A 24-Week (12-Week Extension) Trial of Pemvidutide in Subjects with Non-alcoholic Fatty Liver Disease (NAFLD)

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Forward-looking statements

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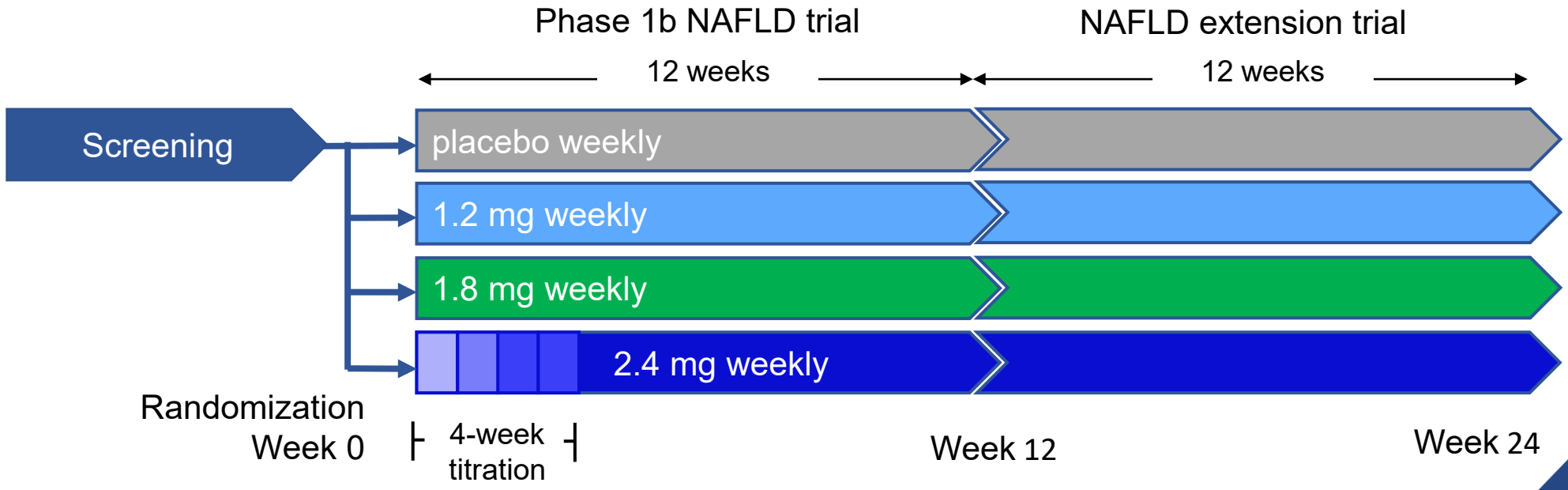
Pemvidutide NAFLD Extension Trial Design

- 12-week extension trial of pemvidutide in subjects with non-alcoholic fatty liver disease (NAFLD)
- 83 subjects who completed the 12-week Phase 1b NAFLD trial were invited to participate, to receive a total of 24 weeks of treatment
- 66 subjects consented to rollover, of whom 64 were eligible to participate



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Study Population—Key Eligibility Criteria

Subjects needed to have completed dosing in the 12-week Phase 1b NAFLD trial and met the following criteria at parent trial entry:

- **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

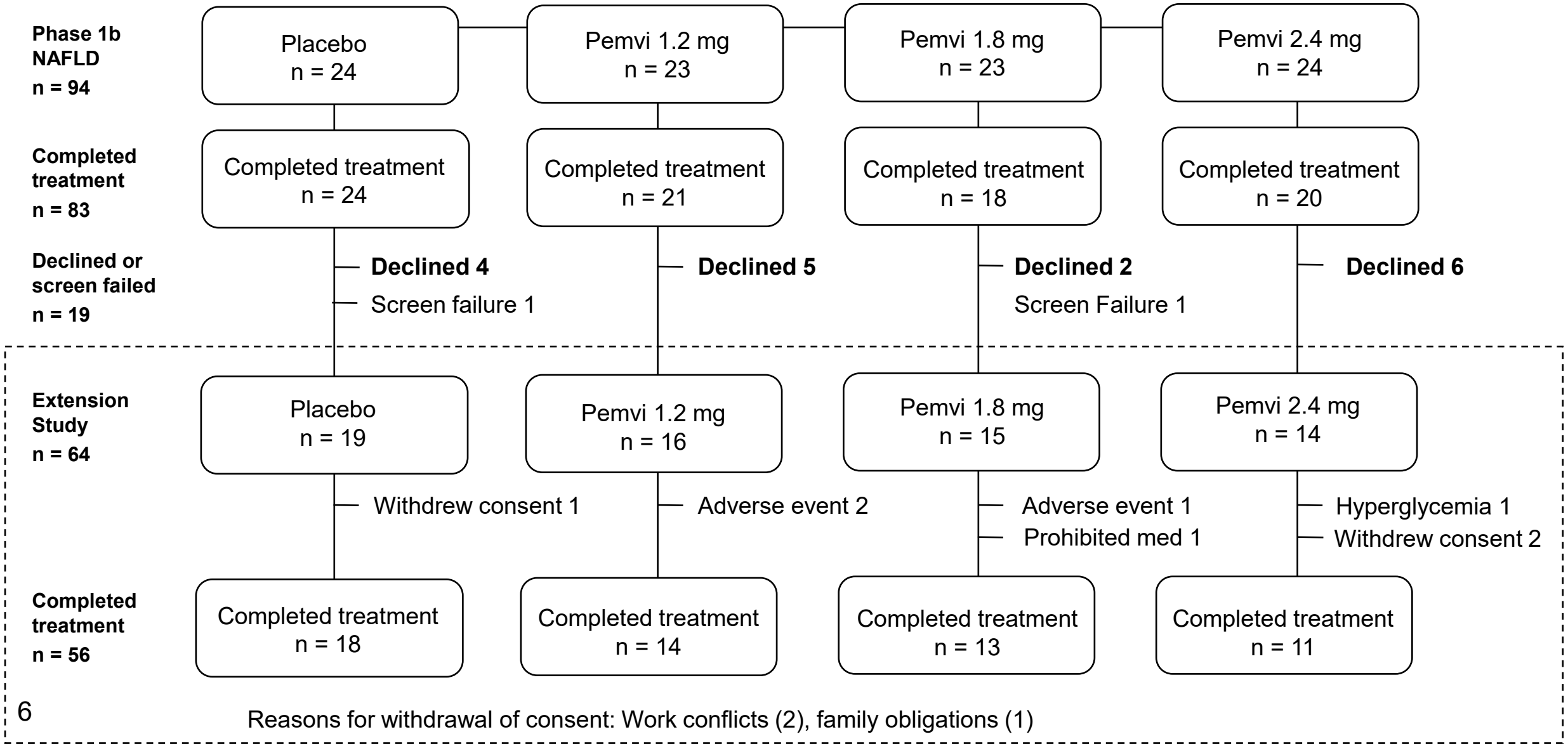
Efficacy

- **Primary Endpoint:**
  - Reduction in liver fat content (LFC) by MRI-PDFF at Week 24 compared to Week 0
- **Key Secondary Endpoints:**
  - Liver inflammation by serum alanine aminotransferase (ALT) levels and corrected T1 (cT1) imaging at Week 24 compared to Week 0
  - Percent (%) weight loss at Week 24 compared to Week 0

Safety

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

Study Disposition



Reasons for withdrawal of consent: Work conflicts (2), family obligations (1)

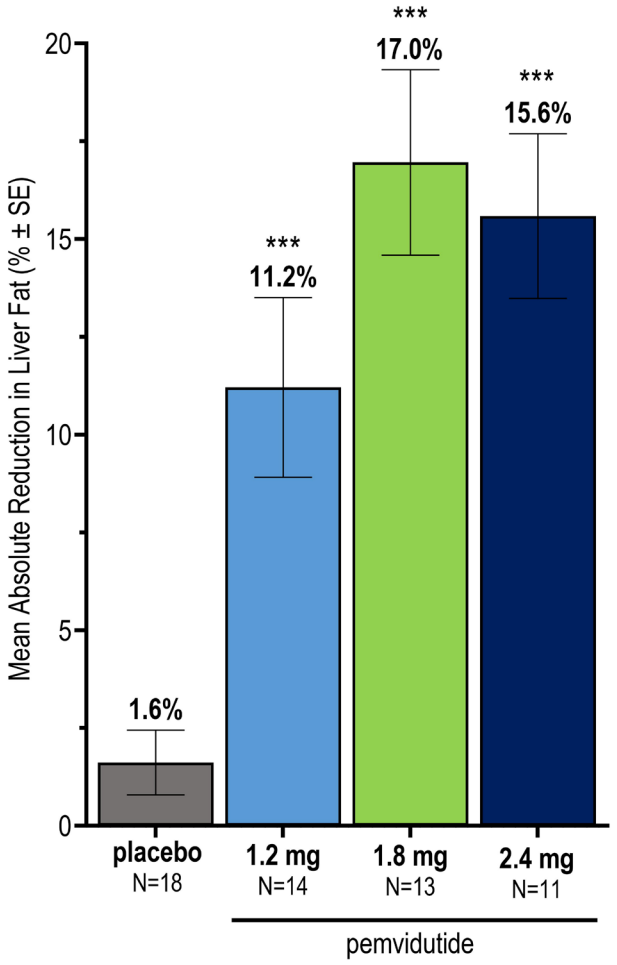
Baseline Characteristics of Extension Study Participants

Characteristic		Treatment			
		Placebo (n = 19)	1.2 mg (n=16)	1.8 mg (n=15)	2.4 mg (n=14)
Age, years	mean (SD)	49.0 (15)	48.6 (11)	49.9 (10)	48.4 (8)
Gender	female, n (%)	11 (57.9%)	7 (43.8%)	8 (53.3%)	8 (57.1%)
Race	white, n (%)	17 (89.5%)	14 (87.5%)	13 (86.7%)	14 (100%)
	other, n (%)	2 (10.5%)	2 (12.5%)	2 (13.3%)	0 (0.0%)
Ethnicity	Hispanic, n (%)	11 (57.9%)	15 (93.8%)	12 (80.0%)	9 (64.3%)
	not Hispanic, n (%)	8 (42.1%)	1 (6.3%)	3 (20.0%)	5 (35.7%)
BMI, kg/m^2	mean (SD)	37.1 (4.9)	36.7 (6.1)	36.0 (3.8)	37.0 (5.3)
Body weight, kg	mean (SD)	104.4 (21.2)	101.4 (16.3)	100.9 (13.2)	107.4 (17.2)
Diabetes status	T2D, n (%)	5 (26.3%)	3 (18.8%)	6 (40.0%)	3 (21.4%)
Liver fat content (LFC), %	mean (SD)	24.0 (9.6)	20.1 (7.7)	23.9 (7.4)	20.5 (6.5)
ALT, IU/L	mean (SD)	41.0 (21.3)	32.4 (14.2)	35.3 (13.0)	39.6 (26.6)
Blood pressure, mm Hg	systolic, mean (SD)	122.7 (10.3)	128.6 (16.0)	123.8 (17.4)	127.6 (9.9)
	diastolic, mean (SD)	79.4 (6.0)	79.4 (9.5)	77.0 (10.9)	82.4 (8.7)

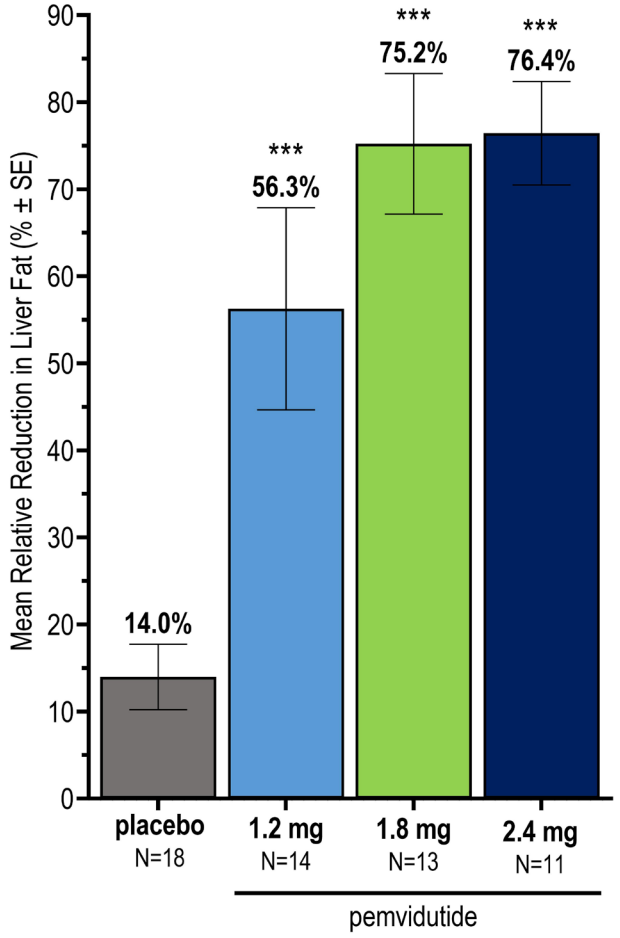
Baseline is defined as Week 0 of the Phase 1b NAFLD trial

Robust Reduction in Liver Fat Content by MRI-PDFF at Week 24

Absolute Reduction



Relative Reduction



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

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial, LS mean ± SE

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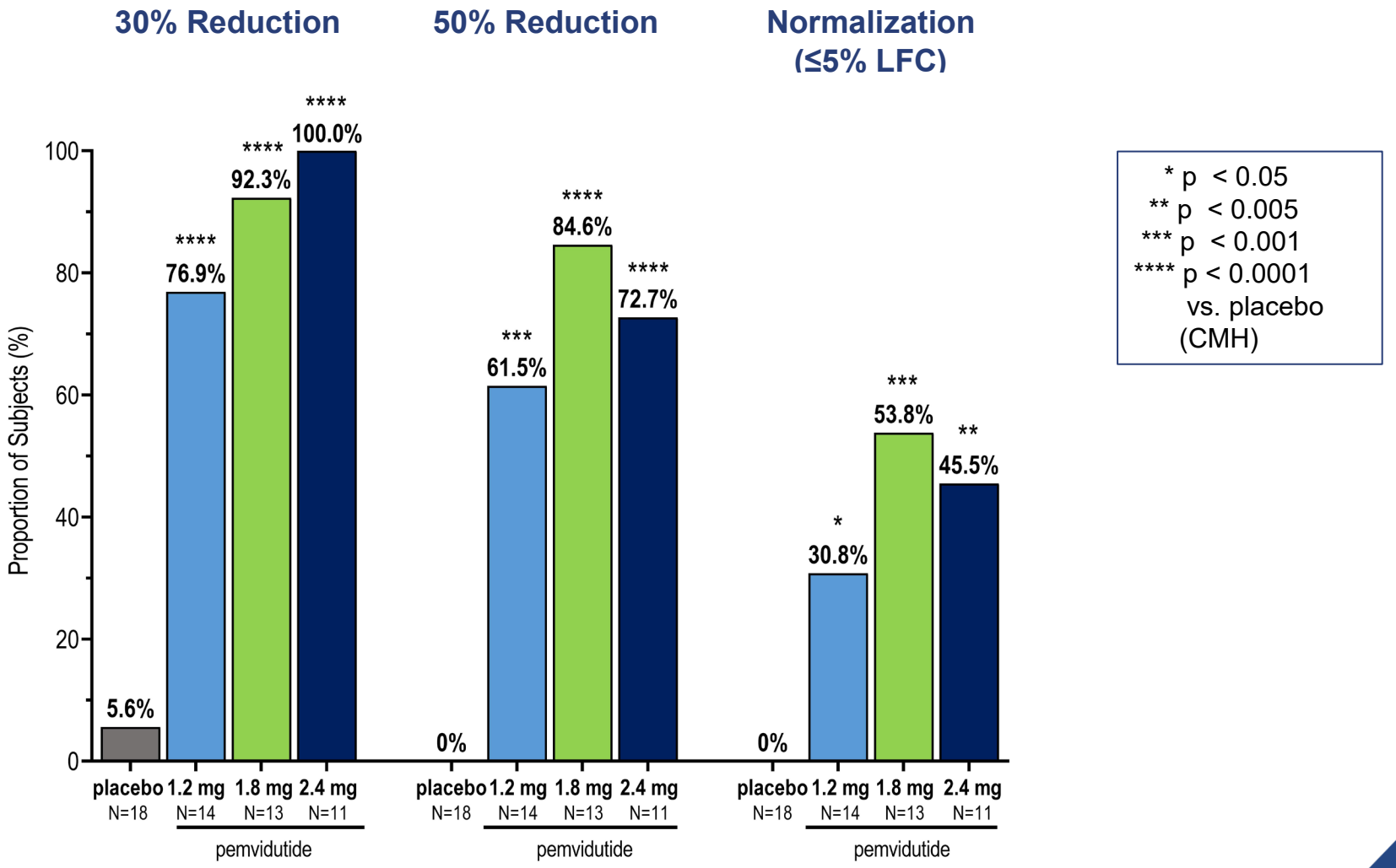
Robust Reduction in Liver Fat Content by MRI-PDFF—Responder Analyses at Week 24



Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial; CMH, Cochran-Mantel-Haenszel

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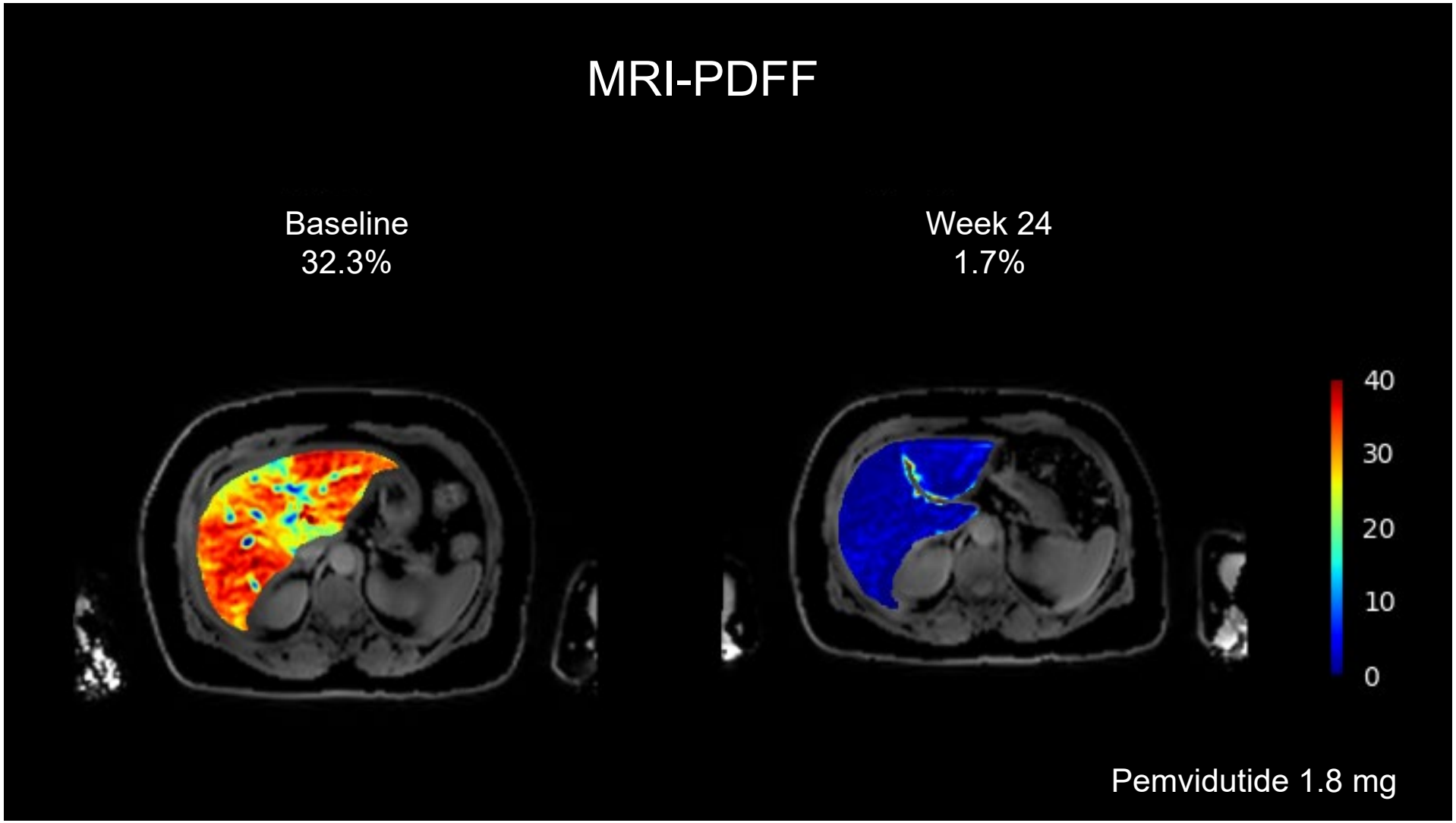
Marked Reduction of Liver Fat Content by MRI-PDFF at Week 24



This reduction was accompanied by a 38.1% decrease in liver volume

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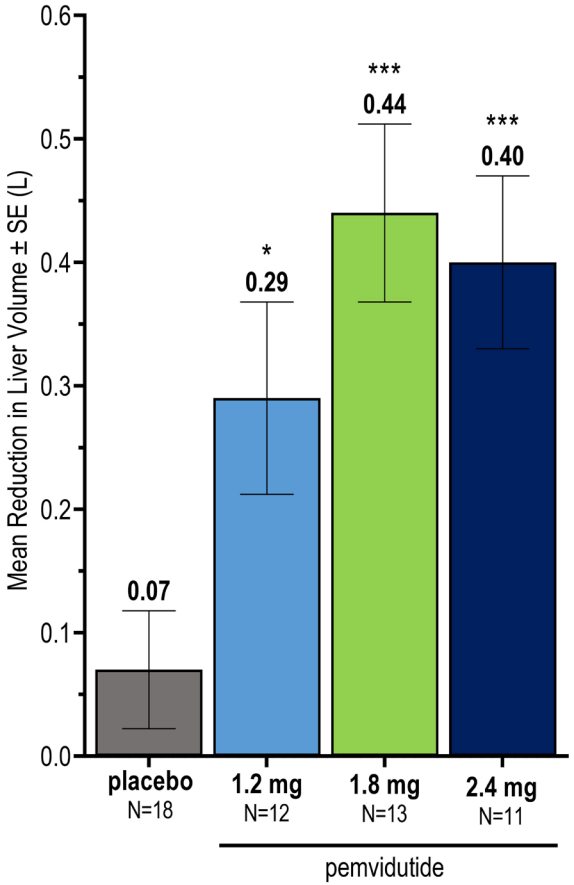
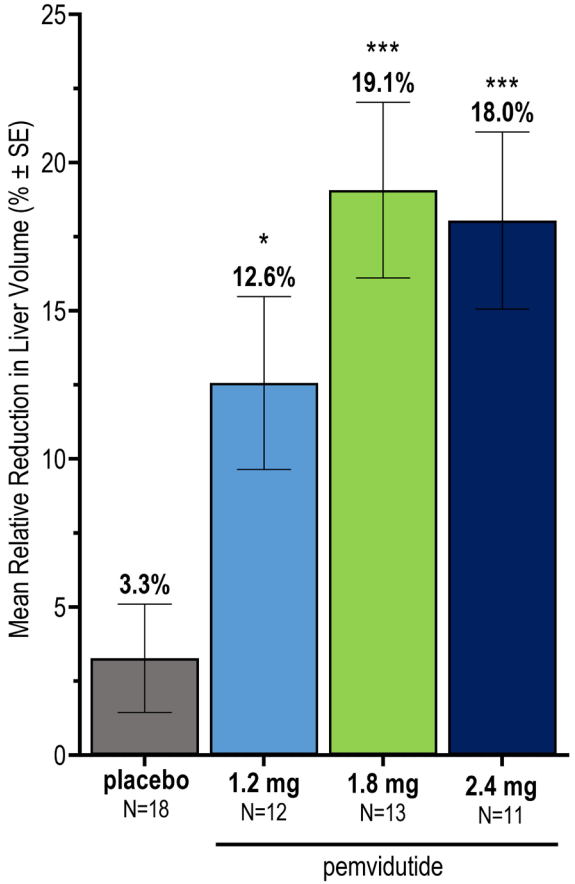
Robust Reduction in Liver Volume by MRI-PDFF at Week 24

Absolute Reduction



Relative Reduction



* p < 0.05
*** p < 0.001
vs. placebo,
(ANCOVA)

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial, LS mean ± SE

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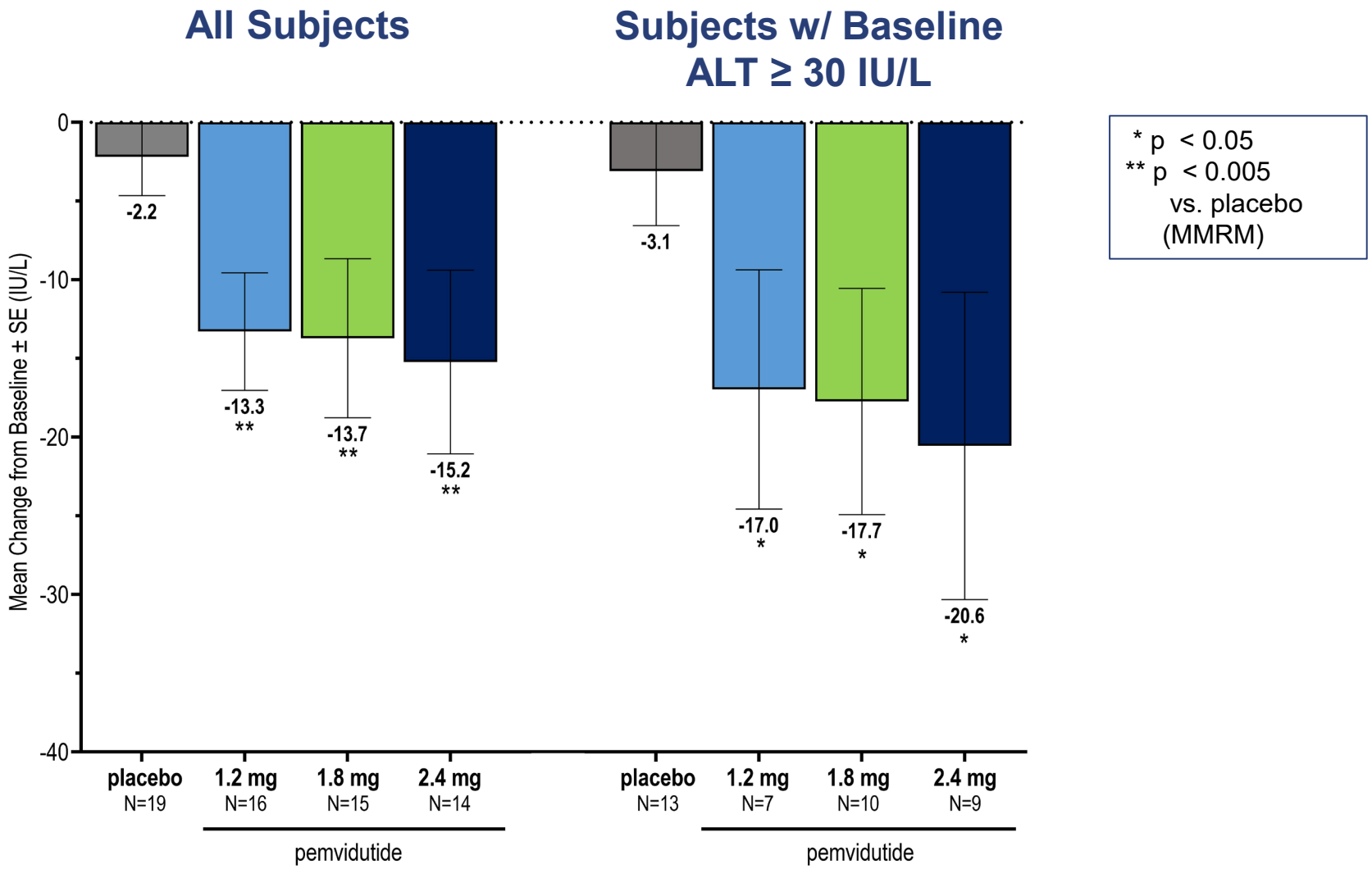
Robust Reduction of Serum ALT at Week 24

BIOMARKER OF LIVER INFLAMMATION



Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial; MMRM, mixed model with repeated measures, LS mean ± SE

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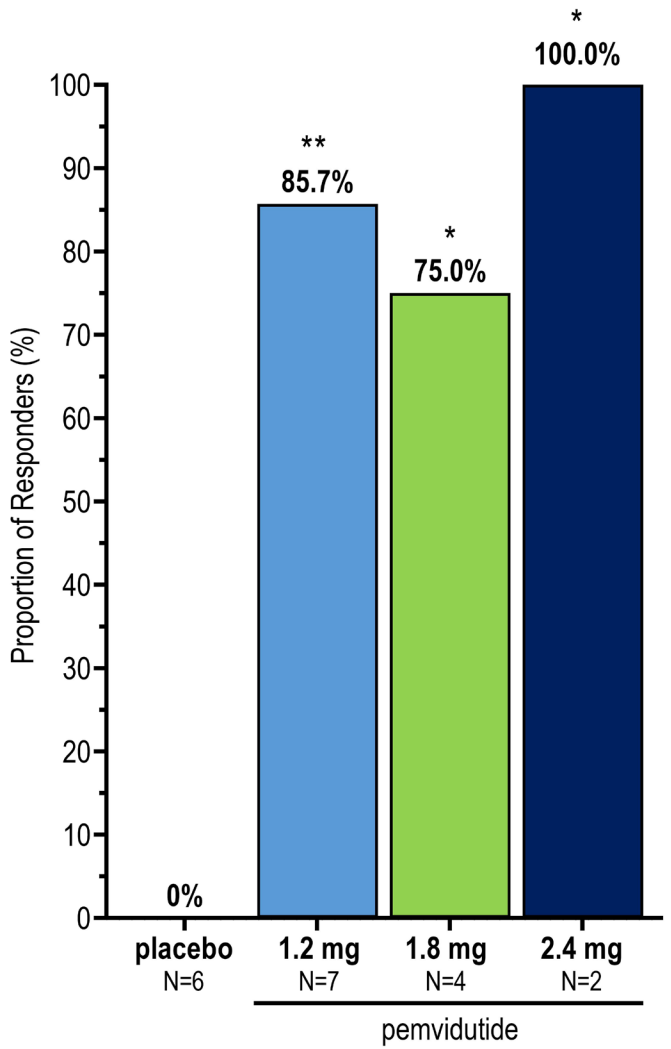
High Rates of cT1 Response at Week 24

RESPONSE DEFINED AS AN 80ms REDUCTION IN cT1 FROM BASELINE



* p < 0.05
** p < 0.005
vs. placebo
(Fisher's Exact Test)

- 80ms reduction in cT1 has been associated with a 2-point reduction of NAFLD Activity Score (NAS)[1]
- Elevated cT1 levels have been associated with increased risk of major adverse cardiac events (MACE) and major adverse liver outcomes (MALO)[2,3]

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial; [1]Dennis A, Front Endocrinol 2021; [2]Jayaswal, A. Liver Int 2020; [3]Roca-Fernandez A, MedRxiv 2022;

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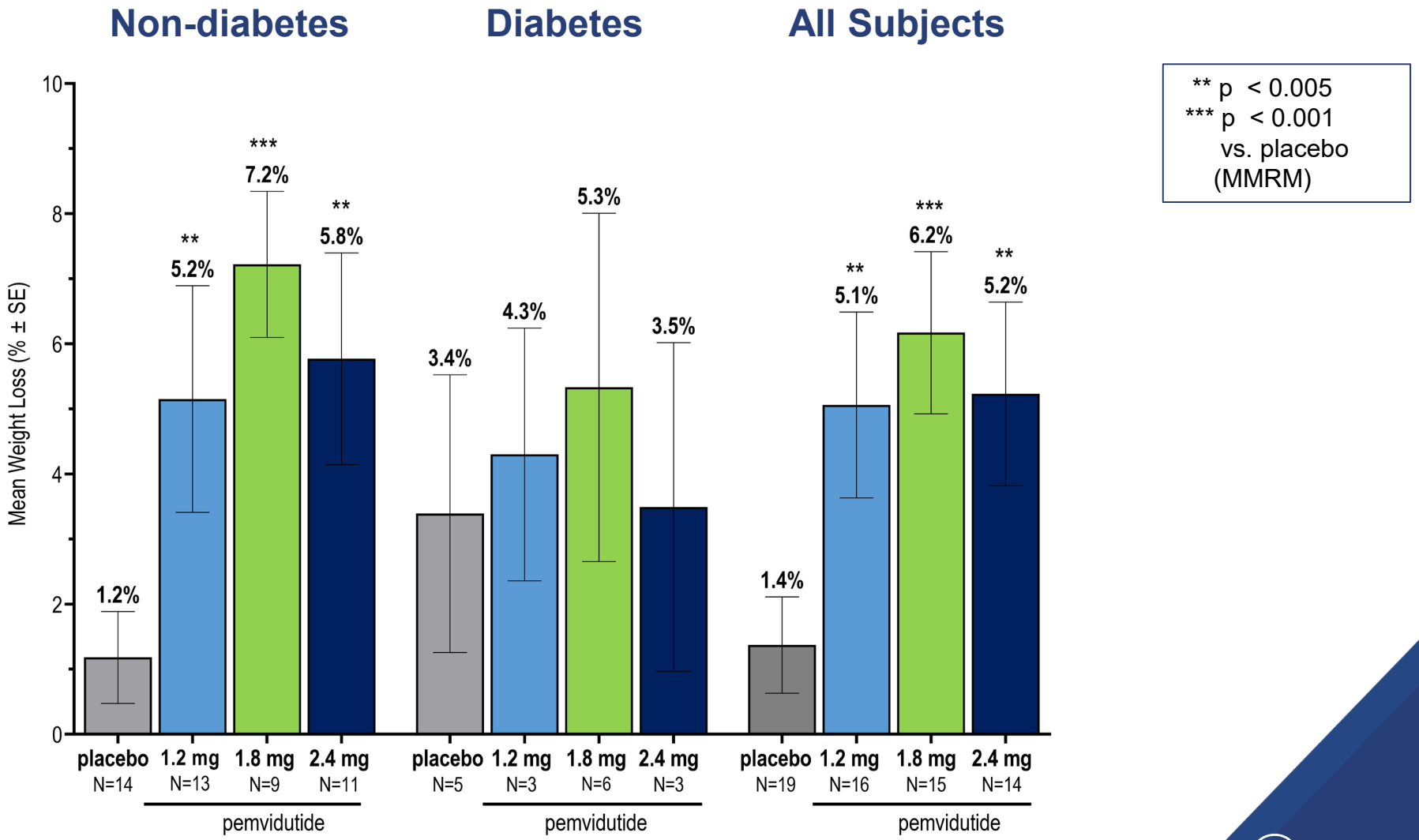
Continued Weight Loss at Week 24—Efficacy Estimand

DIFFERENTIATES PEMVIDUTIDE FROM NASH DRUGS WITH COMPARABLE LEVELS OF LIVER FAT REDUCTION



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

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial; MMRM, mixed model with repeated measures, LS mean ± SE

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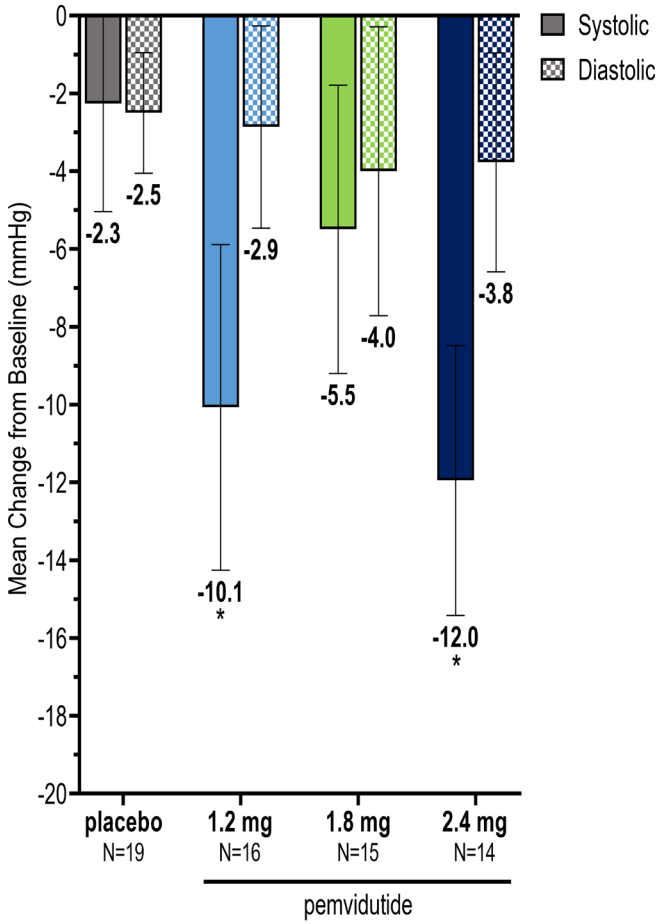
Changes in Serum Lipids at Week 24

Characteristic		Treatment			
		Placebo (n = 19)	1.2 mg (n=16)	1.8 mg (n=15)	2.4 mg (n=14)
Total cholesterol, mean (SD)					
Baseline	mg/dL	181.4 (35.7)	184.1 (46.8)	196.8 (38.6)	187.2 (36.0)
Week 24	mg/dL	169.4 (44.1)	170.9 (40.1)	173.2 (23.7)	162.0 (33.1)
LDL cholesterol, mean (SD)					
Baseline	mg/dL	97.8 (37.1)	95.5 (38.9)	110.6 (36.4)	104.8 (29.6)
Week 24	mg/dL	94.7 (43.7)	95.9 (31.8)	98.6 (26.1)	95.5 (30.9)
HDL cholesterol, mean (SD)					
Baseline	mg/dL	47.2 (7.3)	43.3 (10.2)	45.6 (8.4)	47.2 (6.7)
Week 24	mg/dL	44.9 (7.7)	42.2 (8.9)	41.4 (4.1)	43.3 (6.7)
Triglycerides, mean (SD)					
Baseline	mg/dL	182.5 (96.3)	232.1 (127.2)	217.0 (102.0)	209.9 (146.1)
Week 24	mg/dL	148.8 (78.9)	190.4 (177.0)	167.4 (94.5)	115.1 (37.6)

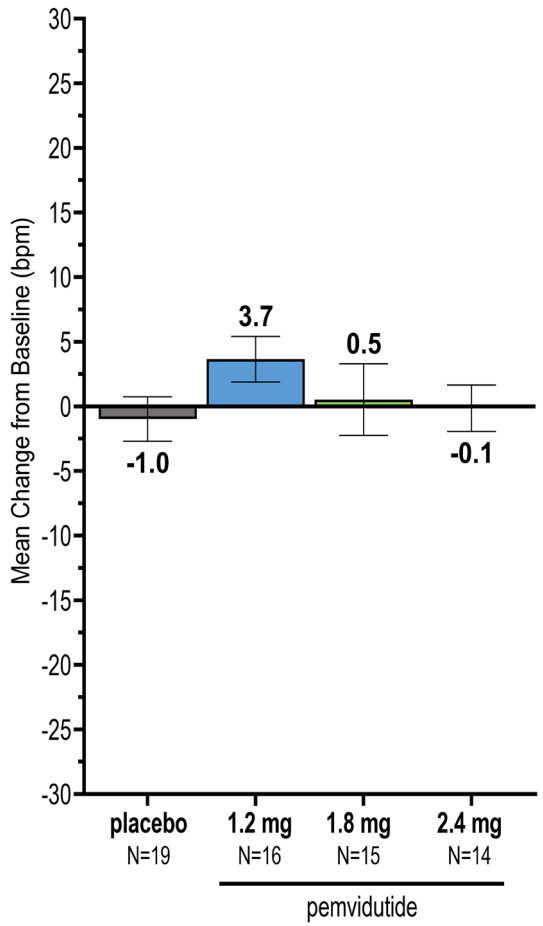
Baseline refers to Week 0 of the Phase 1b NAFLD trial

Improvements in Blood Pressure without Clinically Meaningful Increases in Heart Rate at Week 24

Blood Pressure



Heart Rate



* p < 0.05 vs. placebo (MMRM)

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial; MMRM, mixed model with repeated measures, LS mean ± SE

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Safety Overview—AEs During 12-Week Extension Study

Characteristic		Treatment			
		Placebo (n = 19)	1.2 mg (n=16)	1.8 mg (n=15)	2.4 mg (n=14)
Serious or severe AEs	n (%)	1 (5.3%)	1 (6.3%)	1 (6.7%)	0 (0.0%)
AEs leading to treatment discontinuation	n (%)	0 (0.0%)	2 (12.5%)	1 (6.7%)	0 (0.0%)
Nausea					
Mild	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	3 (20.0%)	0 (0.0%)
Vomiting					
Mild	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diarrhea					
Mild	n (%)	1 (5.3%)	0 (0.0%)	1 (6.7%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)
Constipation					
Mild	n (%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	0 (0.0%)
Moderate	n (%)	1 (5.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)

The serious and severe AEs were the same events: 1) chest pain post elective coronary stent placement (placebo), 2) Salmonella infection (pemvi 1.2 mg), and 3) hypertension >3 weeks post last dose of study medication (pemvi 1.8 mg), all unrelated to study medication, with only the Salmonella infection leading to treatment discontinuation. The other AEs leading to treatment discontinuation were mild (Grade 1) abdominal pain in 2 subjects. No significant ALT elevations were reported.

Glycemic Control at Week 24

Characteristic		Treatment			
		Placebo	1.2 mg	1.8 mg	2.4 mg
NON-DIABETES		N=14	N=13	N=9	N=11
Fasting glucose					
Baseline, mg/dL	mean (SD)	96.2 (12.4)	99.4 (11.9)	96.0 (12.4)	99.3 (13.6)
Week 24, mg/dL	mean (SD)	93.3 (12.1)	99.1 (13.1)	96.9 (12.5)	98.4 (24.5)
HbA1c					
Baseline, %	mean (SD)	5.8 (0.2)	5.7 (0.3)	5.7 (0.2)	5.5 (0.4)
Week 24, %	mean (SD)	5.7 (0.3)	5.8 (0.3)	5.8 (0.3)	5.6 (0.3)
DIABETES		N=5	N=3	N=6	N=3
Fasting glucose					
Baseline, mg/dL	mean (SD)	111.5 (19.2)	132.1 (28.2)	120.2 (37.1)	147.4 (40.4)
Week 24, mg/dL	mean (SD)	109.4 (14.8)	123.4 (50.8)	109.0 (13.1)	75.5 (29.0)
HbA1c					
Baseline, %	mean (SD)	6.1 (0.6)	7.8 (1.4)	6.4 (0.5)	6.8 (1.3)
Week 24, %	mean (SD)	6.4 (1.1)	7.4 (2.3)	6.4 (0.3)	6.3 (1.3)

Baseline refers to Week 0 of the Phase 1b NAFLD trial

Summary and Conclusions

Liver fat reduction

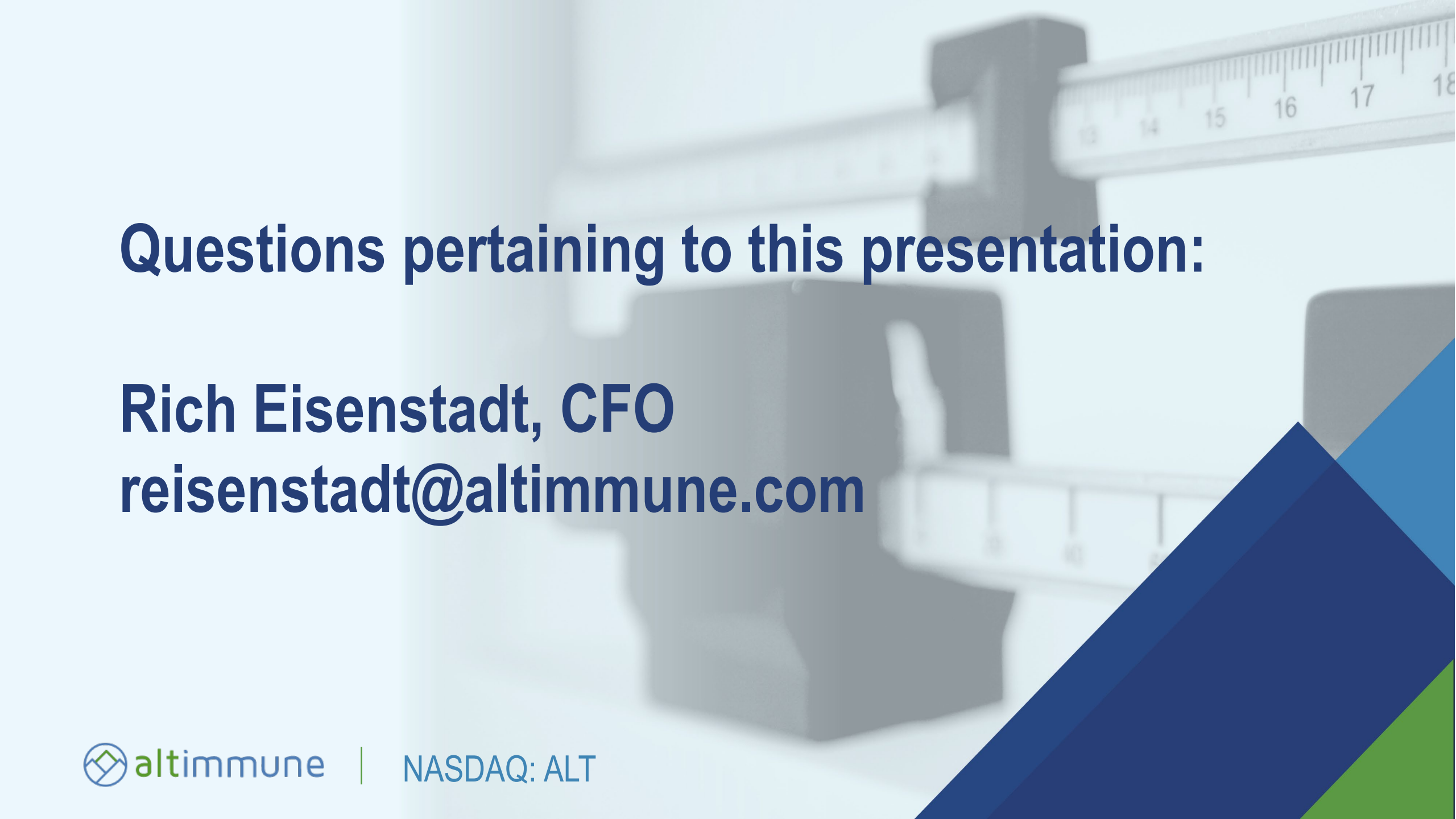
- Greater than 75% relative liver fat reduction at 24 weeks, better than or equal to the effects of other leading NASH candidates
- Significant reductions and normalization in serum ALT and improvement in cT1 point to potent effects in NASH clinical trials

Weight loss

- Non-diabetes—continued weight loss, achieving 7.2% at pemvidutide 1.8 mg at Week 24
- Diabetes—achieved 5.3% weight loss at pemvidutide 1.8 mg at Week 24

Safety and tolerability

- Low rates of AEs leading to treatment discontinuation, no serious/severe AEs related to pemvidutide
- Cardioprotective reductions in blood pressure without increases in heart rate
- Glycemic control maintained with trends toward improvements in fasting glucose and HbA1c in subjects with diabetes
- No clinically significant ALT elevations



Questions pertaining to this presentation:

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