total Mass
Pemvidutide-treated Subjects, Full Analysis Set (n = 50)



Lean Loss Ratio = (lean mass loss)/(lean mass loss + adipose mass loss)

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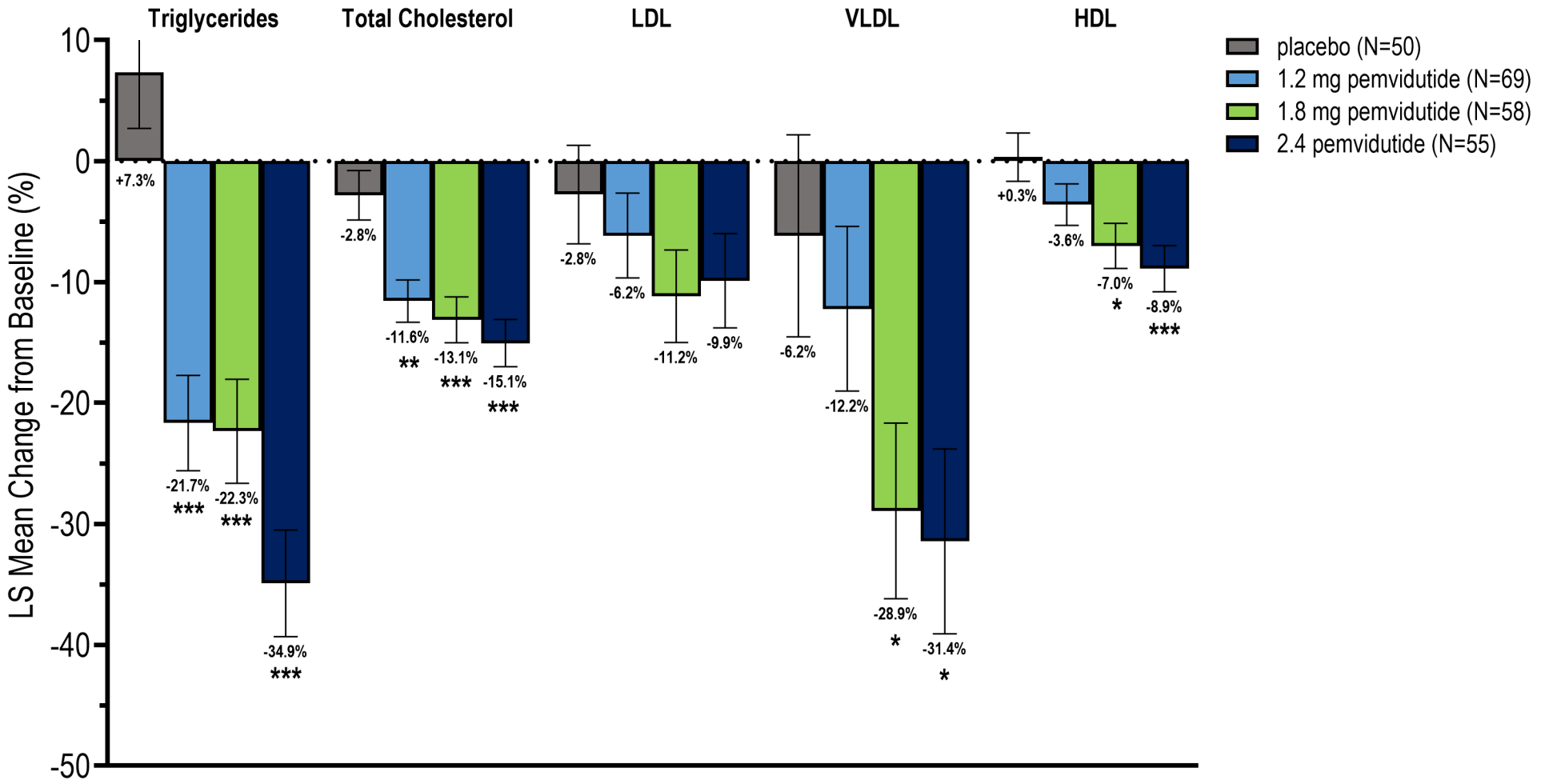
ROBUST REDUCTIONS IN SERUM LIPIDS AT WEEK 48



ANCOVA, analysis of covariance

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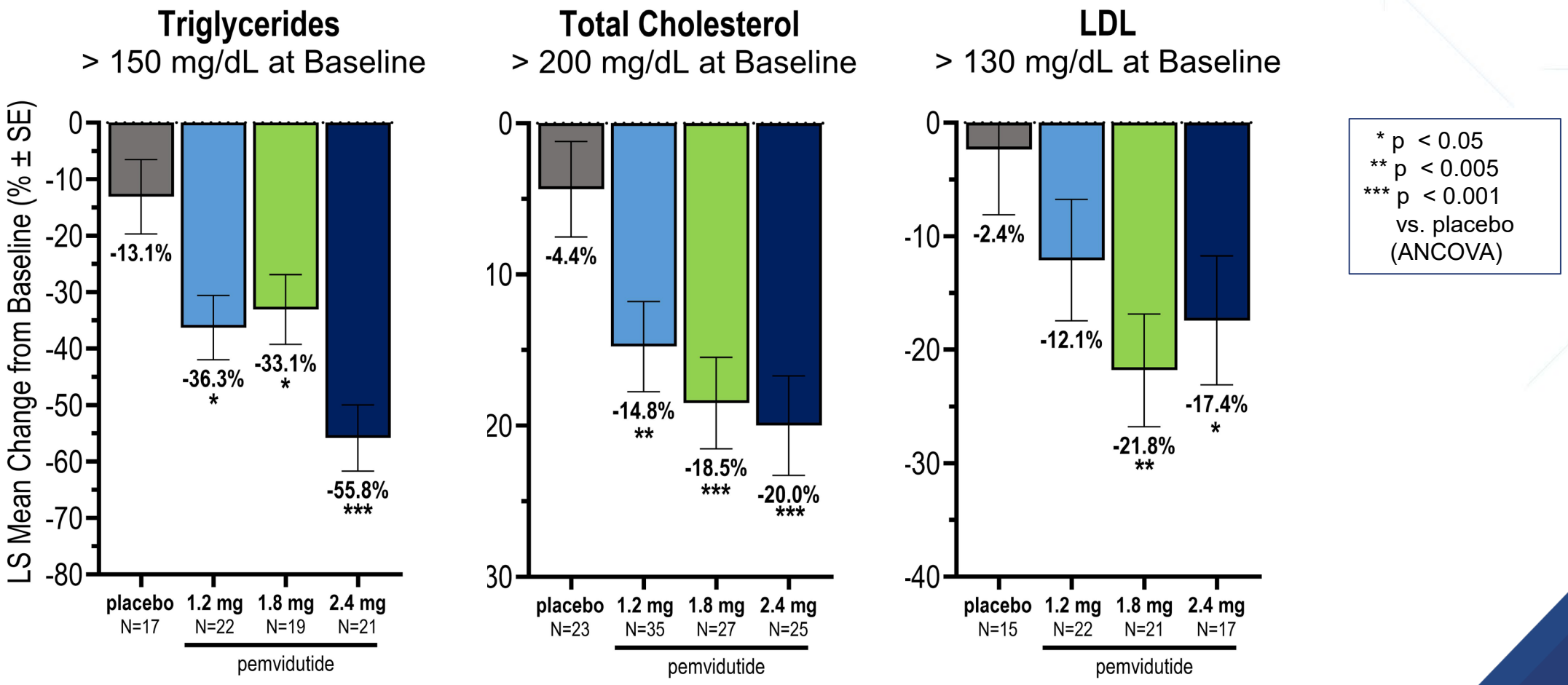
GREATER REDUCTIONS IN TRIGLYCERIDES, TOTAL AND LDL CHOLESTEROL IN SUBJECTS WITH ELEVATED BASELINE LEVELS



ANCOVA, analysis of covariance

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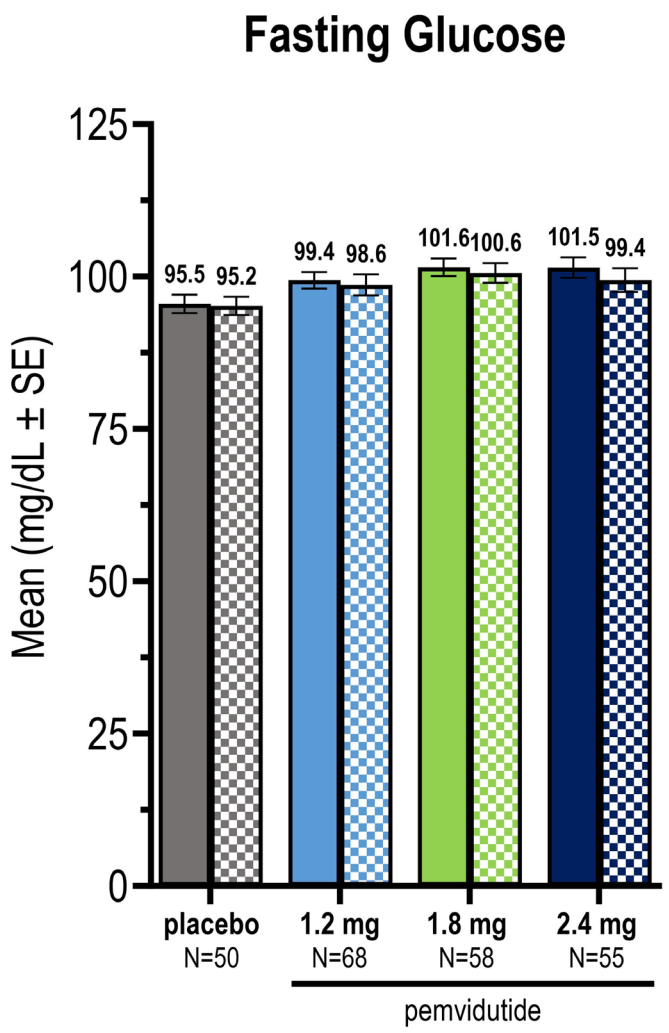
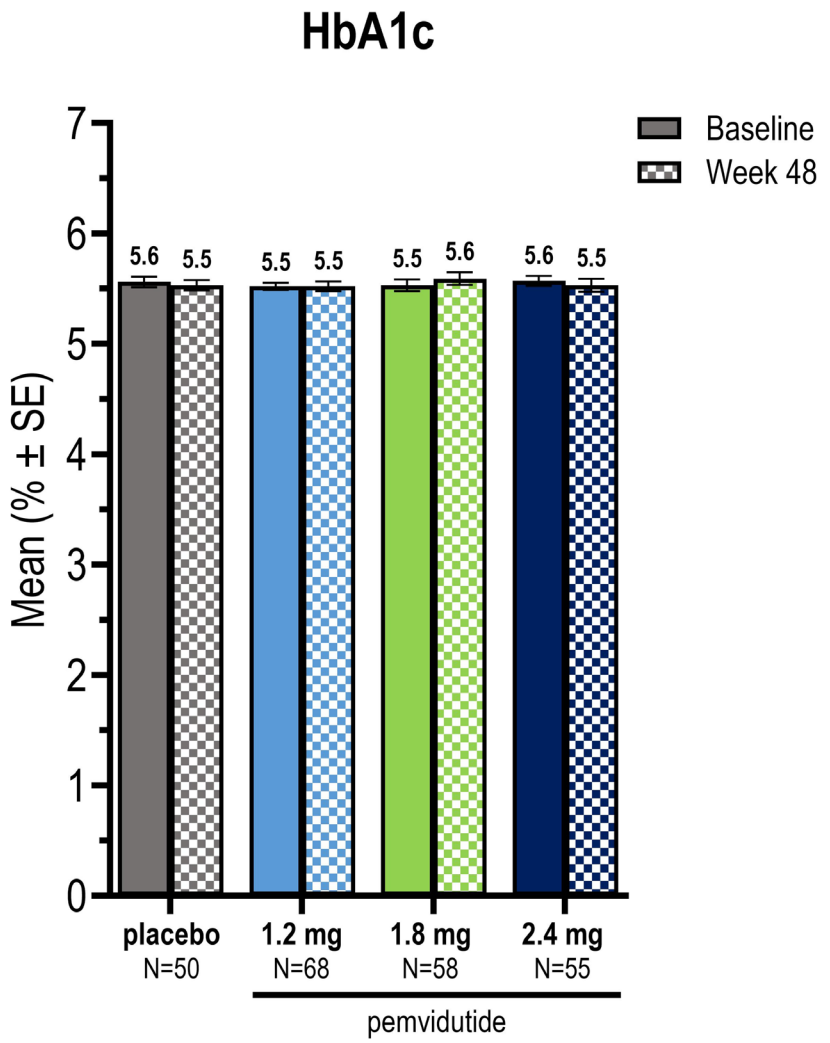
GLUCOSE HOMEOSTASIS MAINTAINED





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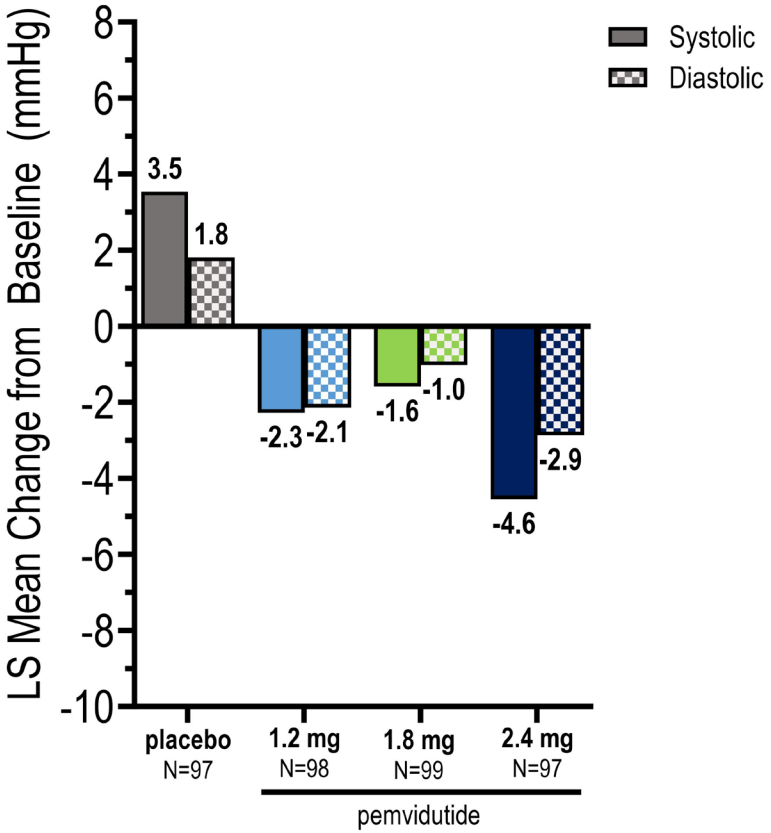
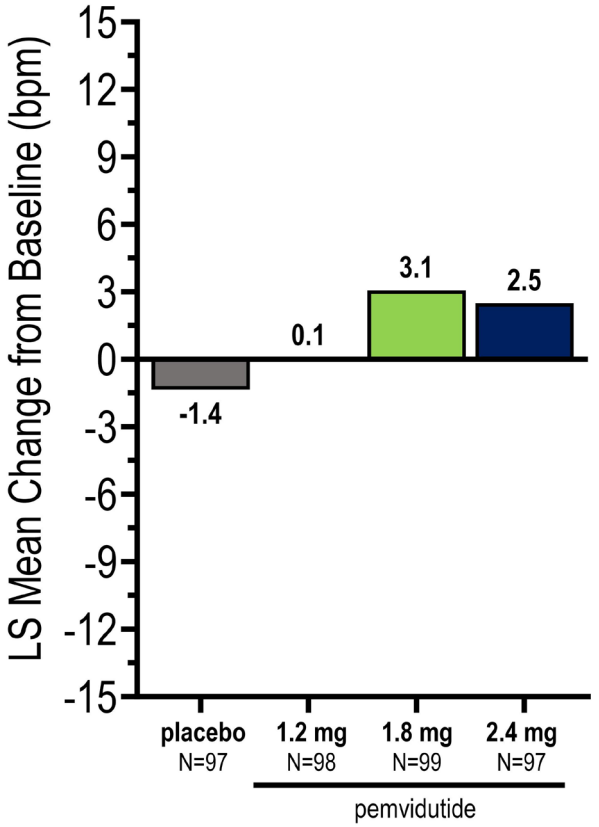
IMPROVEMENTS IN BLOOD PRESSURE WITHOUT CLINICALLY MEANINGFUL INCREASES IN HEART RATE AT WEEK 48

Blood Pressure



Heart Rate



MMRM, mixed model for repeated measures

OVERVIEW OF ADVERSE EVENTS (AEs)

Characteristic		Treatment			
		Placebo (N=97)	1.2 mg (N=98)	1.8 mg (N=99)	2.4 mg (N=97)
SAEs related to study drug	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
AEs leading to study drug discontinuation					
All AEs leading to discontinuation	N (%)	6 (6.2%)	5 (5.1%)	19 (19.2%)	19 (19.6%)
Drug-related AEs leading to discontinuation	N (%)	2 (2.1%)	4 (4.1%)	16 (16.2%)	15 (15.5%)
Gastrointestinal (GI) AEs—mainly mild to moderate					
Nausea	N (%)	11 (11.3%)	25 (25.5%)	59 (59.6%)	50 (51.5%)
Vomiting	N (%)	3 (3.1%)	6 (6.1%)	27 (27.3%)	27 (27.8%)
Diarrhea	N (%)	5 (5.2%)	8 (8.2%)	10 (10.1%)	18 (18.6%)
Constipation	N (%)	8 (8.2%)	17 (17.3%)	13 (13.1%)	22 (22.7%)
AEs of Special Interest (AESI)	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Major Adverse Cardiac Events (MACE)	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac AEs, including arrhythmias	N (%)	4 (4.1%)	3 (3.1%)	4 (4.0%)	3 (3.1%)

- Only 1 drug-related SAE of vomiting
- No AESI or MACE events
- No imbalances in cardiac AEs across treatment groups

MOMENTUM TRIAL – WEEK 48 SUMMARY

Efficacy

- Robust mean weight loss of 15.6% on pemvidutide 2.4 mg at Week 48
- Over 30% of subjects lost 20% or more body weight on 2.4 mg at Week 48
- Continued weight loss on 2.4 mg at Week 48—greater weight loss could potentially be achieved with longer duration of treatment
- Lean loss index of only 21.9%, representing class-leading preservation of lean mass
- Substantial and clinically meaningful reductions in total cholesterol, LDL, triglycerides and blood pressure

Safety and Tolerability

- Gastrointestinal AEs, common to incretin-based agents, mainly mild to moderate in severity
- No imbalance in cardiac AEs, including arrhythmias
- No clinically meaningful increases in heart rate
- Glucose homeostasis maintained