Unlocking Glucagon Biology to Overcome Fibrosis in MASH

M. Scott Harris, MD
Chief Medical Officer
Altimmune, Inc.

MASH Drug Development Summit
25 September 2024

altimmune | NASDAQ: ALT

Forward-looking statements

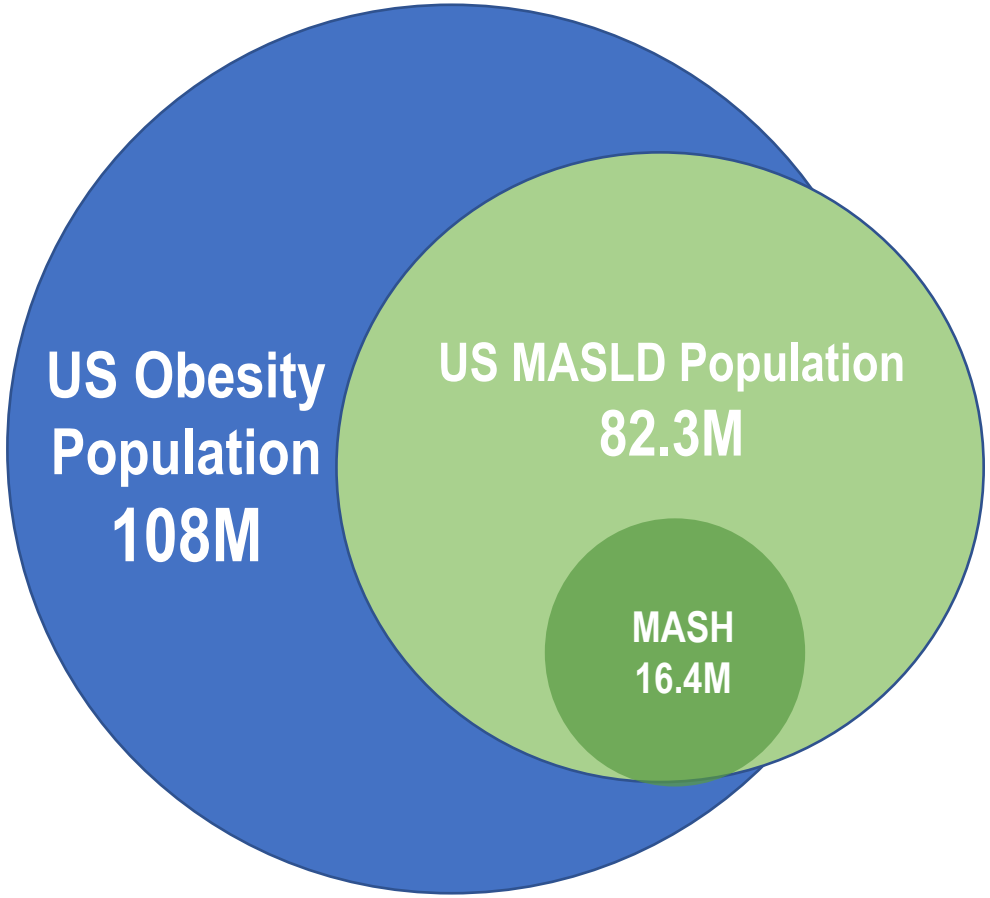
Safe-Harbor Statement

This presentation has been prepared by Altimmune, Inc. ("we," "us," "our," "Altimmune" or the "Company") and includes certain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the timing of clinical development and funding milestones for our clinical assets as well as statements relating to future financial or business performance, conditions, plans, prospects, trends, or strategies and other financial and business matters, and the prospects for commercializing or selling any product or drug candidates. In addition, when or if used in this presentation, the words “may,” “could,” “should,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict” and similar expressions and their variants, as they relate to the Company may identify forward-looking statements. The Company cautions that these forward-looking statements are subject to numerous assumptions, risks, and uncertainties, which change over time. Important factors that may cause actual results to differ materially from the results discussed in the forward looking statements or historical experience include risks and uncertainties, including risks relating to: potential impacts due to the COVID-19 pandemic such as delays in regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy, the timing and reliability of the results of the studies relating to human safety and possible adverse effects resulting from the administration of the Company’s product candidates; our lack of financial resources and access to capital; clinical trials and the commercialization of proposed product candidates (such as marketing, regulatory, product liability, supply, competition, dependence on third parties and other risks); the timing of regulatory applications and the regulatory approval process; dependence on intellectual property and reimbursement and regulation. Further information on the factors and risks that could affect the Company's business, financial conditions and results of operations are contained in the Company’s filings with the U.S. Securities and Exchange Commission, including under the heading “Risk Factors” in the Company’s annual reports on Form 10-K and quarterly reports on Form 10-Q filed with the SEC, which are available at www.sec.gov. The statements made herein speak only as of the date stated herein, and any forward-looking statements contained herein are based on assumptions that the Company believes to be reasonable as of this date. The Company undertakes no obligation to update these statements as result of new information or future events.

altimmune

OBESITY AND FATTY LIVER DISEASE

DISEASES WITH UNMET NEED APPROACHING EPIDEMIC PROPORTIONS



The recent successes of semaglutide (Wegovy®) and tirzepatide (Zepbound®) have created optimism for other incretin-based therapies

- GLP-1/GCG dual receptor agonists
- GLP-1/ amylin combination agents
- GLP-1/GIP mAb
- Oral GLP-1 monotherapies

GLP-1: glucagon-like peptide-1
GCG: glucagon
mAB: monoclonal Ab

Hales CM et al. NCHS Data Brief. 2020 Feb;(360):1-8. PMID: 32487284; Younossi ZM et all. Gut. 2020 Mar;69(3):564-568; https://liverfoundation.org/liver-diseases/fatty-liver-disease/nonalcoholic-steatohepatitis-nash/

altimmune

OBESITY-RELATED CO-MORBIDITIES ARE THE MOST FREQUENT CAUSE OF DEATH IN PATIENTS WITH MASH

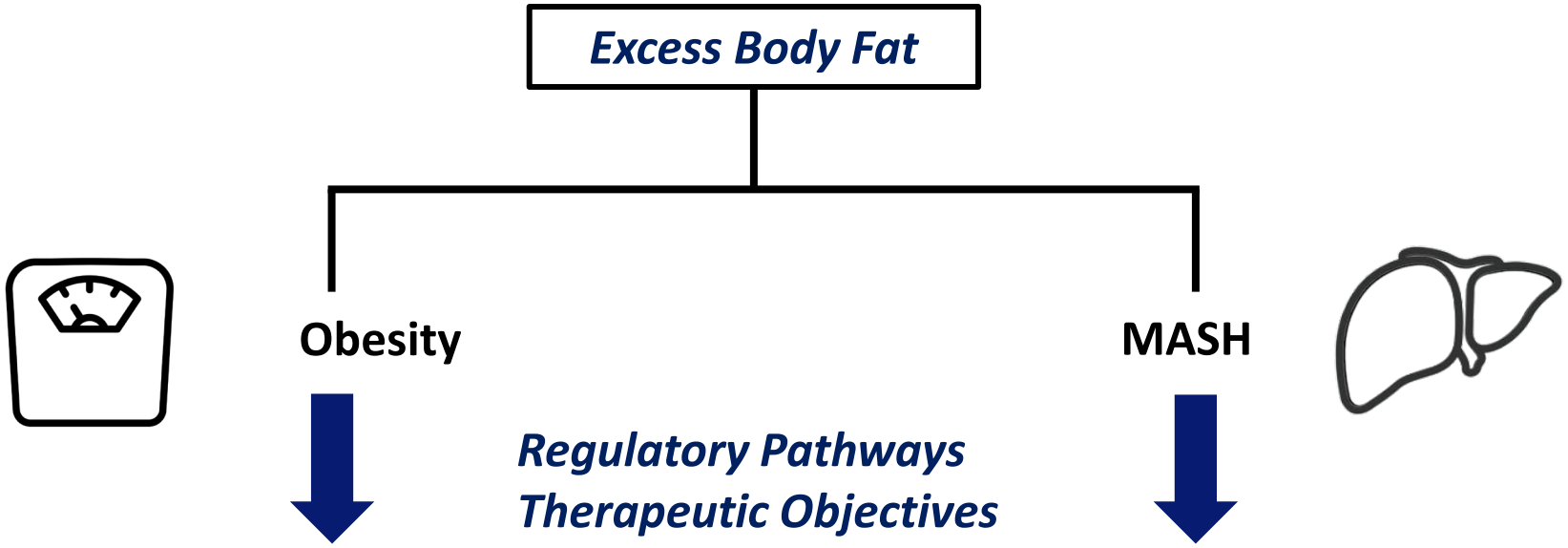
Outcome	n (%)
Death or liver transplantation	193 (100.0)
Cardiovascular disease	74 (38.3)
Non-liver cancer	36 (18.7)
Cirrhosis complications	15 (7.8)
Infections	15 (7.8)
HCC	2 (1.0)
Liver transplantation	1 (0.5)
Other	35 (18.1)
Unknown	15 (7.8)

619 patients with biopsy confirmed MASH

Adapted from Angulo, Gastroenterology 2015;149: 389–397

OBESITY AND MASH SYNERGIES

DISTINCT REGULATORY PATHWAYS BUT SIMILAR THERAPEUTIC OBJECTIVES



- **Reduce body weight**
- Improve serum lipid profile
- Reduce cardiovascular risk factors

- **Reduce liver fat**
- Reduce liver inflammation
- Reduce body weight

NON-INCRETIN AGENTS FAIL TO ACHIEVE MEANINGFUL WEIGHT LOSS

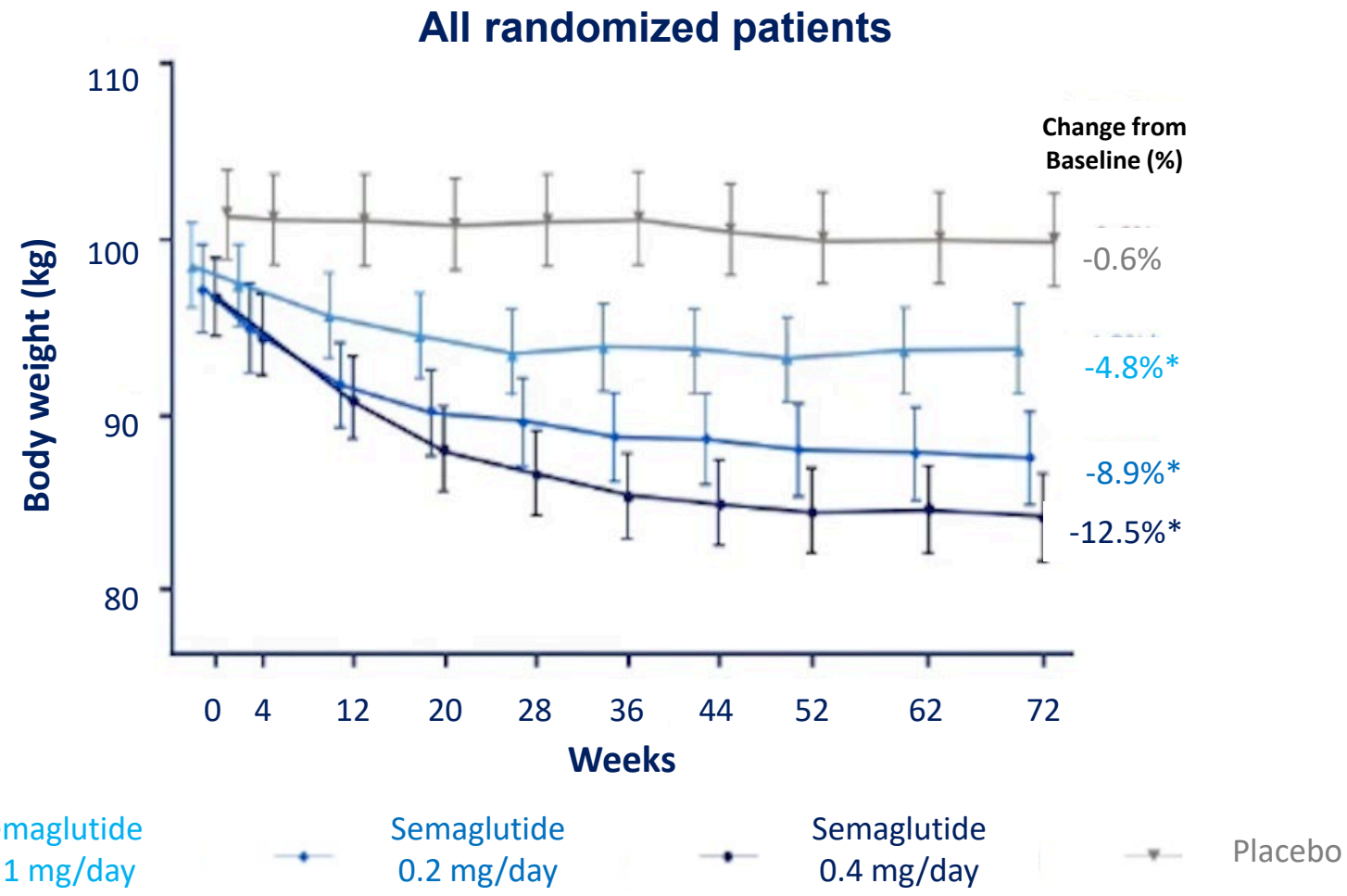
SNAPSHOT OF COMPOUNDS IN ADVANCED MASH DEVELOPMENT

Agent	Mechanism	Change in Body Weight	MASH Resolution	Fibrosis Improvement
Obeticholic acid	FXR agonist	-2%	No	Yes
Resmetirom	THRβ agonist	no change	Yes	Yes
Lanifibranor (1200 mg)	PanPPAR	+3.1%	Yes	Yes
Pegozafermin	FGF21 agonist	-0.6%	Yes	Yes
Efruxifermin (70 mg)	FGF21 agonist	-2.6%	Yes	Yes

Younossi, YM 2019, Lancet 394: 2184-96; Harrison, SA 2019, Lancet 394: 2012-24; Harrison SA 2022 , AASLD2022; Franque SM, 2021; NEJM 385: 1547-57

SEMAGLUTIDE—WEIGHT LOSS IN PHASE 2 MASH CLINICAL TRIAL

SUBJECTS WITH AND WITHOUT DIABETES



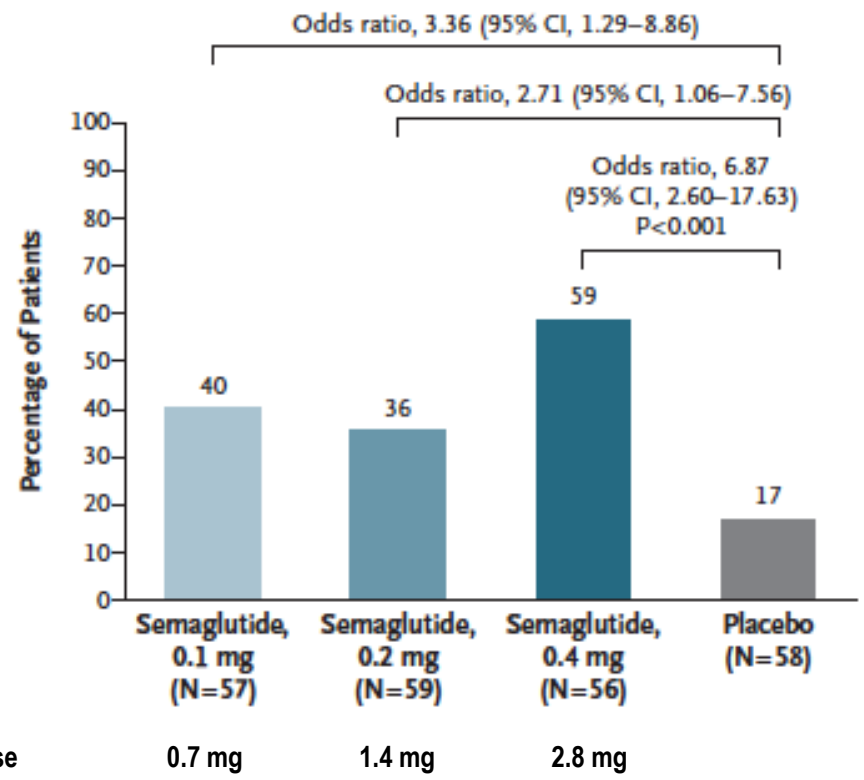
Newsome, NEJM 2020; Nov 13. doi: 10.1056/NEJMoa2028395

altimmune

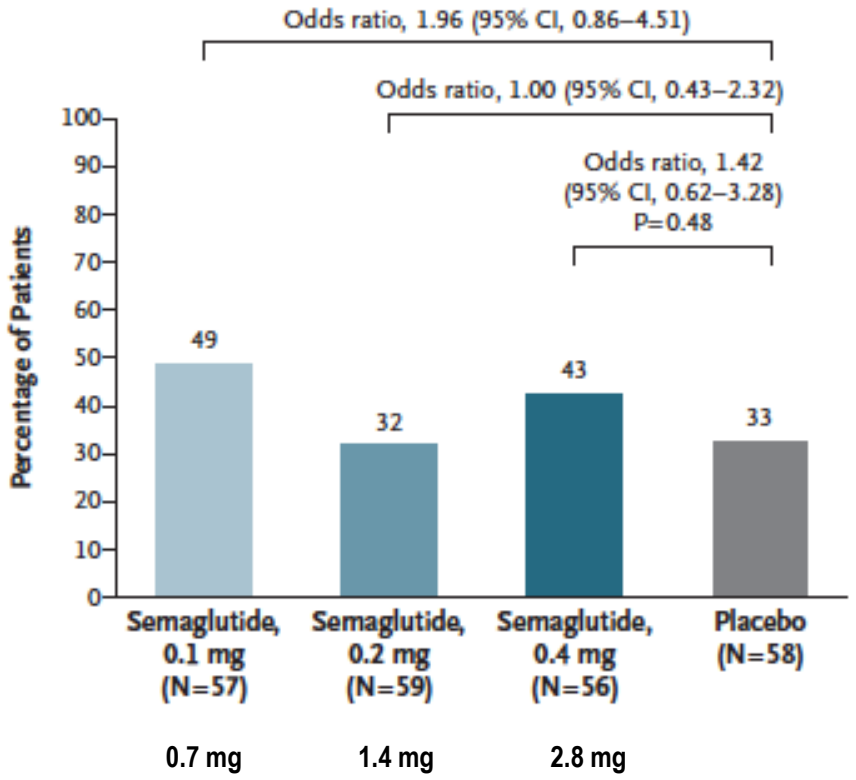
SEMAGLUTIDE—MASH RESOLUTION WITHOUT FIBROSIS IMPROVEMENT

RESULTS OF A 68-WEEK, PHASE 2, MULTICENTER TRIAL

MASH Resolution



Fibrosis Improvement

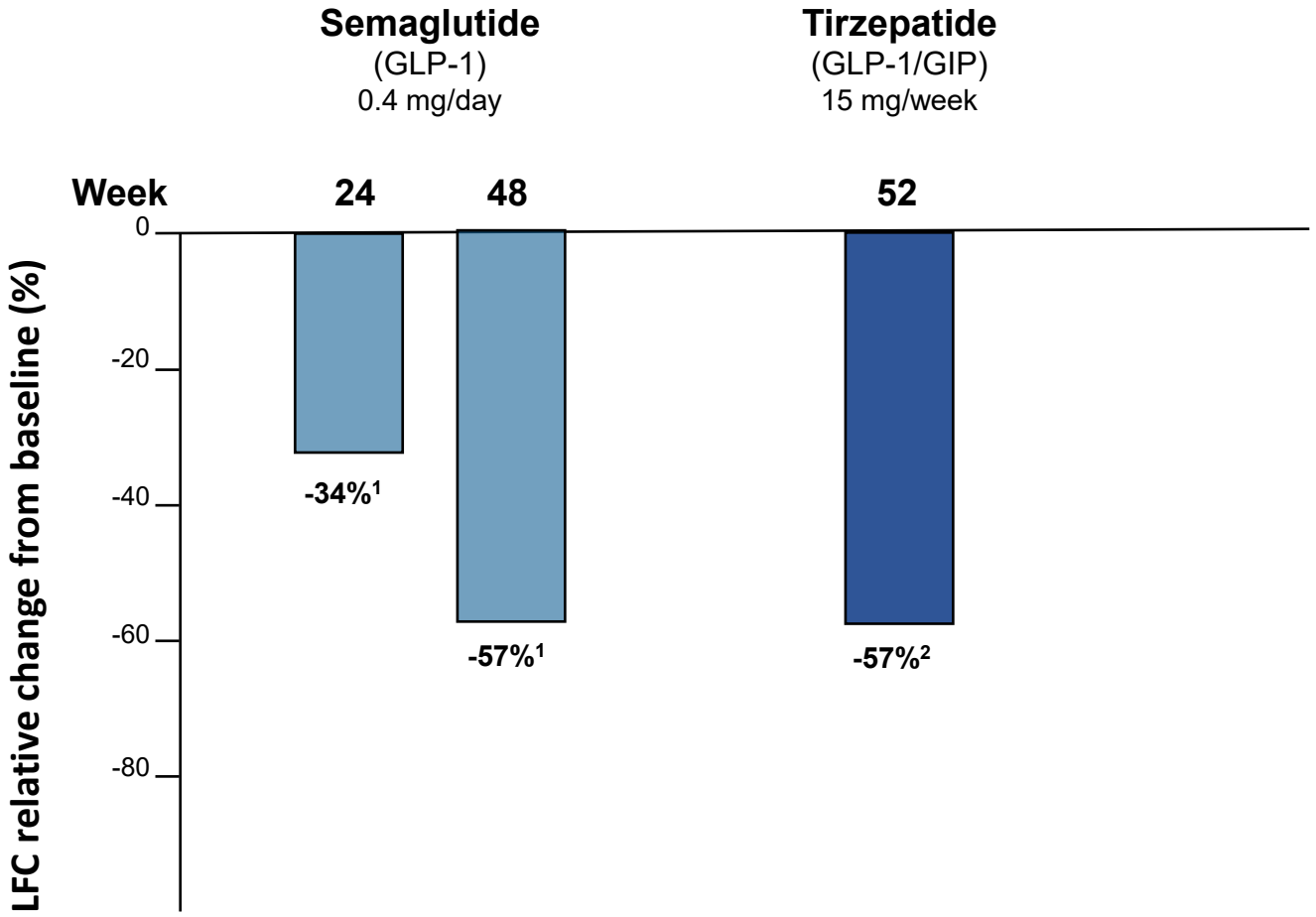


Newsome, NEJM 2020; Nov 13. doi: 10.1056/NEJMoa2028395

altimmune

GLP-1 AND GIP AGENTS HAVE ONLY MODEST EFFECTS ON LIVER FAT CONTENT

EFFECTS DRIVEN BY SOLELY BY WEIGHT LOSS DUE TO ABSENCE OF GLP-1 AND GIP RECEPTORS IN LIVER

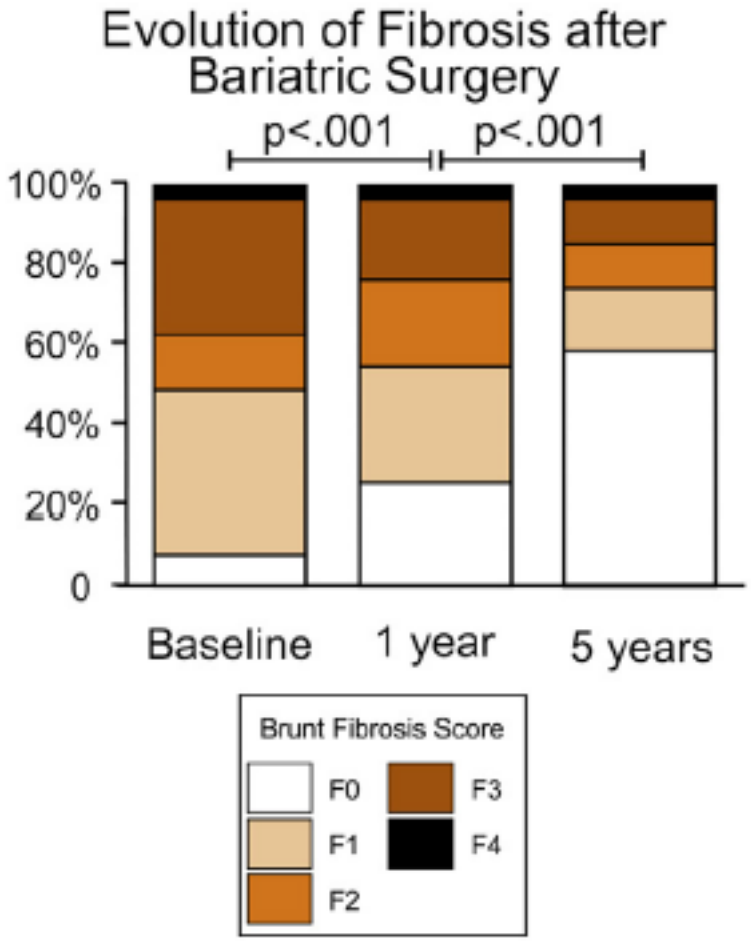


[1] Flint, Aliment Pharm Ther 2021; [2] Sanyal EASL 2024

altimmune

THE IMPACT OF WEIGHT LOSS ON LIVER FIBROSIS MAY BE SLOW

IMPROVEMENT ON FIBROSIS MAY TAKE AS LONG 5 YEARS IN THE ABSENCE OF DIRECT LIVER EFFECTS

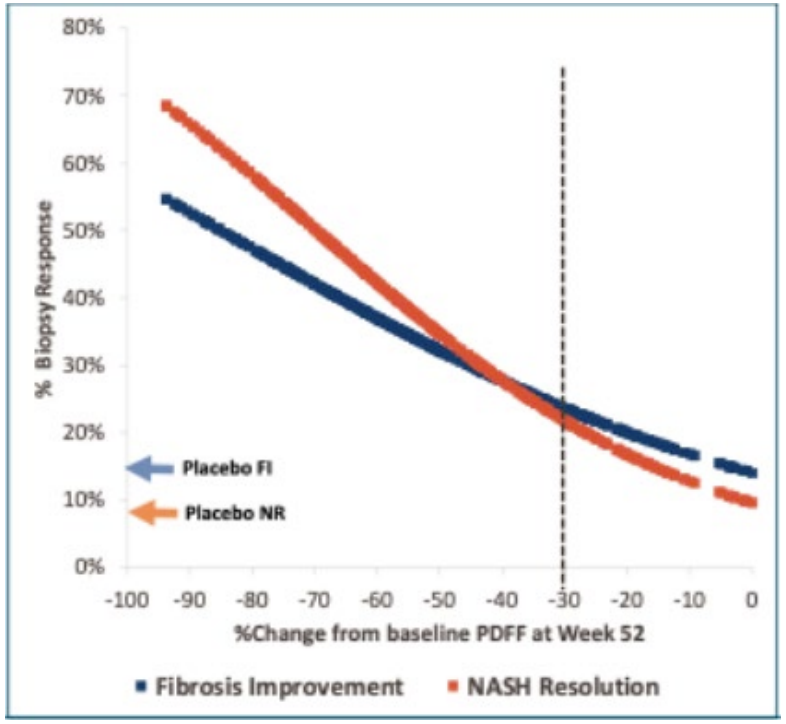


Lassailly Gastroenterology 2020

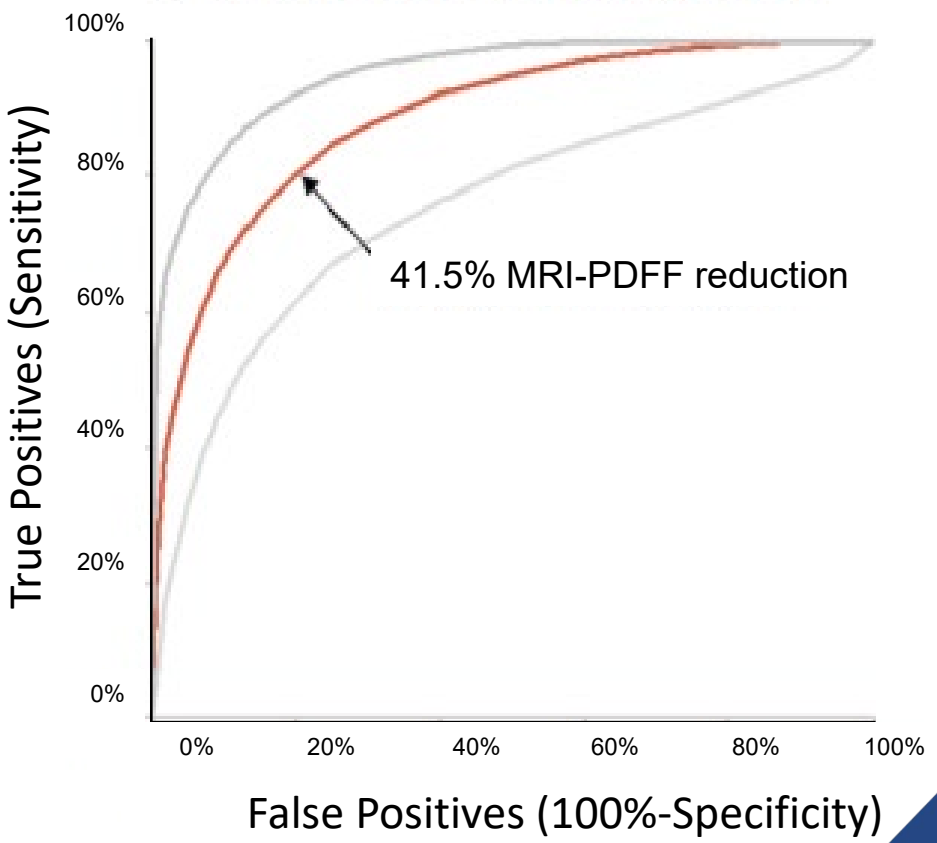
altimmune

MRI-PDFF REDUCTION STRONGLY PREDICTED OF BIOPSY RESPONSES ON NASH RESOLUTION AND FIBROSIS IMPROVEMENT

Relationship of Δ MRI-PDFF and Biopsy Response



Receiver Operating Curve (ROC)



Noureddin, EASL 2024 and Loomba, EASL 2020

FIBROSIS IMPROVEMENT DRIVEN BY LIVER FAT REDUCTION

Fibrosis Improvement Achieved

Compound	Dose	Mechanism	Liver Fat Reduction	Duration of Treatment	Fibrosis Improvement		
					Treatment	Placebo	Δ
Resmetirom	100 mg QD	THR-β	48%	52 weeks	26%	14%	12%
Pegozafermin	44 mg Q2W	FGF21	54%	24 weeks	27%	7%	20%
Tirzepatide	15 mg QW	GLP-1/GIP	57%	52 weeks	51%	30%	21%
Survodutide	6.0 mg QW	GLP-1/GCG	64%	48 weeks [2]	42%	18%	24%
Efruxifermin	50 mg QW	FGF21	64%	24 weeks	41%	20%	21%
Pemvidutide	1.8 mg QW	GLP-1/GCG	75%	24 weeks	TBD	TBD	TBD

Fibrosis Improvement Not Achieved

Compound	Dose	Mechanism	Liver Fat Reduction	Duration of Treatment	Fibrosis Improvement		
					Treatment	Placebo	Δ
Semaglutide	0.4 mg QD	GLP-1	30-35%[1]	72 weeks	43%	33%	10%

[1] Estimated at Week 24; [2] ITT analysis

12

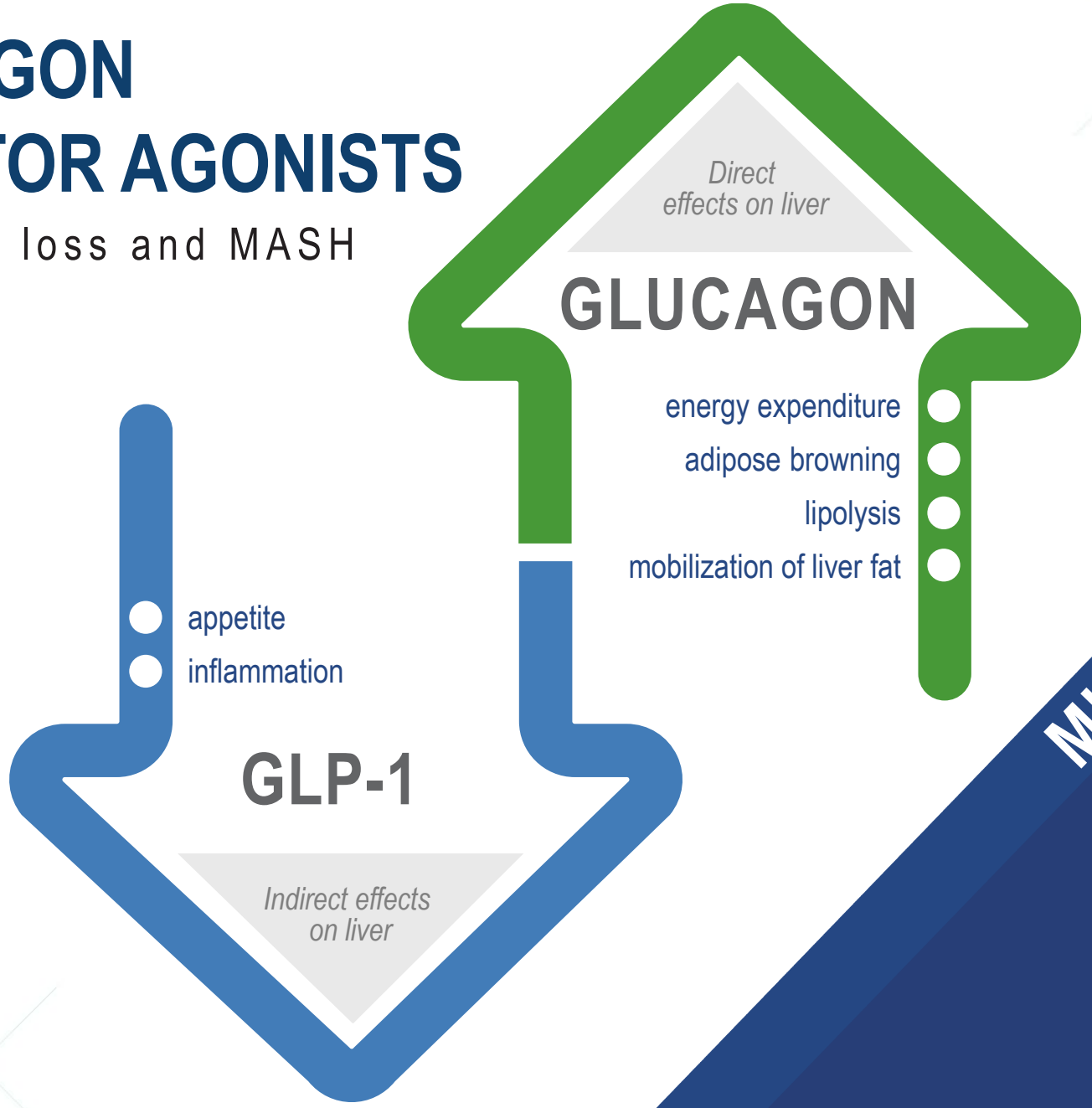
GLP-1/GLUCAGON DUAL RECEPTOR AGONISTS

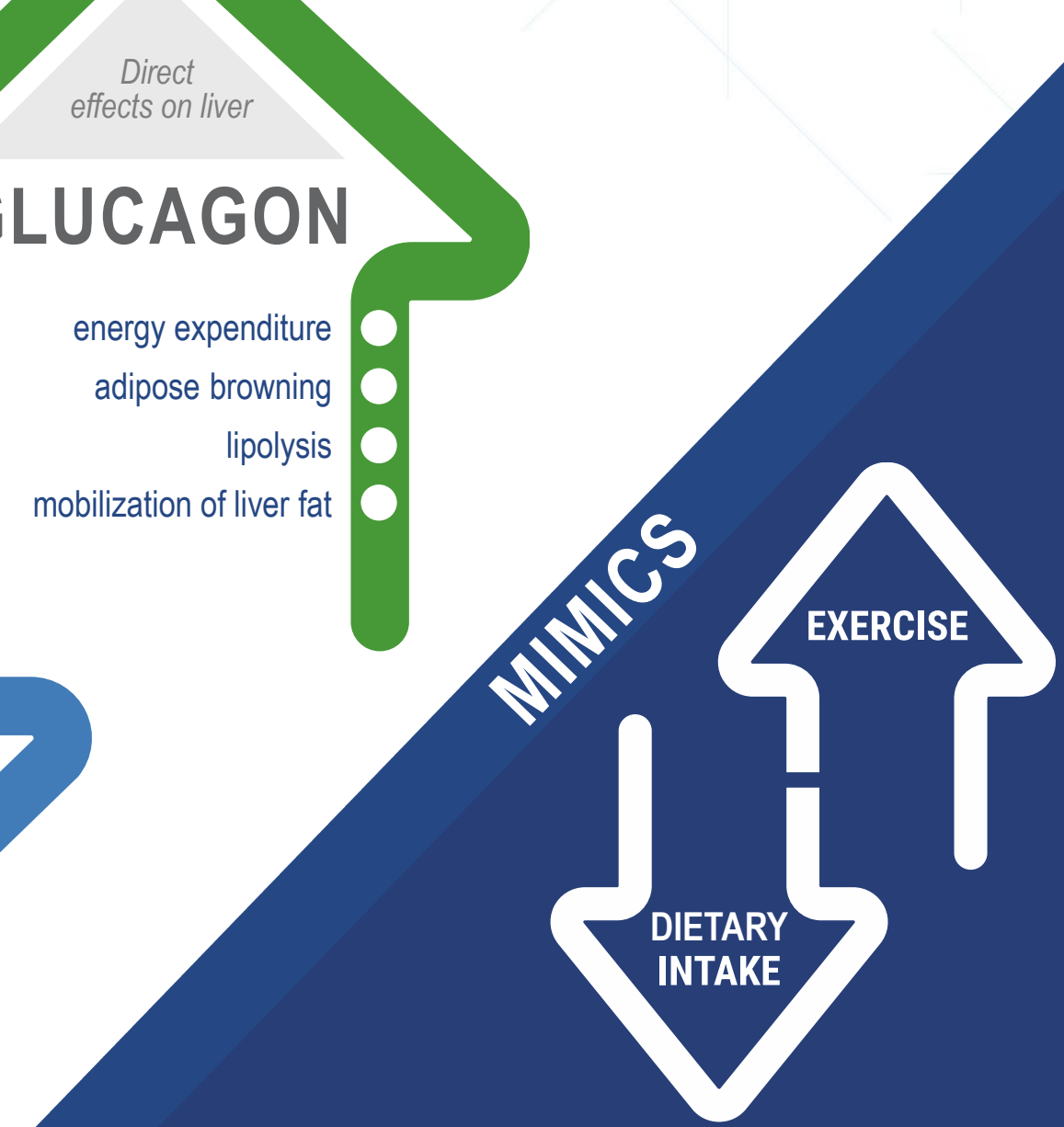
Optimized for weight loss and MASH

Designed for significant reductions in:

BODY WEIGHT

LIVER FAT, INFLAMMATION, & RESULTING FIBROSIS

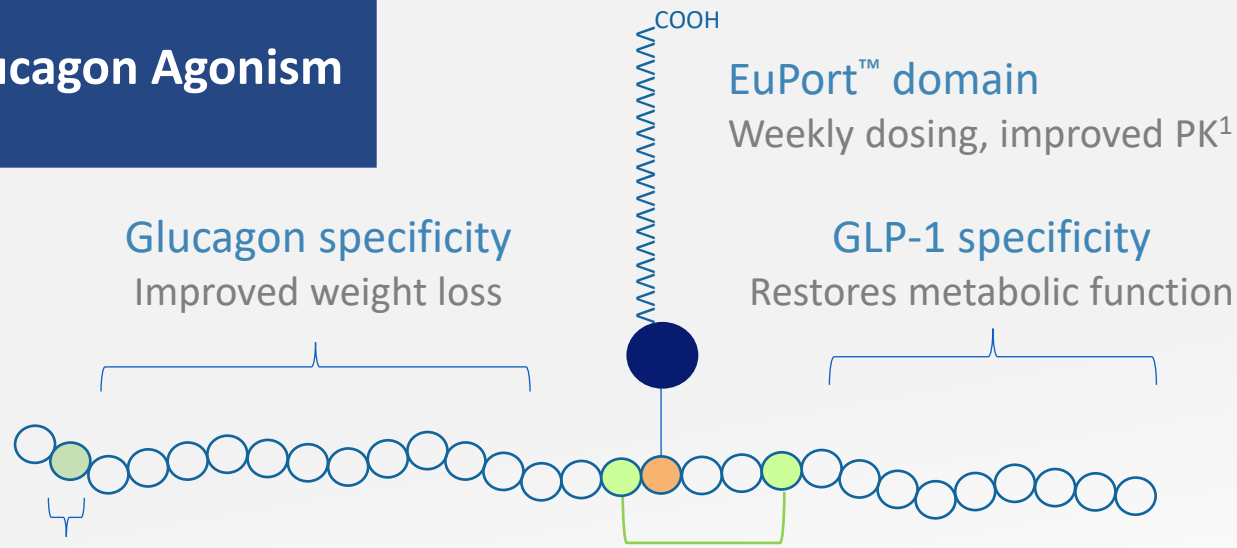




PEMVIDUTIDE

BALANCED AGONIST WITH PROLONGED SERUM HALF-LIFE AND DELAYED TIME TO PEAK CONCENTRATION

Pemvidutide:
Balanced GLP-1: Glucagon Agonism

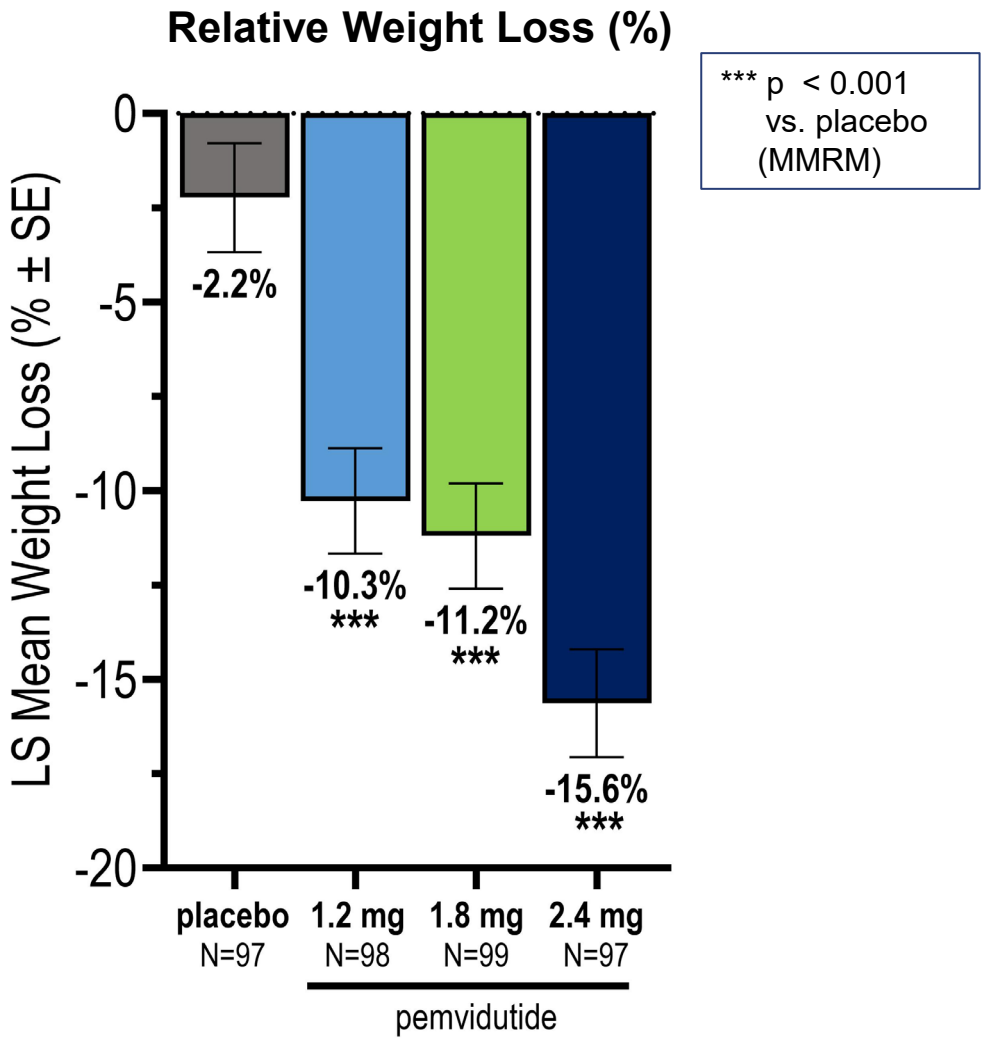


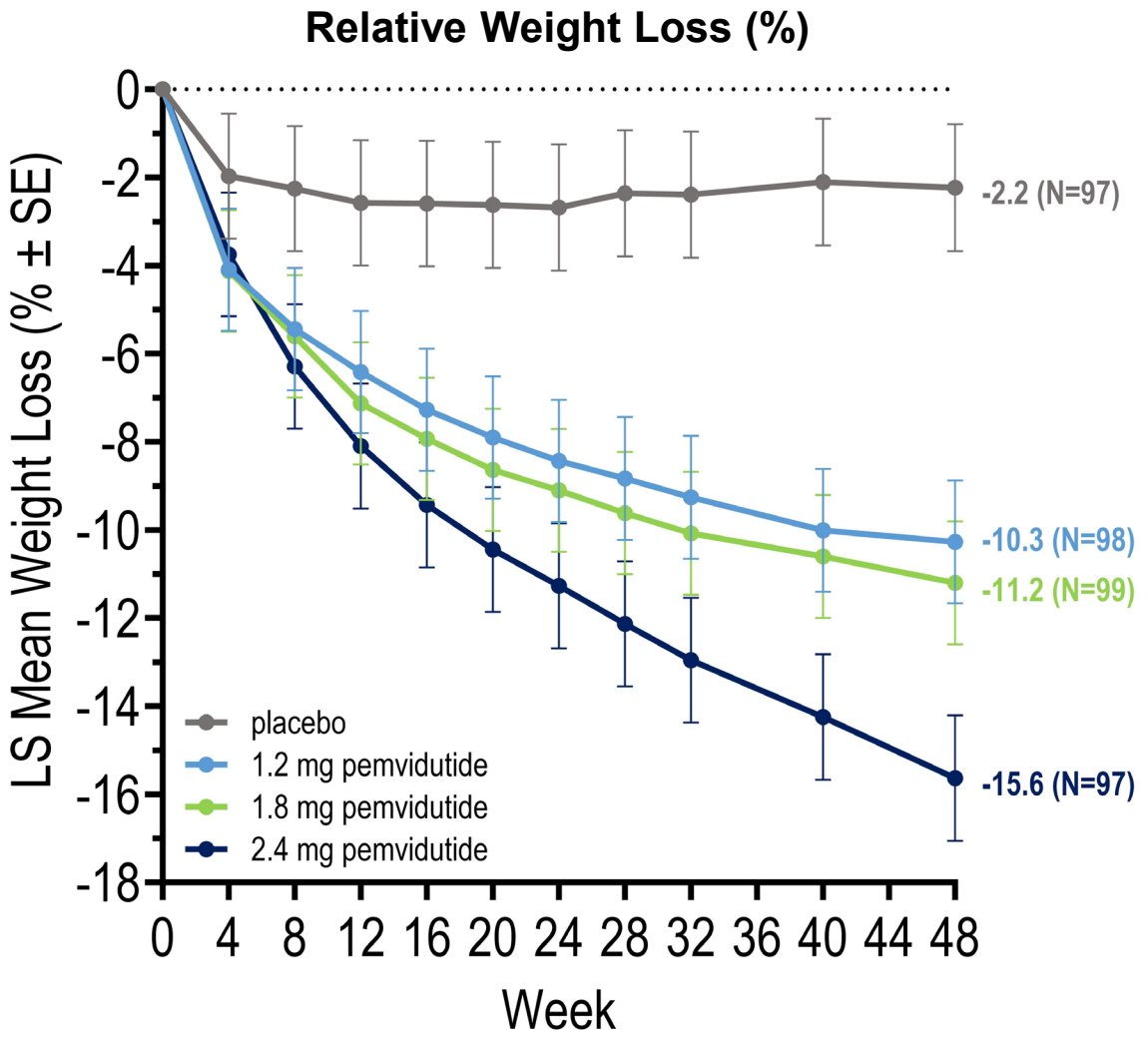
Nestor JJ et al, Peptide Science. 2021;113:e24221

altimmune

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





MMRM, mixed model for repeated measures

PEMVIDUTIDE—CLASS-LEADING EFFECTS ON LEAN MASS PRESERVATION

POTENTIALLY SUPERIOR TO THE 25% LEAN LOSS HISTORICALLY ASSOCIATED WITH DIET AND EXERCISE[1]

LEAN LOSS INDEX

Drug	Study	Study duration	LBM loss index
Pemvidutide	MOMENTUM Phase 2	48 weeks	21.9%[2]
Tirzepatide	SURMOUNT 1 Phase 3	72 weeks	26.0%[3,4]
Retatrutide	Phase 2 obesity study	36 weeks	37.7%[4]
Semaglutide	STEP-1 Phase 3	68 weeks	39.9%[5]

Lean loss index = loss of lean mass/total mass loss

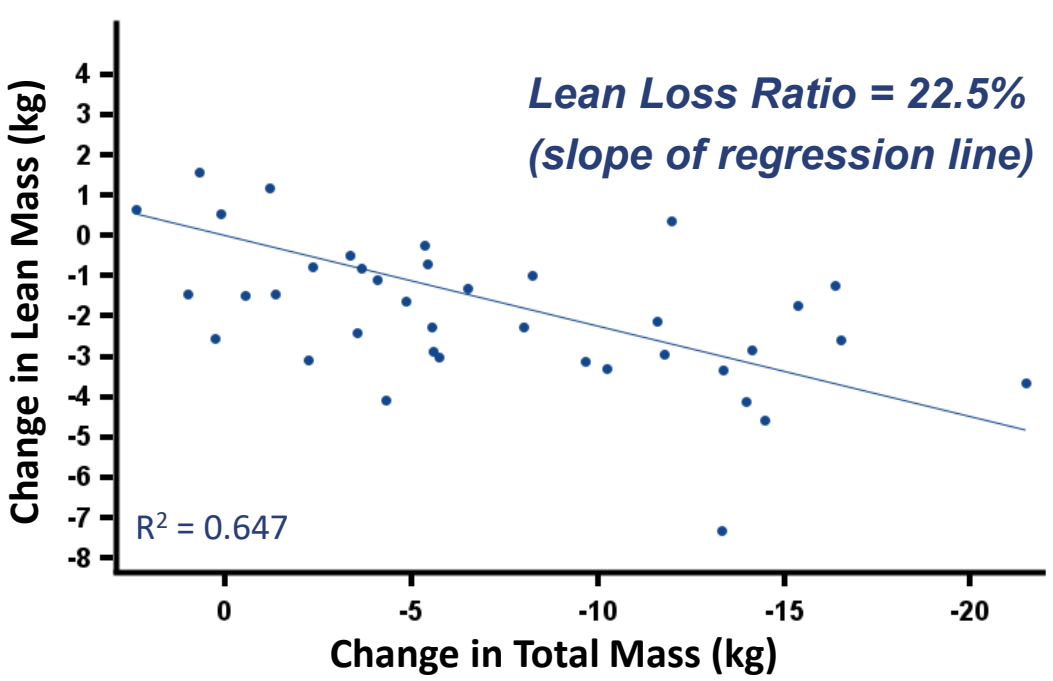
Excessive loss of lean mass has been associated an increased risk of frailty fractures, cardiovascular disease, dementia, cancer and increased all-cause mortality [5, 6]

1. Heymsfield Obes Rev. 2014 April; 15(4): 310–321; 2. Aronne LA, 84th ADA Meeting, June 2024; 3. Kushner RF, Obesity Week 2022; 4. Harris C, Obesity Week 2023; 5. Wegovy Prescribing Information. 2024; 6 Wei, Front. Endocrinol. 2023. 14:1185221

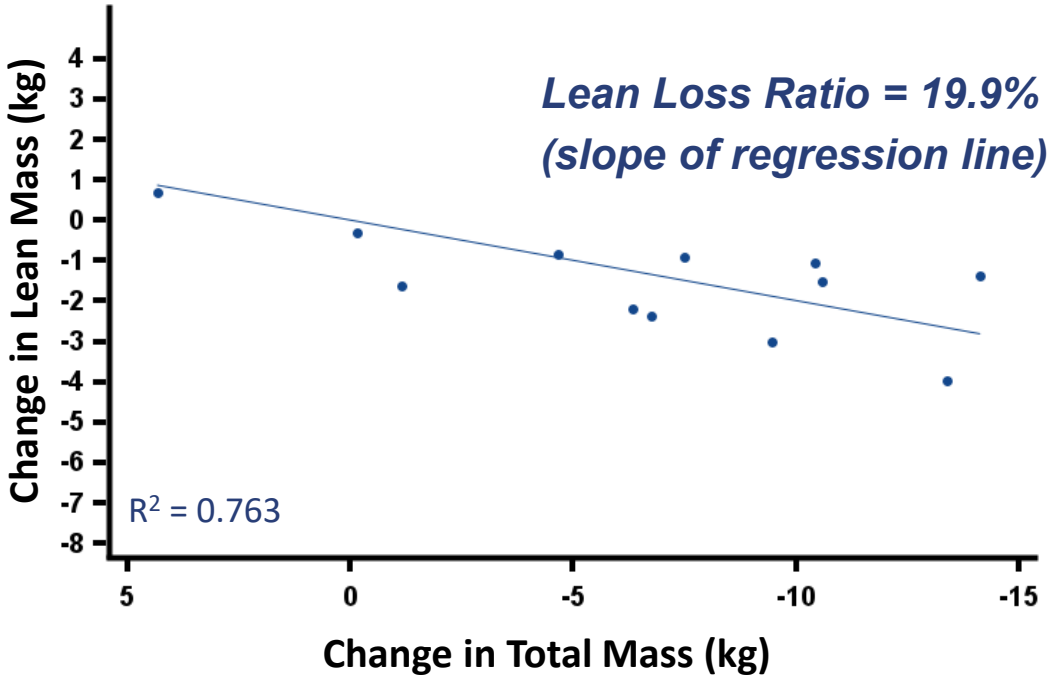
LEAN MASS PRESERVATION MAINTAINED IN OLDER SUBJECTS

PREVENTING LEAN MASS LOSS IN THE ELDERLY MAY REDUCE RISK OF FALLS AND FRACTURES

SUBJECTS < 60 YEARS OLD (N=38)



SUBJECTS ≥ 60 YEARS OLD (N=12)



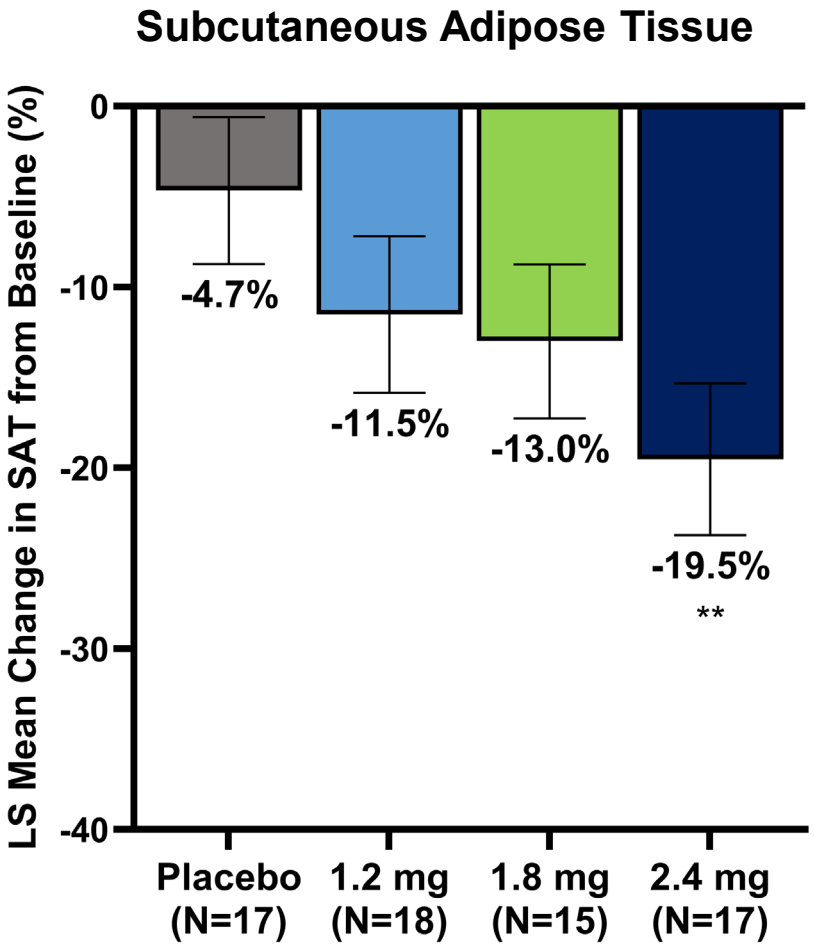
*Change in Total Mass = Lean Mass Loss + Adipose Mass Loss

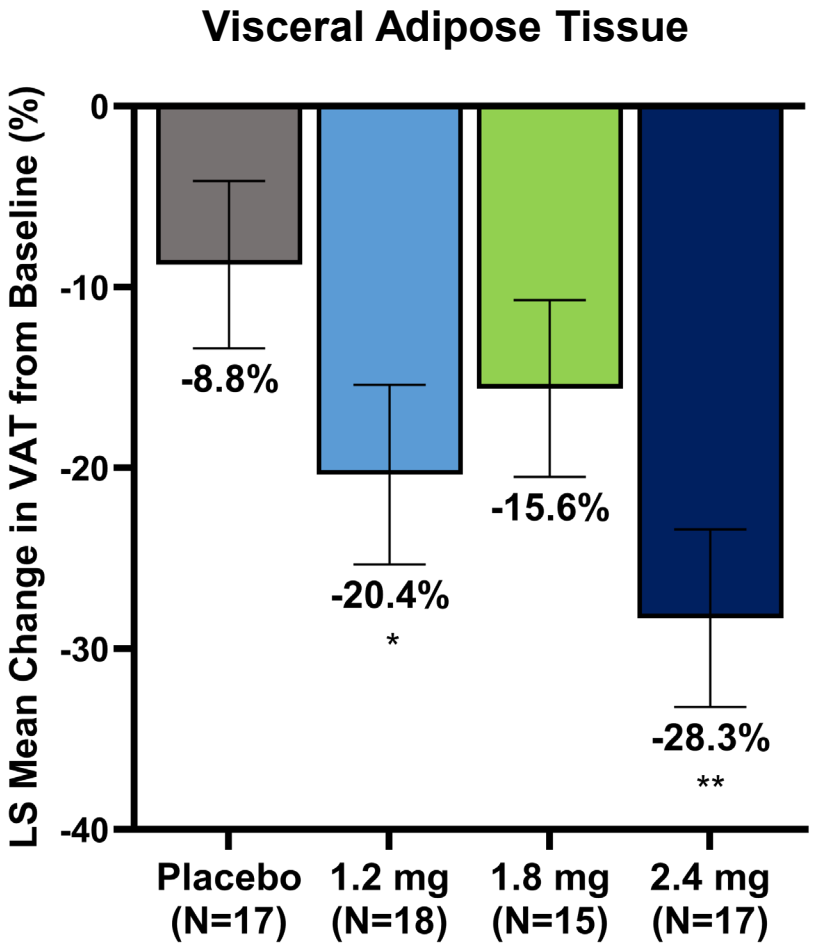
Heymsfield, EASD 2024

altimmune

VISCERAL ADIPOSE TISSUE REDUCED BY 28.3% AT WEEK 48 ON 2.4 MG

PREFERENTIAL REDUCTION OF VAT, THE ADIPOSE TISSUE DEPOT ASSOCIATED WITH CV RISK





Data are means ± SE. * p<0.05, ** p<0.01, *** p<0.001 vs placebo (ANCOVA)

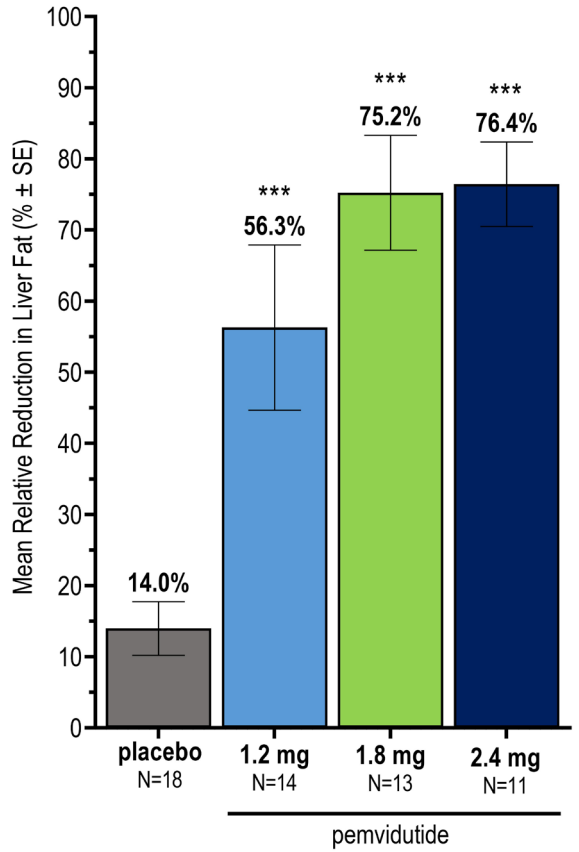
Heymsfield, EASD 2024

altimmune

PEMVIDUTIDE— ROBUST REDUCTIONS IN LIVER FAT CONTENT AT 24 WEEKS

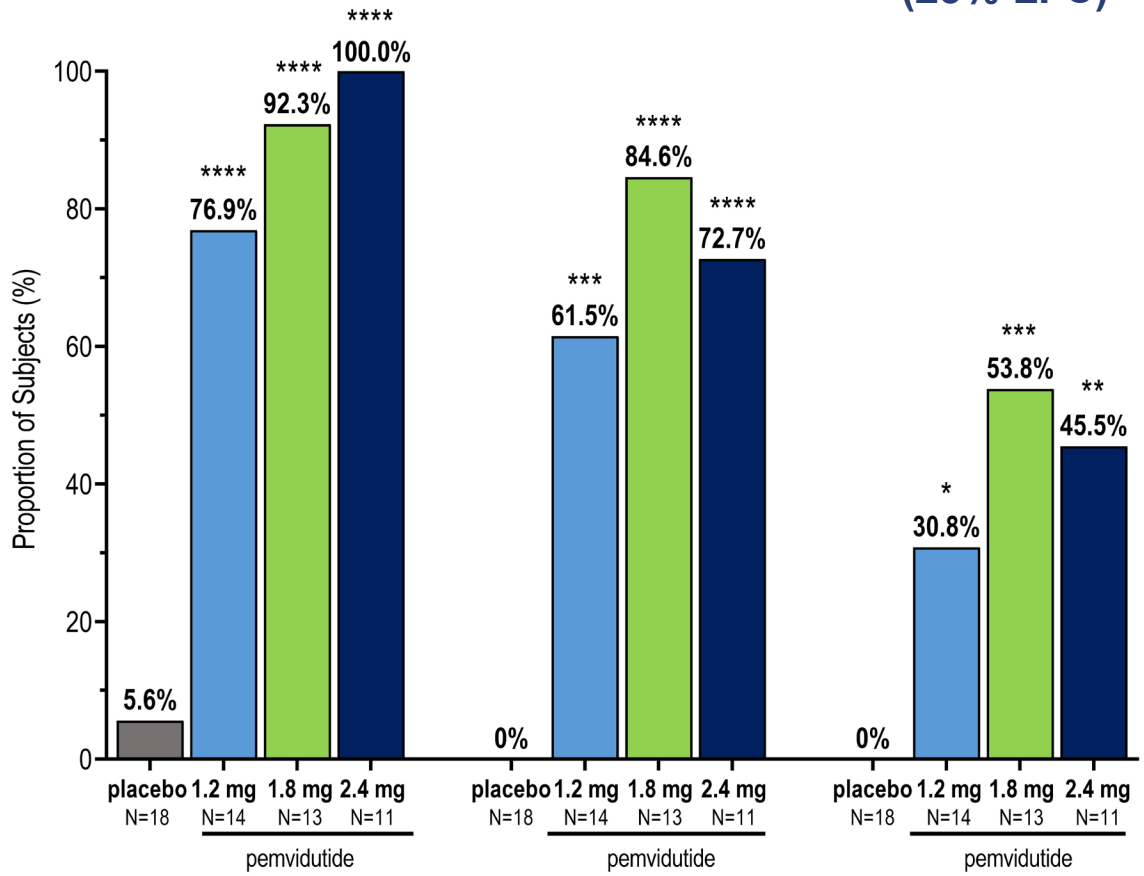
CORRELATES WITH MASH RESOLUTION AND FIBROSIS IMPROVEMENT

Relative Reduction



*** p < 0.001 vs placebo ANCOVA, LS mean ± SE

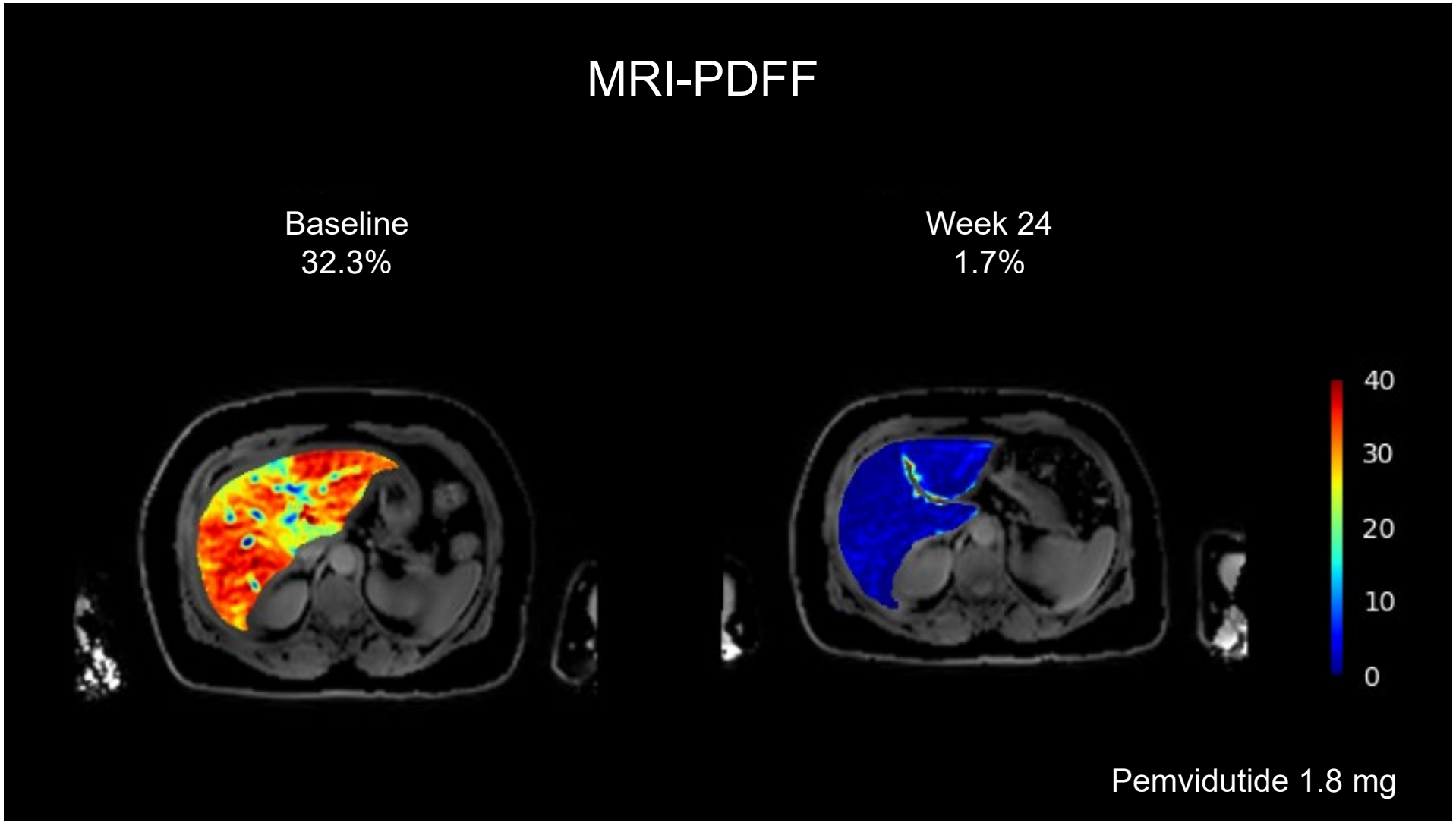
30% Reduction 50% Reduction Normalization (≤5% LFC)



* p < 0.05, *** p < 0.001, ****, p < 0.0001 vs placebo, Cochran-Mantel-Haenszel

altimmune

PEMVIDUTIDE— MARKED REDUCTION OF LIVER FAT CONTENT BY MRI-PDFF AT WEEK 24



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

Study ALT-801-106 MASLD Trial

altimmune

GLP-1 BASED AGENTS IN DEVELOPMENT[1] FOR MASH AND OBESITY

HIGH GLUCAGON CONTENT DRIVES POTENT EFFECTS ON LIVER FAT AND BODY WEIGHT

Agent	Class	Agonist Ratios[2]	Dose Titration	LFC Reduction	Weight Reduction
Semaglutide	GLP-1	—	yes	+	++++
Tirzepatide	GLP-1/GIP	1:15	yes	+	++++
Cotadutide	GLP-1/GCG	5:1	yes	++	+
Retatrutide	GLP-1/GIP/GCG	1:6:0.1	yes	++++	++++
Survodutide	GLP-1/GCG	8:1	yes	+++	++++
Efinopegdutide	GLP-1/GCG	2:1	yes	++++	++++
Pemvidutide	GLP-1/GCG	1:1	no	++++	++++

[1] Phase 2 and later; [2] based on cell-based potency assays
GLP-1, glucagon-like peptide-1; GIP, gastric inhibitory polypeptide; GCG, glucagon

IMPACT TRIAL

PHASE 2 TRIAL ASSESSING THE EFFECTS OF PEMVIDUTIDE IN THE TREATMENT OF MASH

- Multicenter, randomized, placebo-control trial of pemvidutide in the treatment of MASH
- Enrollment of 190 subjects was rapid, completed in only 12 months
- Primary endpoint of MASH resolution and fibrosis improvement will be assessed at only 24 weeks
    - Rapid effects at 24-week will be evidence of the potency of pemvidutide, differentiating it from other incretin agents, which have read out at 48-68 weeks of treatment
- Trial readout Q1 2025

THANK YOU