12-Week, Phase 1b Study of Pemvidutide in Overweight and Obese Subjects with Non-Alcoholic Fatty Liver Disease (NAFLD)—Topline Results

Stephen Harrison, MD, Lead Investigator

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Forward-looking statements

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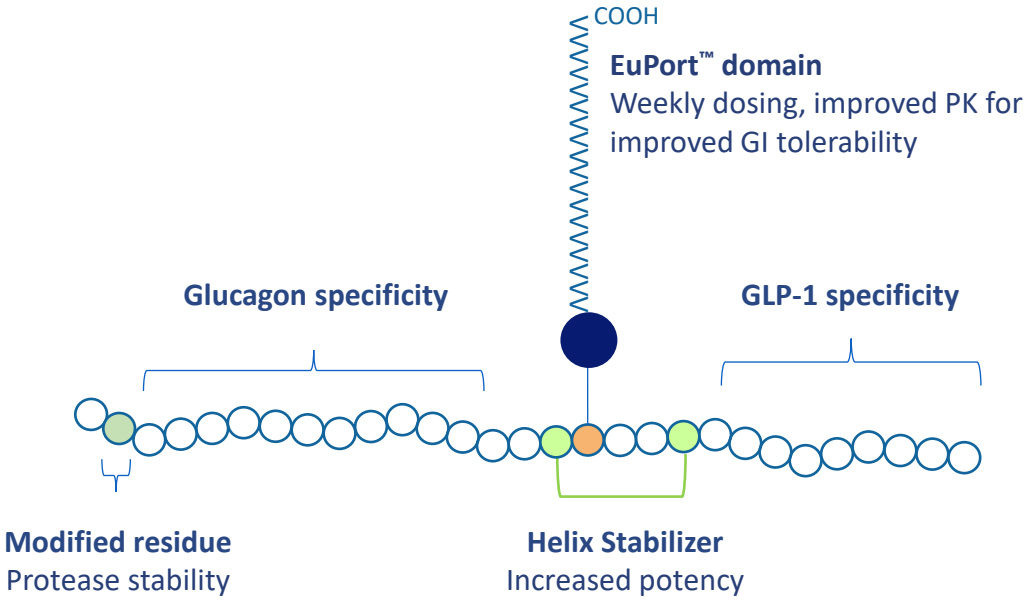
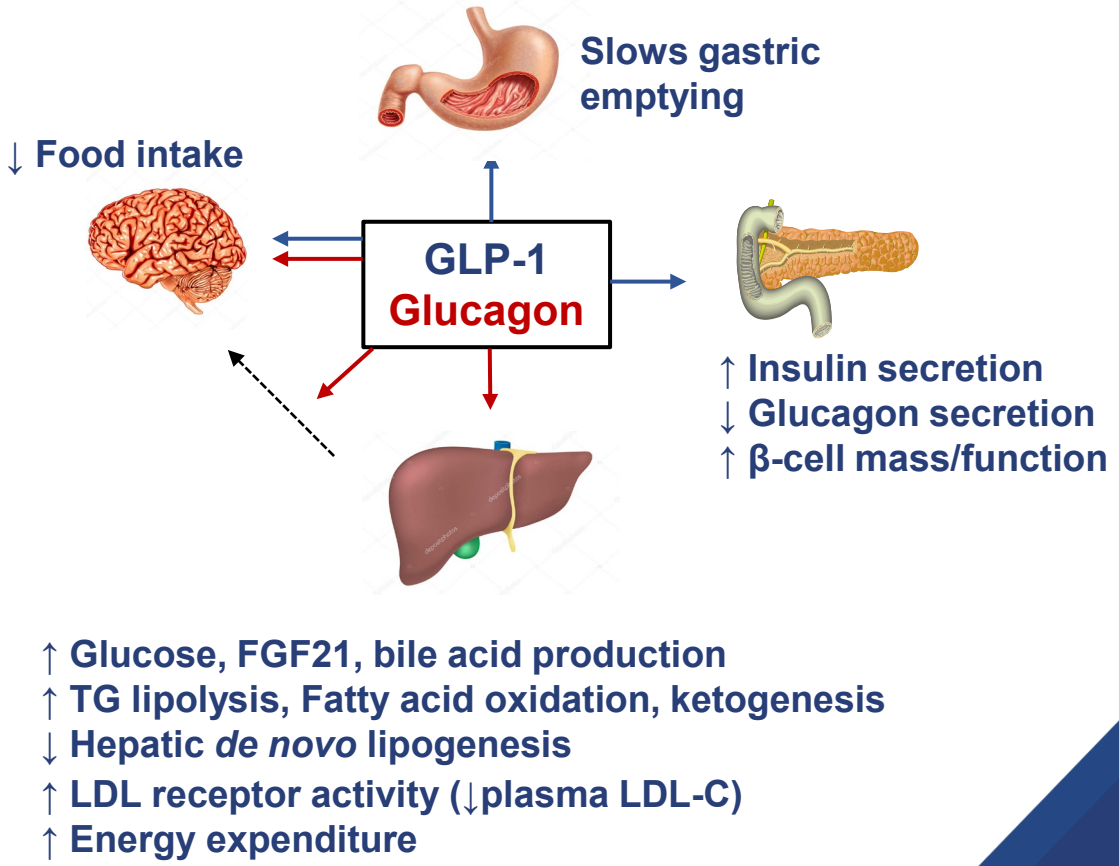
Pemvidutide[1]

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





[1]proposed INN

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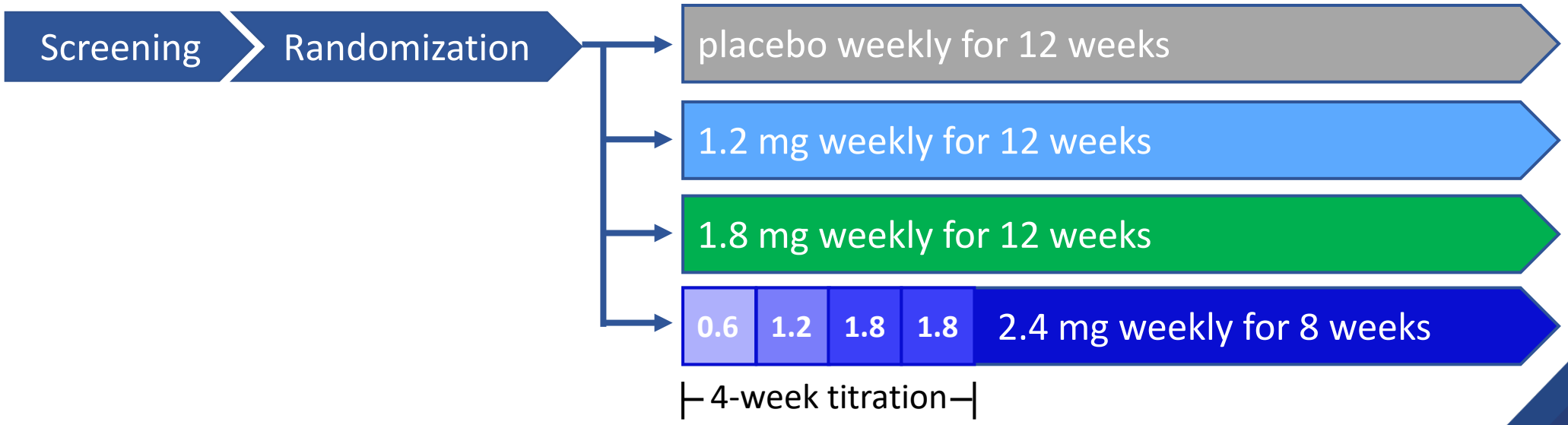
Pemvidutide Phase 1b NAFLD Trial Design

- 12-week, randomized, placebo-controlled study of pemvidutide in subjects with overweight/obesity and non-alcoholic fatty liver disease (NAFLD)
- 94 subjects randomized 1:1:1:1 and dosed across 13 US sites to 1 of 4 treatment arms, stratified by the presence or absence of type 2 diabetes (T2D)



- No caloric restriction or lifestyle intervention

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Study Population—Key Eligibility Criteria

- **Men and women, ages 18-65 years**
- **BMI ≥ 28 kg/m^2**
- **NAFLD, defined as liver fat content (LFC) by MRI-PDFF ≥ 10%**
- **Absence of significant fibrosis, defined as FibroScan® LSM < 10kPa**
- **Non-diabetes OR diabetes if:**
  - Stable dose (≥ 3 months) metformin or SLGT-2 therapy AND
  - No use of insulin, sulfonylureas, DPP-4, GLP-1 treatment
- **HbA1c < 9.5%**
- **Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) laboratory values ≤ 75 IU/L**

Study Endpoints

Efficacy

- **Primary Endpoint: Reduction in liver fat content by MRI-PDFF**
- **Key Secondary Endpoint: Percent (%) weight loss**

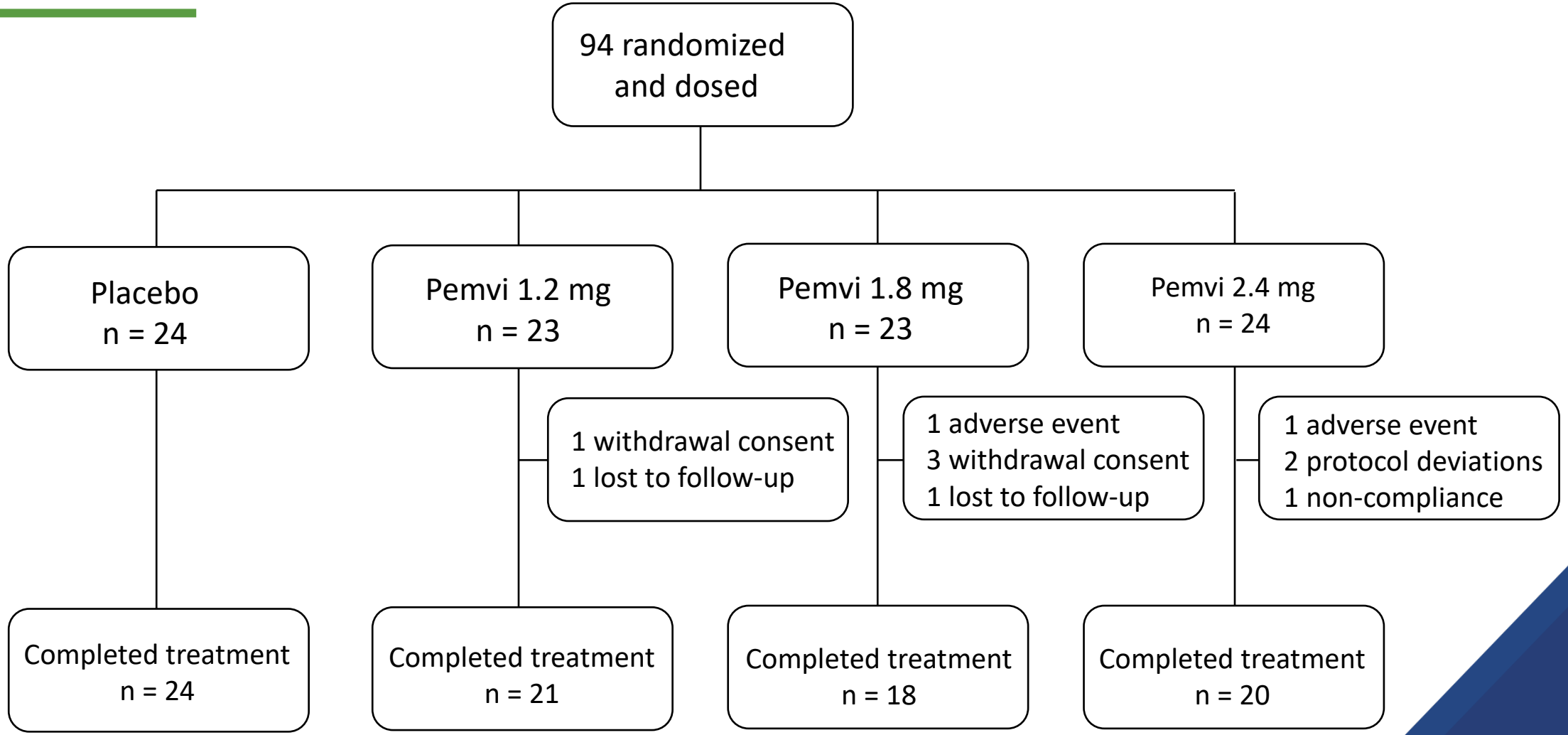
Safety

- **Adverse events (AEs)**
  - Serious and severe AEs
  - AEs leading to discontinuation
  - GI tolerability
- **ALT elevations**
- **Vital signs**
- **Glycemic control (fasting glucose, HbA1c)**

Characteristics of Study Participants

Characteristic		Treatment			
		Placebo (n = 24)	1.2 mg (n=23)	1.8 mg (n=23)	2.4 mg (n=24)
Age, years	mean (SD)	47.9 (14)	48.6 (11)	50.3 (9)	48.8 (8)
Gender	female, n (%)	14 (58.3%)	9 (39.1%)	12 (52.2%)	15 (62.5%)
Race	white, n (%)	21 (87.5%)	21 (91.3%)	20 (87.0%)	24 (100%)
	other, n (%)	3 (12.5%)	2 (8.7%)	3 (13.0%)	0 (0.0%)
Ethnicity	Hispanic, n (%)	14 (58.3%)	20 (87.0%)	19 (82.6%)	18 (75.0%)
	not Hispanic, n (%)	10 (41.7%)	3 (13.0%)	4 (17.4%)	6 (25.0%)
BMI, kg/m^2	mean (SD)	36.9 (4.7)	36.3 (5.6)	35.4 (3.9)	35.3 (5.0)
Body weight, kg	mean (SD)	105.1 (20.8)	102.4 (14.6)	98.9 (19.7)	98.2 (18.9)
Diabetes status	T2D, n (%)	6 (25.0%)	7 (30.4%)	7 (30.4%)	7 (33.3%)
Liver fat content (LFC), %	mean (SD)	23.8 (9.2)	21.6 (7.3)	21.8 (8.0)	20.2 (7.0)
ALT, IU/L	mean (SD)	39.5 (21.4)	32.4 (13.8)	36.4 (15.6)	37.8 (24.4)
Blood pressure, mm Hg	systolic, mean (SD)	122.8 (11.4)	129.0 (14.1)	123.2 (15.9)	125.9 (12.3)
	diastolic, mean (SD)	79.6 (6.0)	79.3 (9.1)	77.8 (9.7)	80.1 (8.6)
Total cholesterol, mg/dL	mean (SD)	181.4 (39.0)	186.9 (44.8)	200.0 (35.2)	182.2 (39.7)
LDL cholesterol, mg/dL	mean (SD)	100.0 (38.2)	100.2 (34.3)	116.6 (33.6)	101.3 (33.0)
Triglycerides, mg/dL	mean (SD)	169.3 (90.1)	224.9 (119.1)	192.2 (114.9)	220.0 (169.3)
HDL cholesterol, mg/dL	mean (SD)	47.5 (6.8)	42.6 (9.1)	47.0 (9.9)	45.3 (7.3)

Study Disposition



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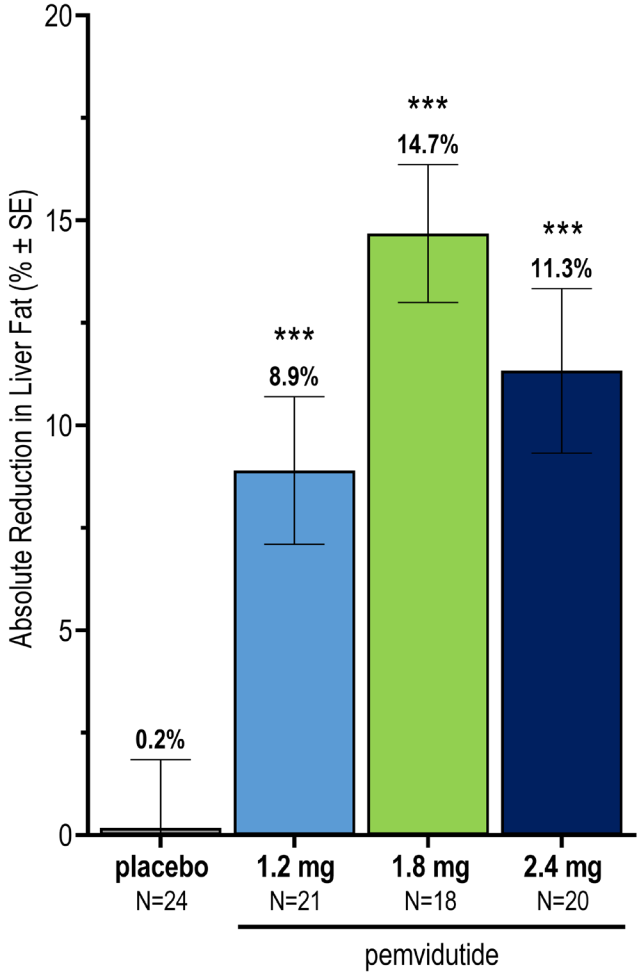
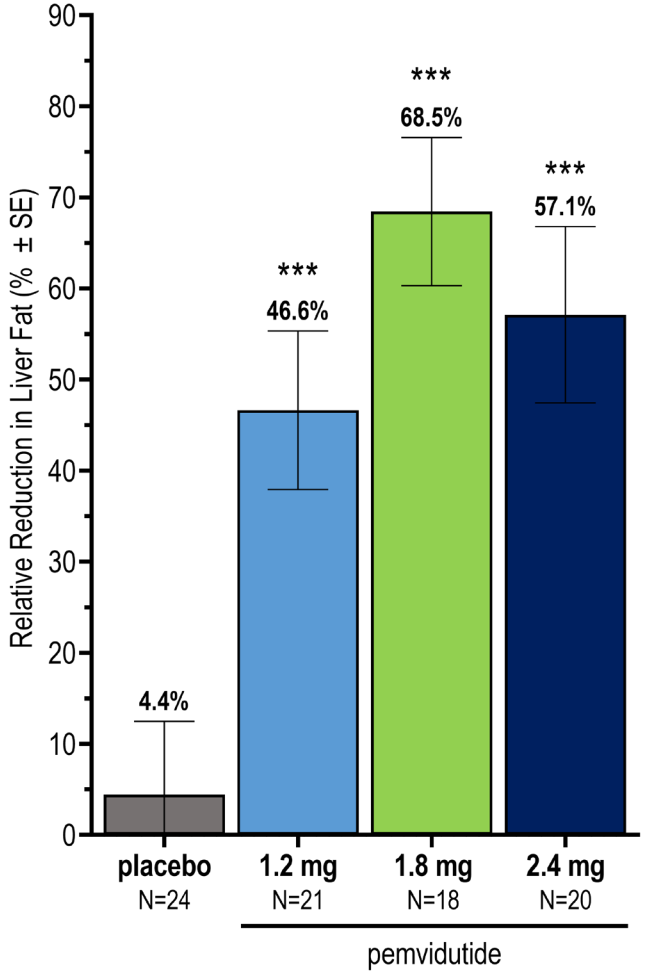
Reduction in Liver Fat Content by MRI-PDFF at Week 12

Absolute Reduction



Relative Reduction



*** p < 0.001 vs. placebo, (ANCOVA)

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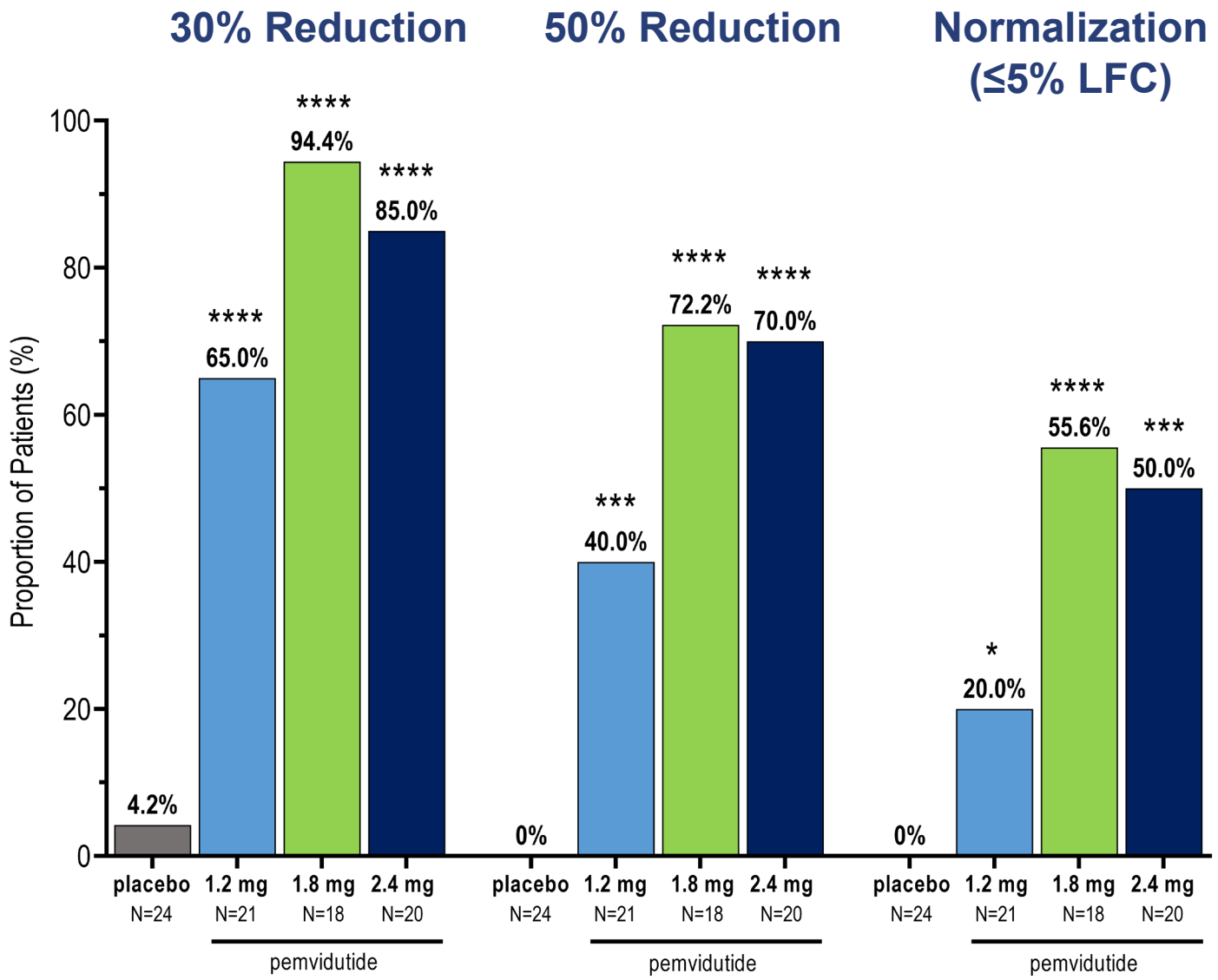
Reduction in Liver Fat Content by MRI-PDFF at Week 12—Responder Analyses



* p < 0.05
*** p < 0.001
**** p < 0.0001 vs. placebo, (CMH[1])

[1]Cochran-Mantel-Haenszel

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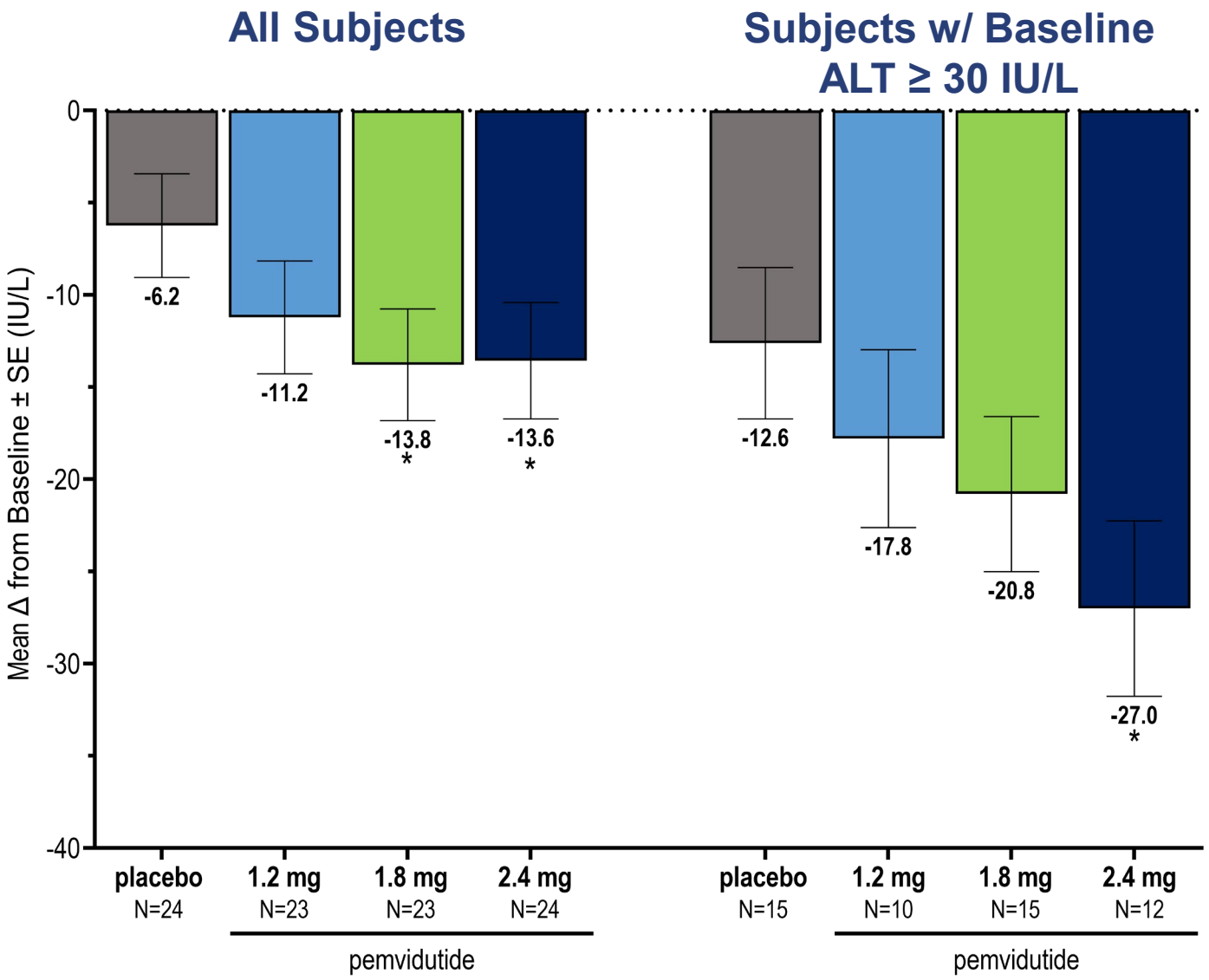
ALT Reduction at Week 12



* p < 0.05 vs. placebo, (MMRM[1])

[1]Mixed Model Repeated Measures

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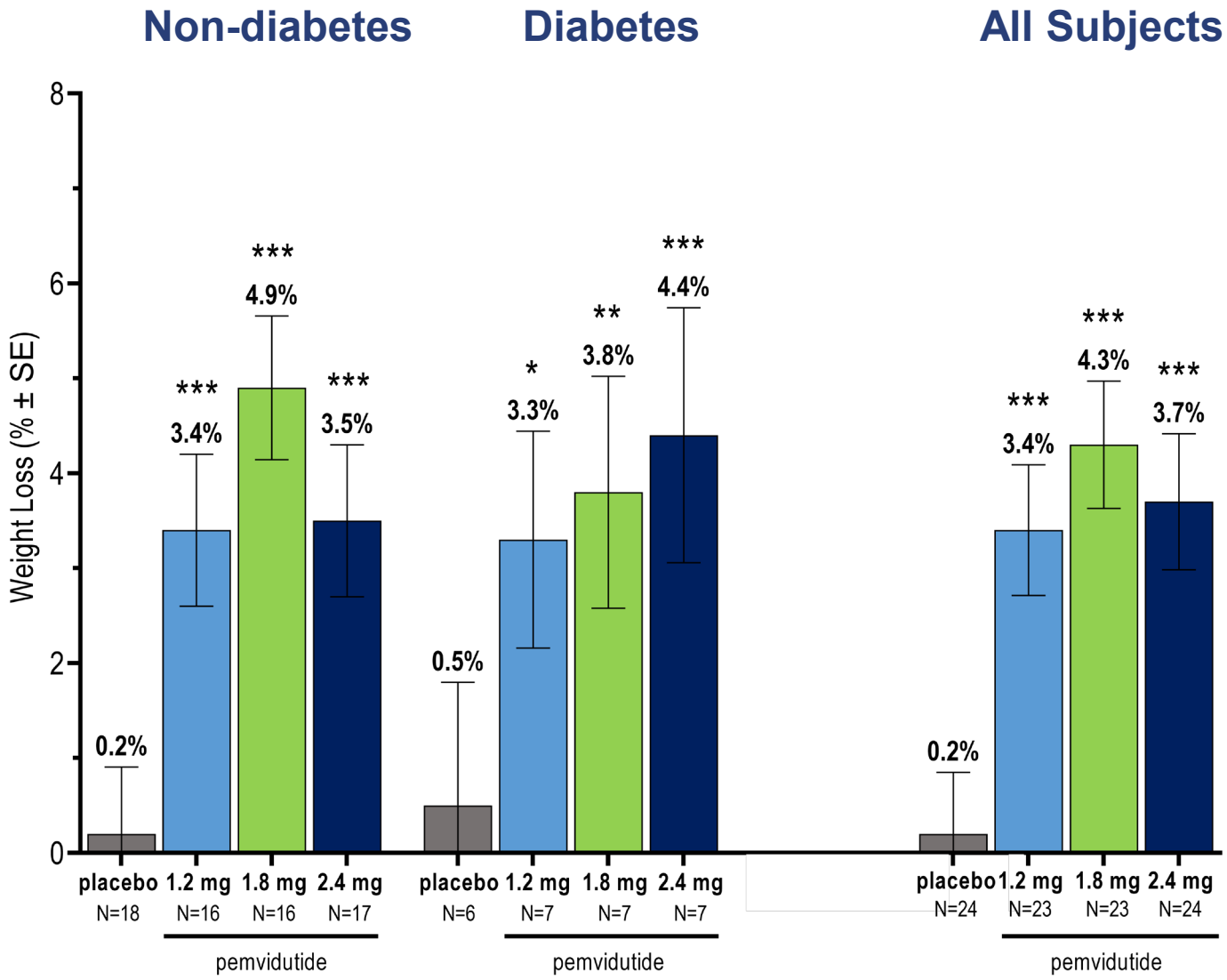
Weight Loss at Week 12—Efficacy Estimand



* p < 0.05
** p < 0.005
*** p < 0.001
vs. placebo,
(MMRM)

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Changes in Serum Lipids at Week 12

Characteristic		Treatment			
		Placebo (n = 24)	1.2 mg (n=21)	1.8 mg (n=18)	2.4 mg (n=20)
% Change from baseline to Week 12					
Total cholesterol, mean (SE)	%	-5.9 (4.4)	-10.1 (4.7)	-9.0 (4.5)	-12.2 (5.1)
LDL, mean (SE)	%	4.2 (8.1)	1.2 (8.6)	2.7 (8.1)	0.5 (9.6)
HDL, mean (SE)	%	-5.3 (3.3)	-1.1 (3.5)	-9.7 (3.3)	-6.9 (3.8)
Triglycerides, mean (SE)	%	-18.7 (14.7)	-42.8 (15.6)	-33.7 (14.7)	-44.6 (16.8)

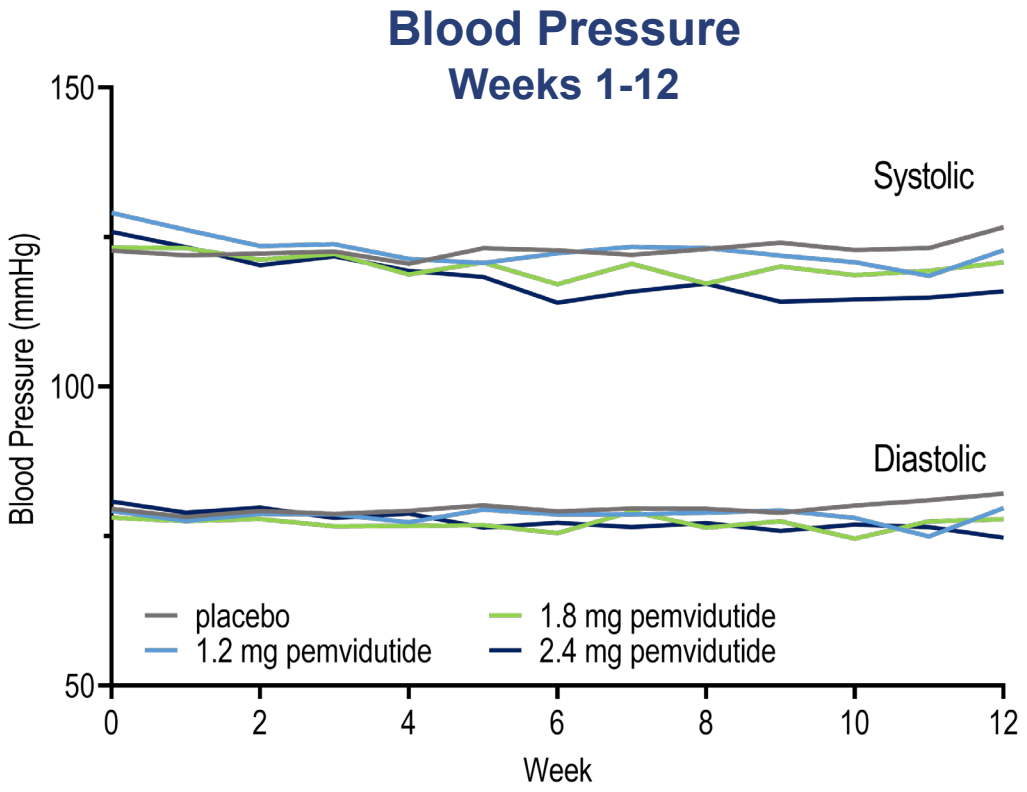
ANCOVA model

Safety Overview

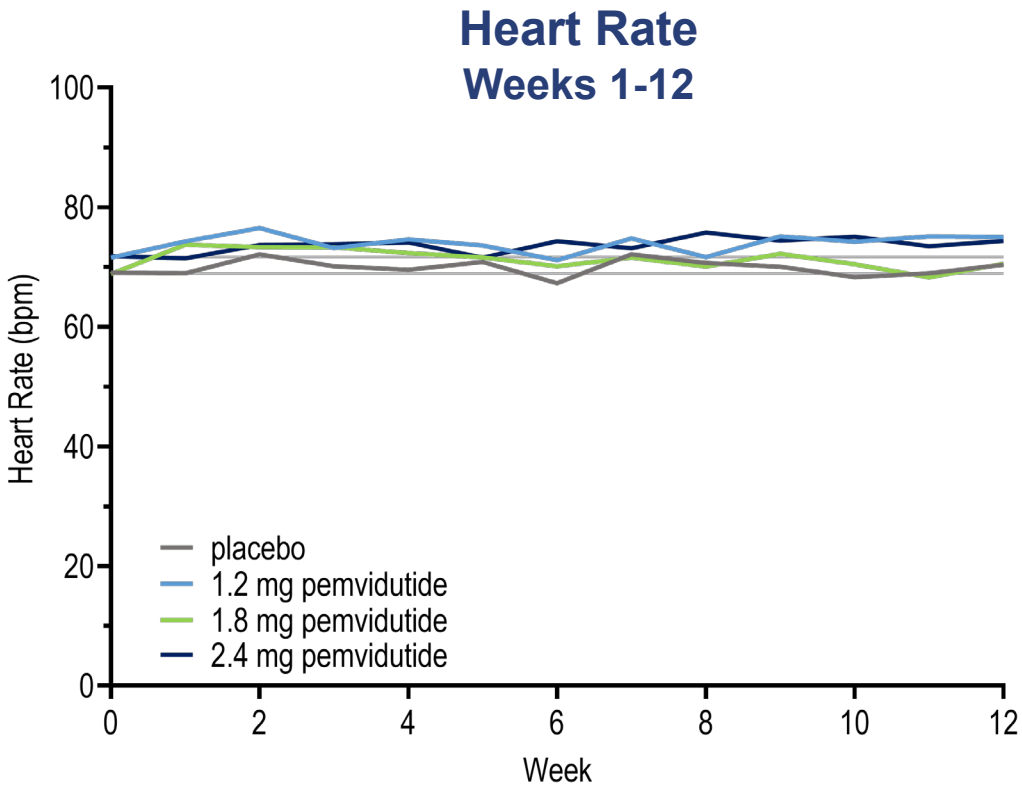
Characteristic		Treatment			
		Placebo (n = 24)	1.2 mg (n=23)	1.8 mg (n=23)	2.4 mg (n=24)
Severe AEs	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
SAEs	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
AEs leading to treatment discontinuation	**n (%)**	**0 (%)**	**0 (%)**	**1 (4.3%)**	**1 (4.2%)**
Nausea					
Mild	n (%)	3 (12.5%)	3 (13.0%)	6 (26.1%)	6 (25.0%)
Moderate	n (%)	0 (0.0%)	1 (4.3%)	6 (26.1%)	3 (12.5%)
Vomiting					
Mild	n (%)	0 (0.0%)	3 (13.0%)	2 (8.7%)	2 (8.3%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diarrhea					
Mild	n (%)	4 (16.7%)	3 (13.0%)	5 (21.7%)	1 (4.2%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation					
Mild	n (%)	0 (0.0%)	3 (13.0%)	4 (17.4%)	1 (4.2%)
Moderate	n (%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)

No clinically significant increases in ALT (defined as > 3x above ULN)

Blood Pressure and Heart Rate



Mean systolic BP decreases of 6-10 mmHg compared to placebo
Mean diastolic BP decreases of 3-7 mmHg compared to placebo



Mean HR increases of 1-3 bpm compared to placebo

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Glycemic Variables — Non-diabetes and Diabetes

Characteristic		Treatment			
		Placebo	1.2 mg	1.8 mg	2.4 mg
NON-DIABETES		N=18	N=16	N=16	N=17
Fasting glucose					
Baseline, mg/dL	mean (SD)	99.9 (13.6)	99.4 (12.4)	95.1 (10.3)	97.9 (13.6)
Week 12, mg/dL	mean (SD)	101.6 (16.7)	99.5 (12.5)	96.0 (10.8)	100.1 (11.0)
HbA1c					
Baseline, %	mean (SD)	5.8 (0.2)	5.7 (0.3)	5.7 (0.3)	5.6 (0.4)
Week 12, %	mean (SD)	5.8 (0.2)	5.9 (0.4)	5.6 (0.4)	5.8 (0.3)
DIABETES		N=6	N=7	N=7	N=7
Fasting glucose					
Baseline, mg/dL	mean (SD)	114.0 (18.1)	124.4 (26.1)	117.3 (34.7)	166.1 (49.6)
Week 12, mg/dL	mean (SD)	128.5 (33.9)	118.4 (36.8)	135.9 (65.5)	129.9 (52.6)
HbA1c					
Baseline, %	mean (SD)	6.2 (0.6)	6.6 (1.4)	6.4 (0.5)	7.5 (1.3)
Week 12, %	mean (SD)	6.3 (0.8)	6.4 (1.6)	6.9 (1.5)	7.7 (1.2)

Summary and Conclusions

Liver fat reduction

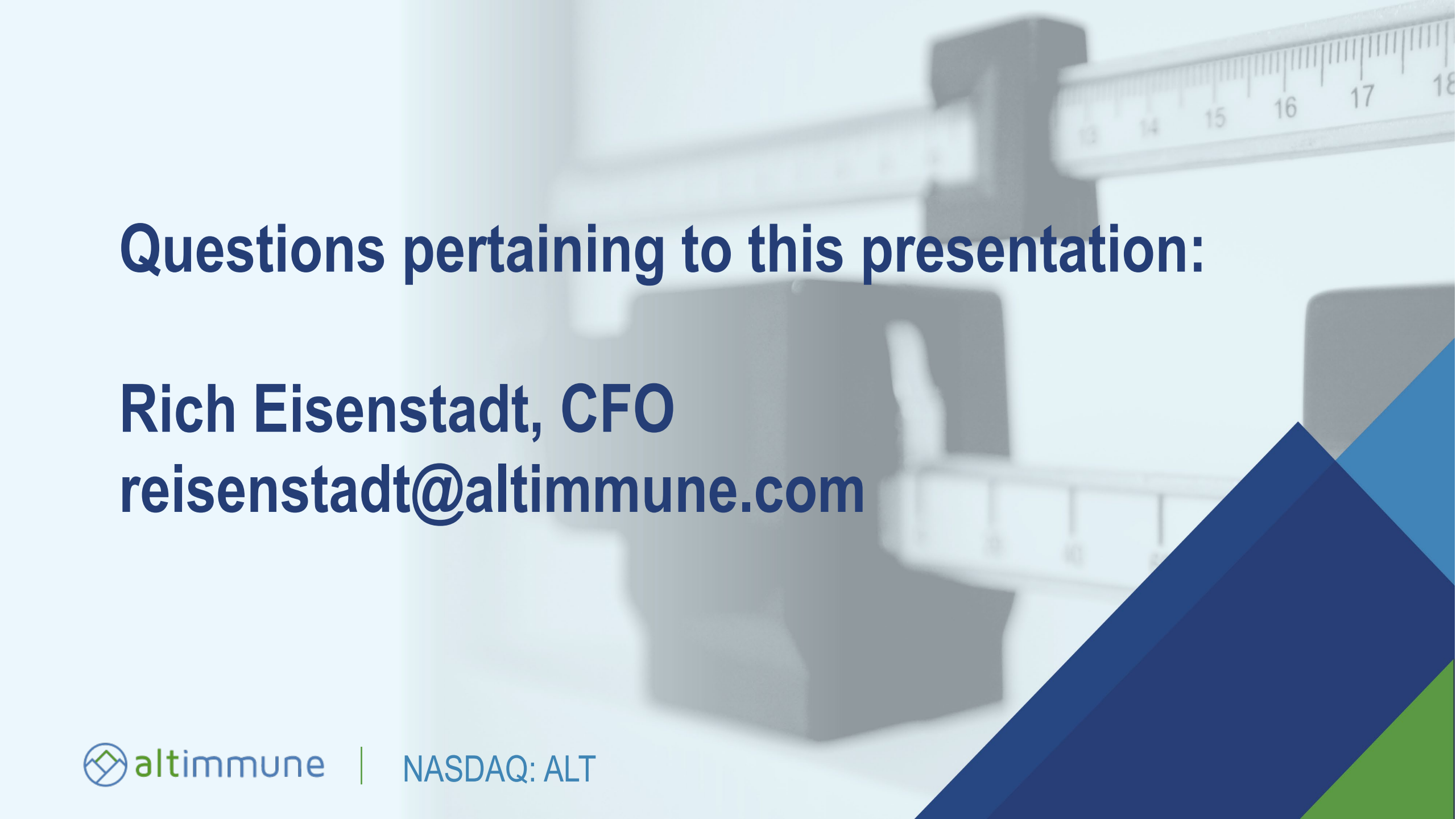
- Robust (>68%) relative liver fat reductions at 12 weeks, better than or equal to the effects of other leading NASH candidates
- Significant reductions in serum ALT point to potent effects in NASH clinical trials

Weight loss

- Non-diabetes—placebo-adjusted weight loss (4.7%) at Week 12
- Diabetes—placebo-adjusted weight loss (3.9%) at Week 12

Safety and tolerability

- No severe or serious AEs and low rates of AEs leading to treatment discontinuations
- Well-tolerated without the need for dose titration, consistent with prior experience
- No clinically significant ALT elevations
- Glycemic control maintained



Questions pertaining to this presentation:

Rich Eisenstadt, CFO
reisenstadt@altimmune.com