Weight Loss—
The Preferred Treatment for NASH

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altimmune | NASDAQ: ALT

Forward-looking statements

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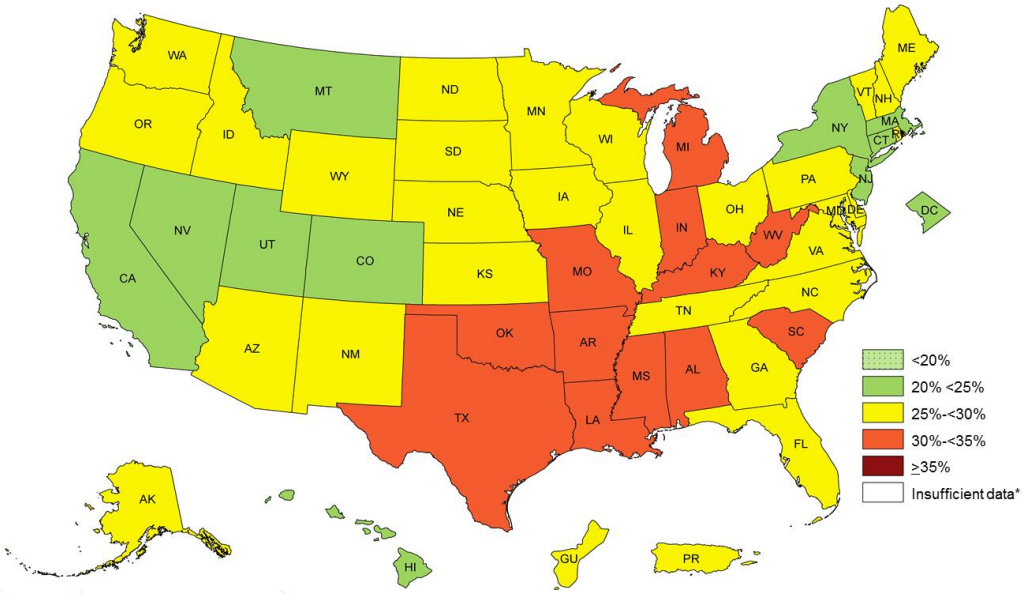
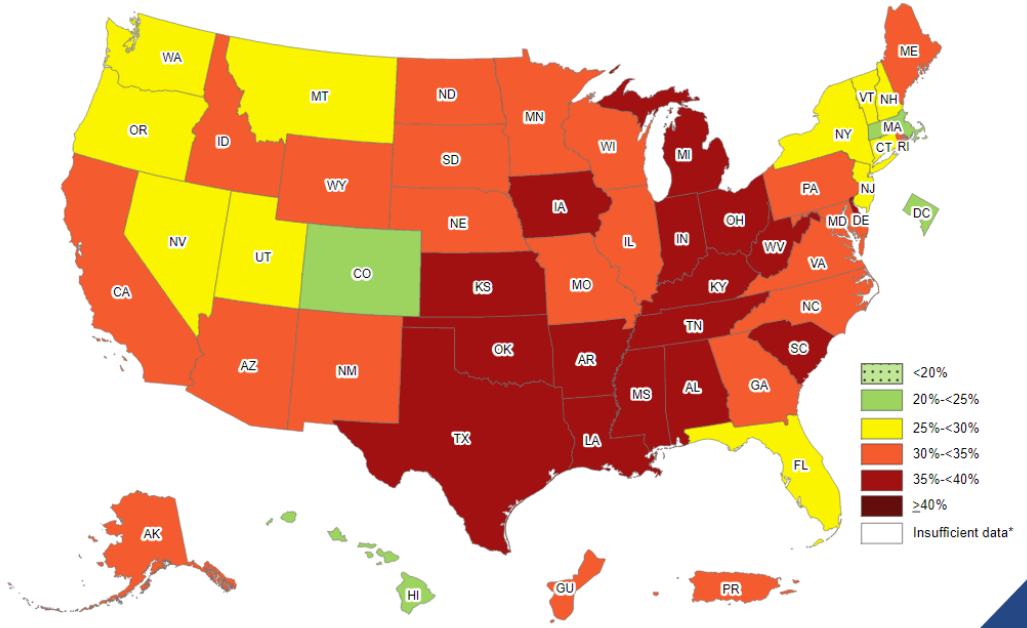
CDC: OBESITY IN U.S. DRAMATICALLY INCREASING

PREVALENCE OF SELF-REPORTED OBESITY AMONG U.S. ADULTS BY STATE AND TERRITORY[1]

2011



2020



1 - https://www.cdc.gov/obesity/data/prevalence-maps.html#race

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OBESITY: SIGNIFICANT BURDEN TO HEALTHCARE SYSTEM

OPPORTUNITY TO ADDRESS MANY COMORBIDITIES THROUGH THE TREATMENT OF OBESITY

IMPACT OF OBESITY

- Obesity is implicated in **two thirds of the leading causes of death** from non-communicable diseases worldwide[1]
- Total obesity related medical care in the U.S. estimated to be **$147 billion** per CDC[2]
- Global market size for medical weight loss alone was **$8.36 billion** in 2020, and is estimated to reach **$27.1 billion** by 2028[3]

COMORBIDITIES

- High blood pressure
- High cholesterol
- Type 2 diabetes
- Coronary heart disease
- Stroke
- Gallbladder disease
- Osteoarthritis
- Sleep apnea and breathing problems
- Certain cancers
- NASH

1 - https://www.sciencedaily.com/releases/2019/10/191024143218.htm
2 - https://www.cdc.gov/obesity/adult/causes.html
3 - https://www.biospace.com/article/obesity-treatment-market-size-to-reach-usd-27-10-billion-in-2028/

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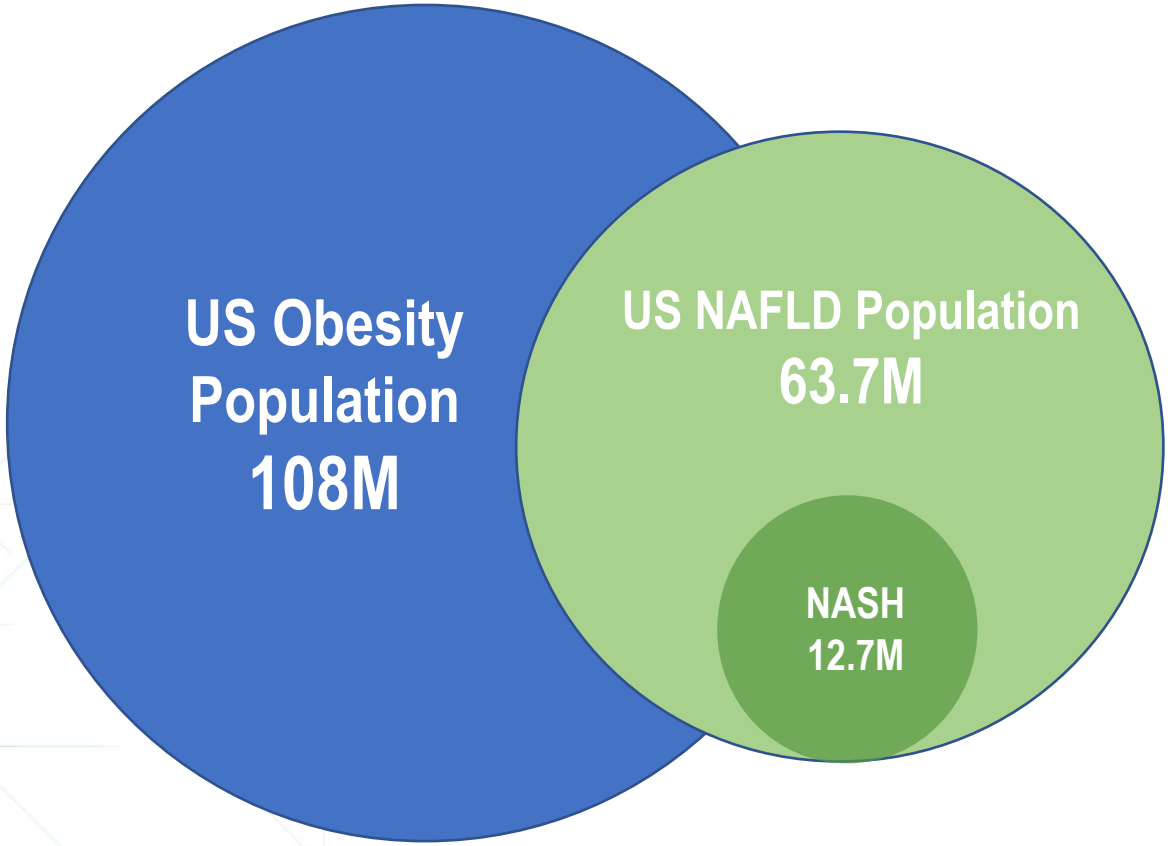
OBESITY AND FATTY LIVER DISEASE

DISEASES WITH UNMET NEED APPROACHING EPIDEMIC PROPORTION



- The treatment of obesity is the cornerstone of treating NASH and the principal co-morbidities of NASH[1,2]
- Previous approaches to the treatment of obesity have been associated with safety concerns limiting success
- The recent success of semaglutide (Wegovy™) has created a regulatory pathway for other incretin-based approaches

[1]Glass LM, Fed Pract 2019; [2]Perazzo H, Liver Int 2017

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DEATHS IN NAFLD: COMPLICATIONS OF OBESITY

LIVER DISEASE ACCOUNTS FOR ONLY A MINORITY OF DEATHS

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)
Liver transplantation	1 (0.5)
Other	35 (18.1)
Unknown	15 (7.8)

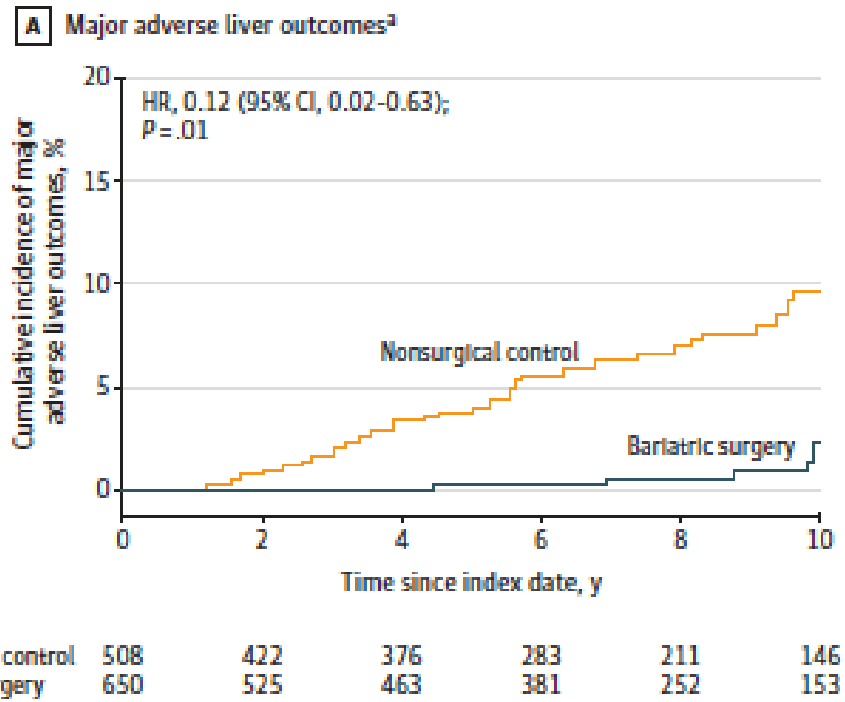
619 patients with biopsy confirmed NAFLD (1975-2005)

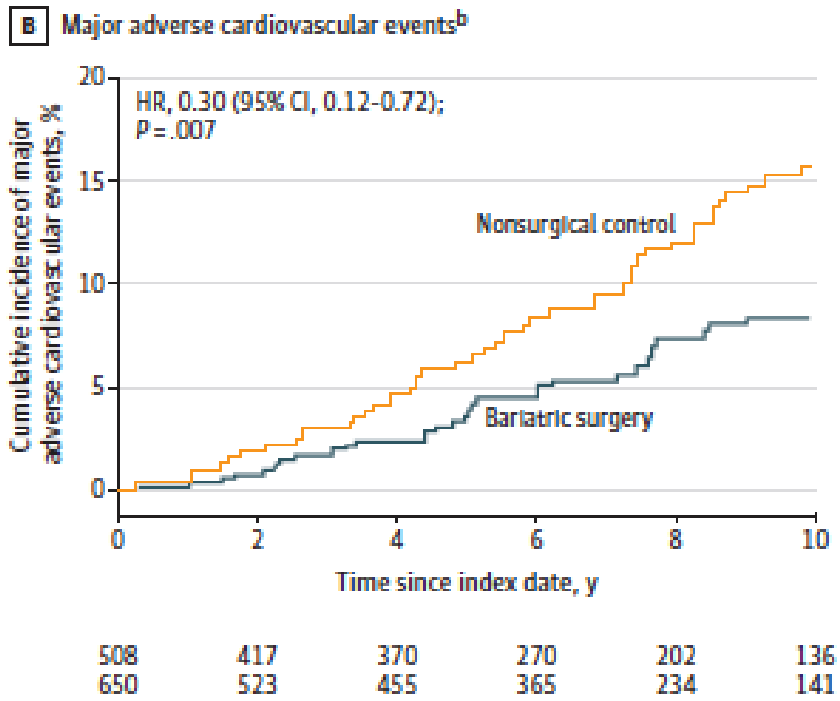
Median follow-up 12.6 years (range 0.3-35)

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

BARIATRIC SURGERY IMPROVES NASH OUTCOMES

LOWERS ADVERSE LIVER OUTCOMES AND MAJOR ADVERSE CARDIOVASCULAR EVENTS





Aminian, JAMA 2021

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WEIGHT LOSS AND IMPROVEMENT OF OBESITY COMPLICATIONS

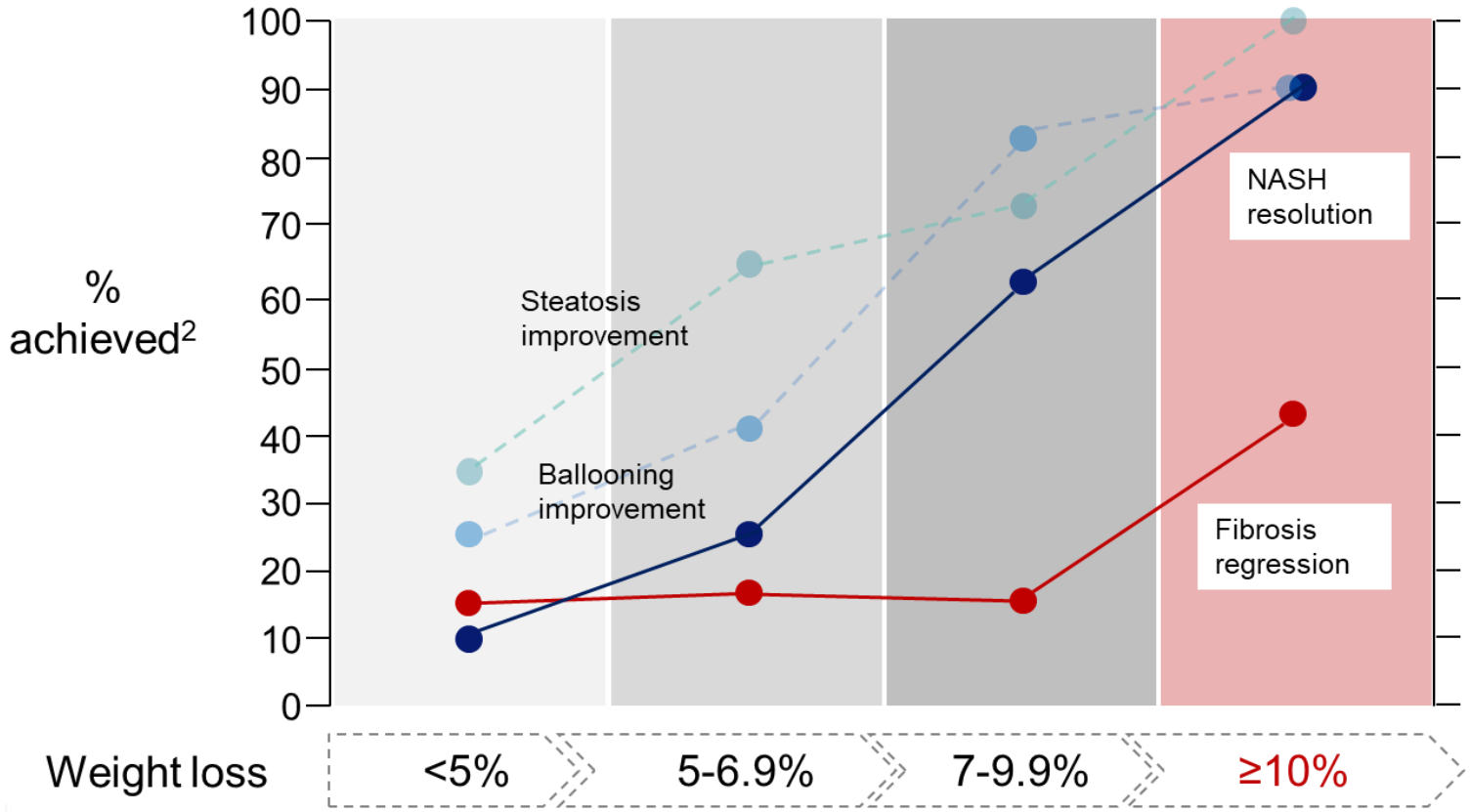
AN EFFECTIVE THERAPY WOULD ACHIEVE AT LEAST 10% WEIGHT LOSS

Complication	Weight Loss Target (%)
NASH	10
Type 2 diabetes	5-15
Hyperlipidemia	10-15
Hypertension	15
Osteoarthritis	5-15
Sleep apnea	10
Gastroesophageal reflux	10-15
Stress incontinence	10

Adapted from Cefalu, Diabetes Care 2015

TREATING OBESITY IS THE CORNERSTONE OF NASH THERAPY

10% OR MORE WEIGHT LOSS MUST BE ACHIEVED[1]



[1] *Promrat et al Hepatology 2010; Glass et al Dig Dis Sci 2015; Vilar-Gomez et al Gastroenterology 2015; Marchesini et al Hepatology 2016; Koutowkidis et al JAMA Intern Med 2019*

[2] *Adapted from Harrison, EASL 2019, Traber, Discovery on Target: Targeting NASH 2019, and Vilar-Gomez, Gastroenterology 2015*

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MOST NASH AGENTS FAIL TO ACHIEVE MEANINGFUL WEIGHT LOSS

SNAPSHOT OF COMPOUNDS IN ADVANCED NASH DEVELOPMENT

Agent	Author (year)	Mechanism	Weight Loss (%)
Obeticholic acid	Younossi, ZM 2019[1]	FXR agonist	~2%
Resmetirom	Harrison, SA 2018[2]	THRβ agonist	no change
Aldafermin (3mg)†	Harrison, SA 2019[3]	FGF19 agonist	1.3%
Pegbelfermin (10 mg)††	Sanyal, A 2018[4]	FGF21 agonist	2.2%
AKR-001 (70 mg)	Ritchie, M 2020[5]	FGF21 agonist	no change; 3.7%†††
Firsocostat	Lawitz, EJ 2018[6]	ACC inhibitor	no change
Lanifibranor (1200 mg)	Franque, S 2020[7]	PanPPAR	increases 3.1%

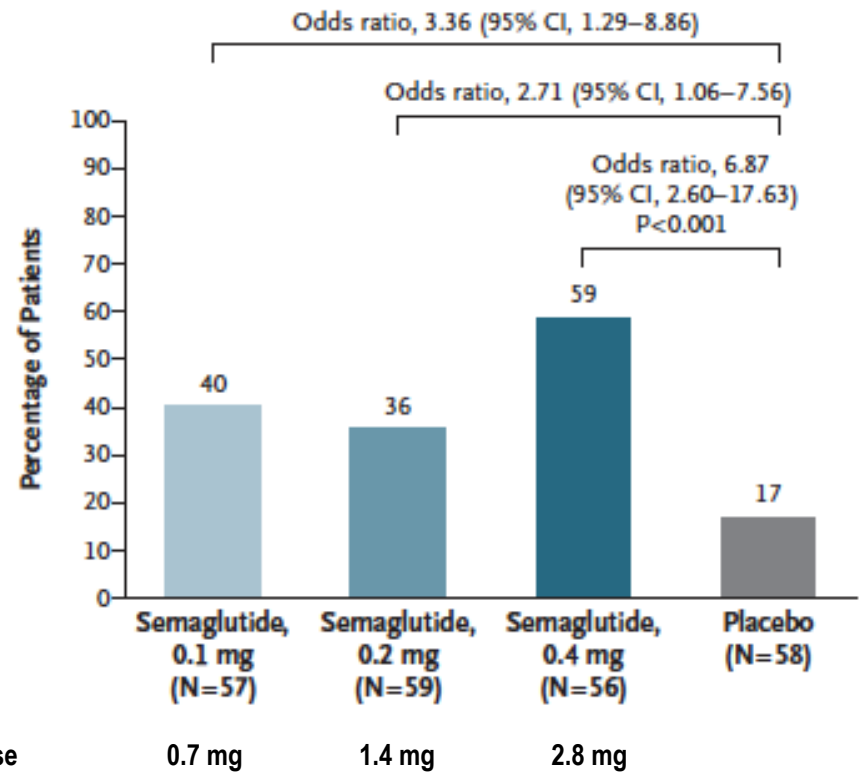
† No information has been made public on 1mg dose
†† Gain of 0.6% on 20mg dose
††† BALANCED study (June 30 corporate deck)

[1]Younossi, YM, et al. (2019) Lancet 394: 2184-96; [2]Harrison, SA, et al. Lancet 394: 2012-24; [3] Harrison, SA, et al. (2019) Lancet 391:1174-85; [4]Sanyal, A, et al. (2018) Lancet 392:2705-17; [5]Ritchie, M, et al. (2020) Exp Opin Invest Drugs, 29:2, 197-204; [6] Lawitz, EJ, et al. (2018) Clin Gastroenterol Hepatol 16:1983-91; [7]Franque S, AASLD 2020

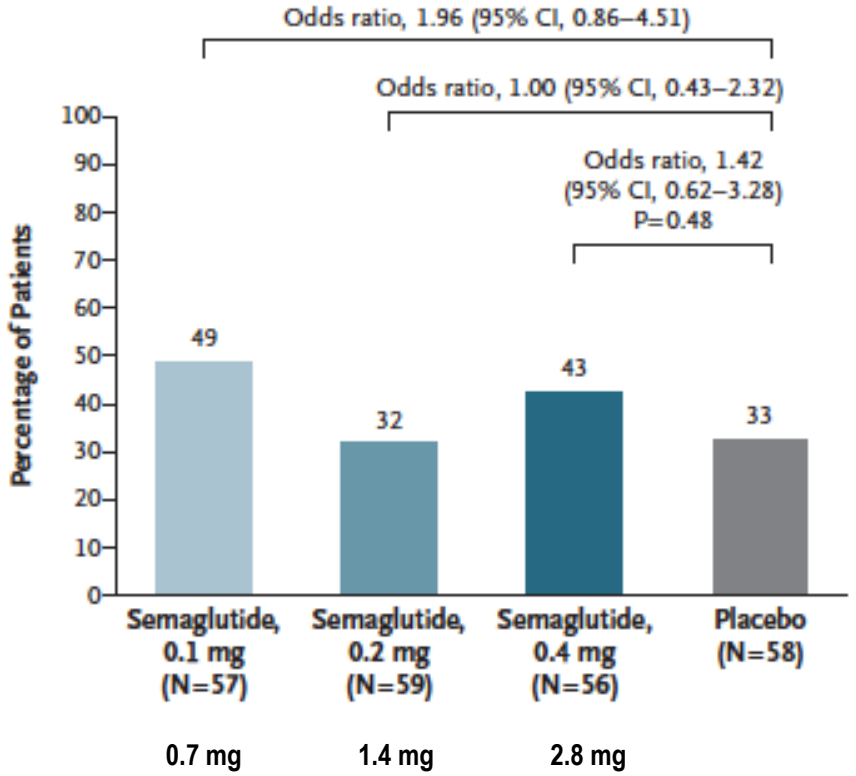
SEMAGLUTIDE—NASH RESOLUTION WITHOUT FIBROSIS IMPROVEMENT

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

NASH Resolution



Fibrosis Improvement



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

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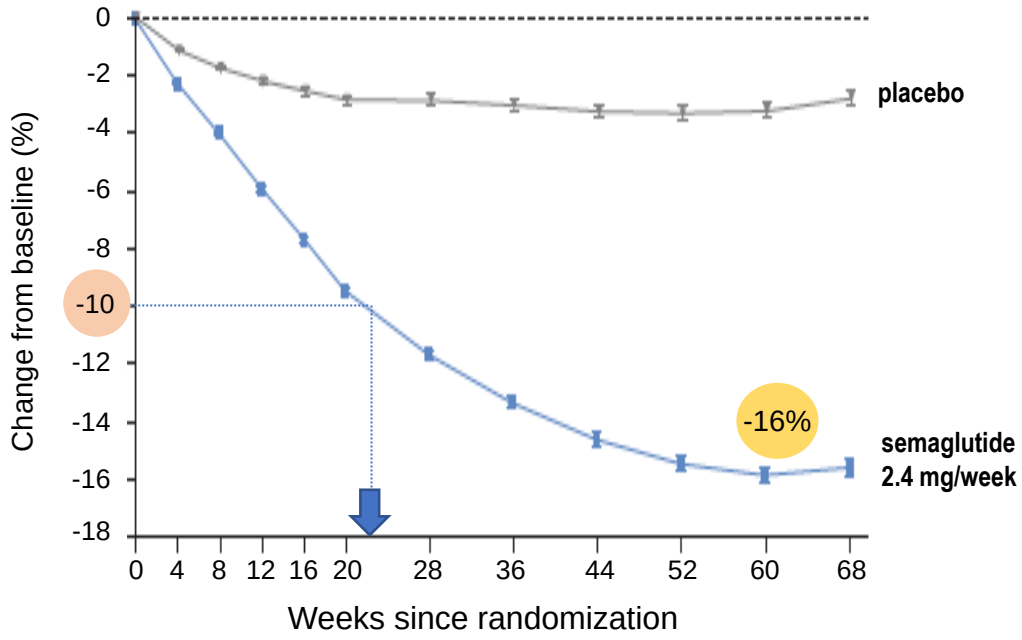
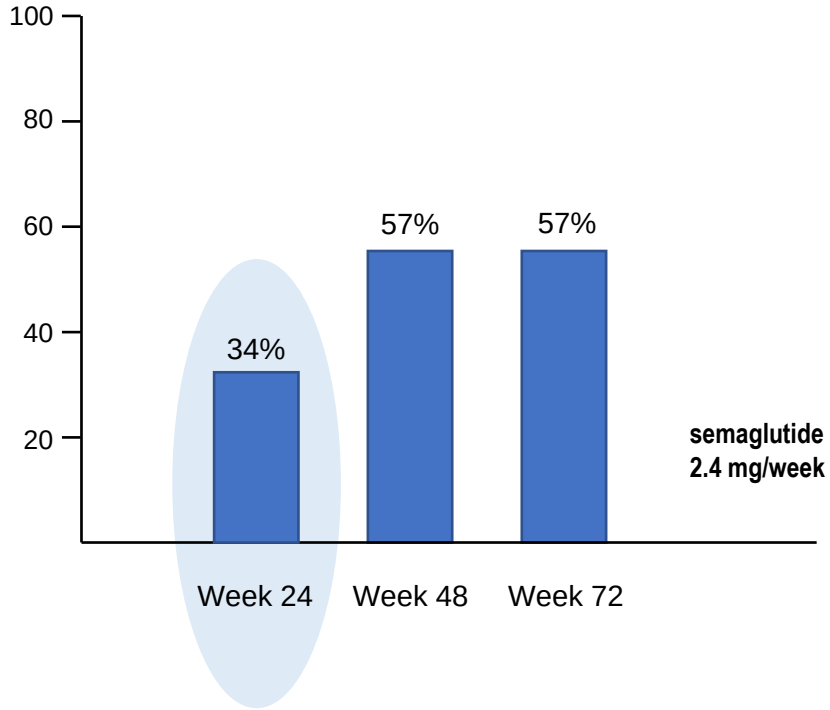
SEMAGLUTIDE—BODY WEIGHT AND LIVER FAT EFFECTS DELAYED

FIBROSIS IMPROVEMENT MAY NOT HAVE BEEN REALIZED WITHIN TREATMENT PERIOD

Body weight, change from baseline



Relative reduction in liver fat (%), estimated



Adapted from Wilding, NEJM 2021, and Flint, Aliment Pharm Ther 2021

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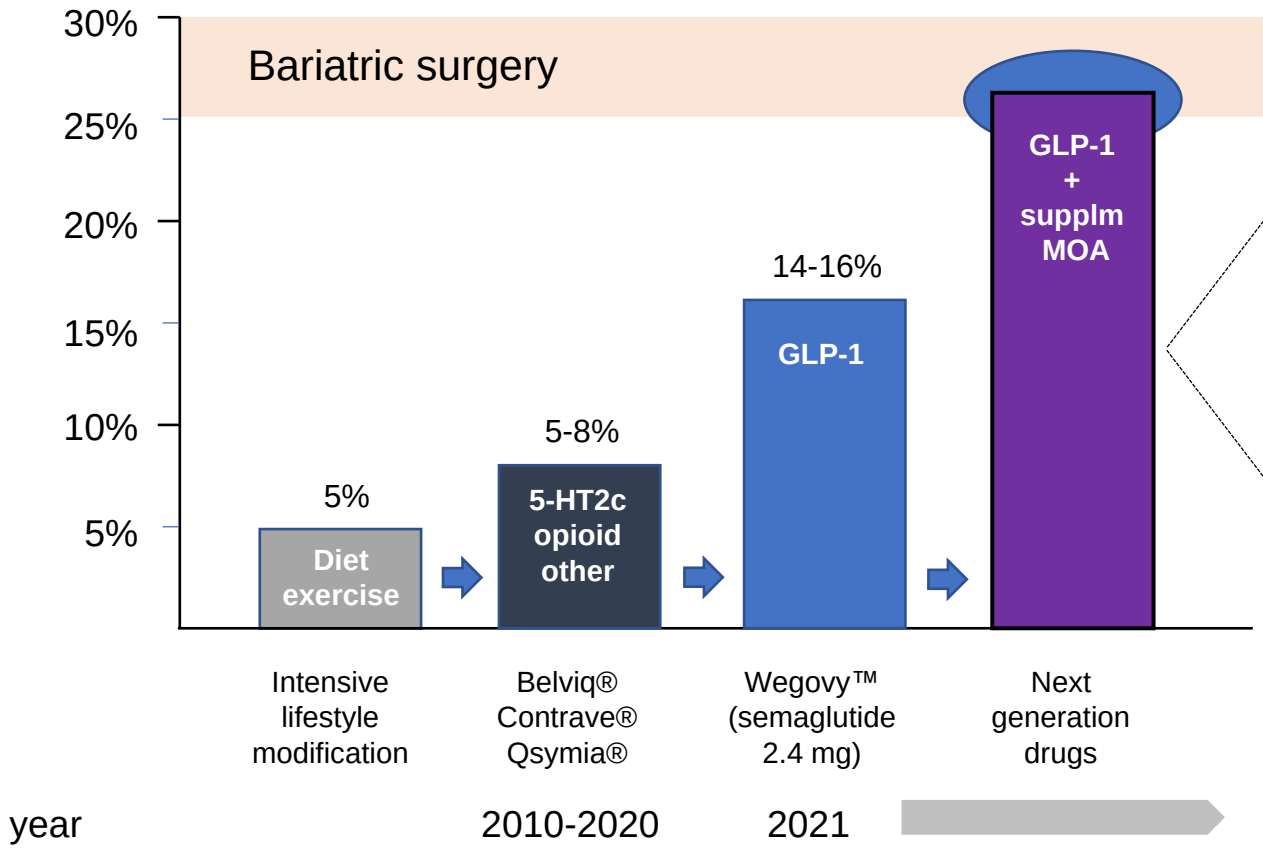
DOSE TITRATION FACES CHALLENGES

PRICE PAID FOR PROLONGED 16-WEEK TO 20-WEEK TITRATION REGIMENS

- Clinical trial results are affected
- Negative impact on patient satisfaction and compliance
  - Willingness to pay co-pays can be affected by perception of slower results
- Difficulties encountered as weight loss and NASH treatments move to primary care
  - Primary care physicians have limited times and resources to oversee these regimens
  - Some insurance companies have treated titration steps as a separate medications, requiring approval for each dose change

MEDICATIONS STRIVE TO ACHIEVE BARIATRIC SURGERY WEIGHT LOSS

SUPPLEMENTING GLP-1 WITH ADDITIONAL MECHANISMS



Drugs in clinical trials for weight loss

2nd Agent	
Additional mechanism	Example
Amylin	Cagrilintide

Dual and triple agonists	
Additional mechanism	Example
GLP-GIP	Tirzepatide
GLP-glucagon	Pemvidutide (ALT-801)
GLP-GIP-glucagon	LY3437943

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PEMVIDUTIDE[1] (ALT-801)
DUAL RECEPTOR AGONIST

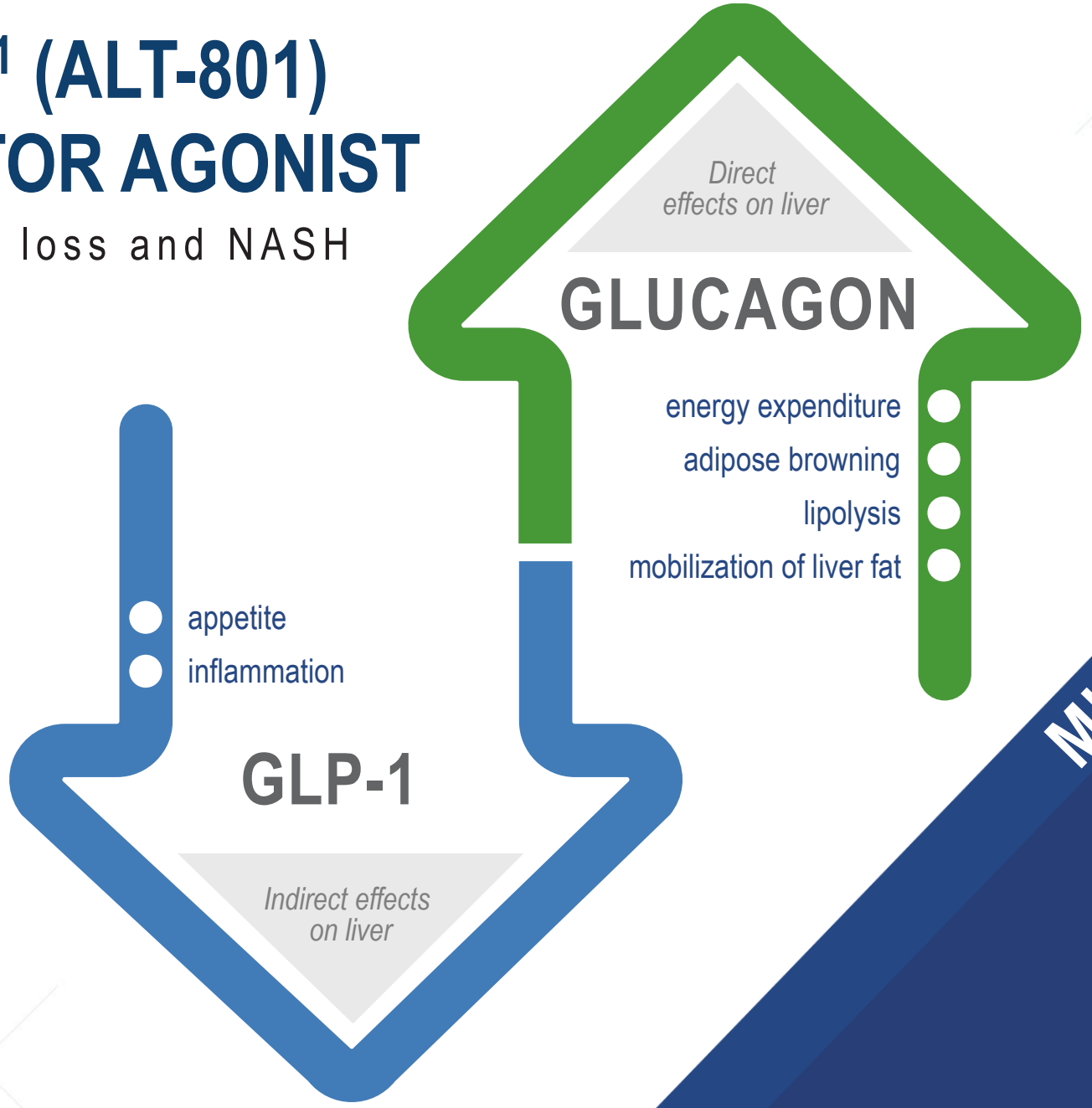
Optimized for weight loss and NASH

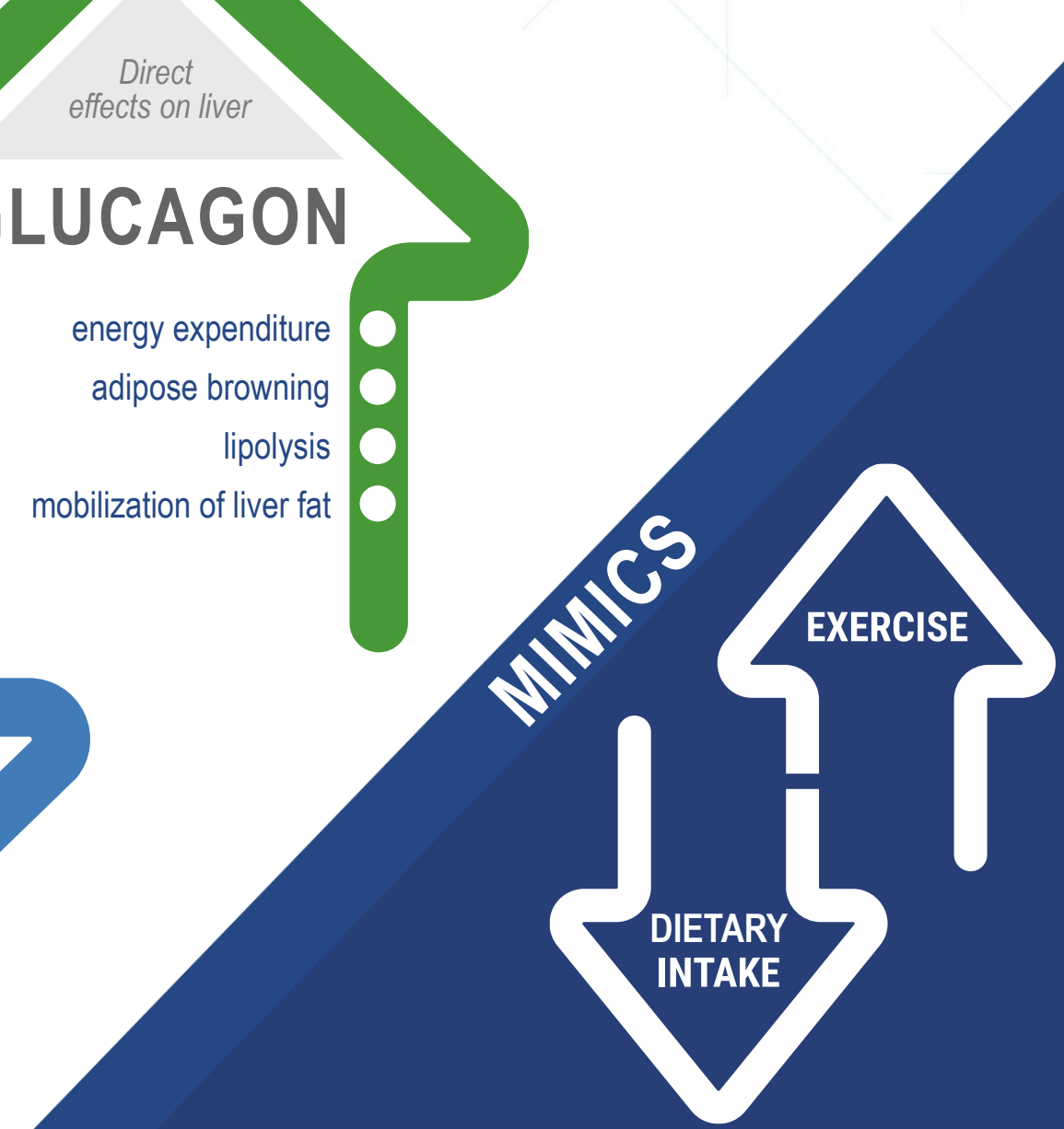
Designed for significant reductions in:

BODY WEIGHT

LIVER FAT, INFLAMMATION, & RESULTING FIBROSIS

[1] proposed INN

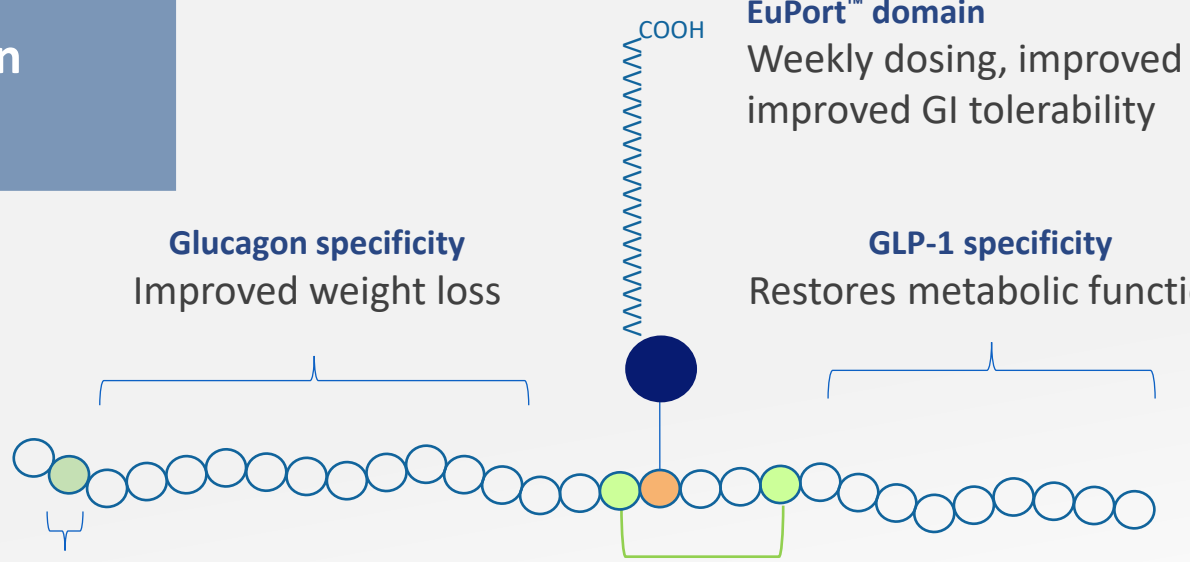




PEMVIDUTIDE (ALT-801)

BALANCED (1:1) DUAL AGONIST WITH ENHANCED PHARMACOKINETIC PROPERTIES

Balanced (1:1) GLP-1:Glucagon Agonism



EuPort™ domain
Weekly dosing, improved PK for improved GI tolerability

Glucagon specificity
Improved weight loss

GLP-1 specificity
Restores metabolic function

Modified residue
Protease stability

Helix Stabilizer
Increased potency[2]

[2]Guarracino DA et al., Chem Rev. 2019 Sep 11;119(17):9915-9949

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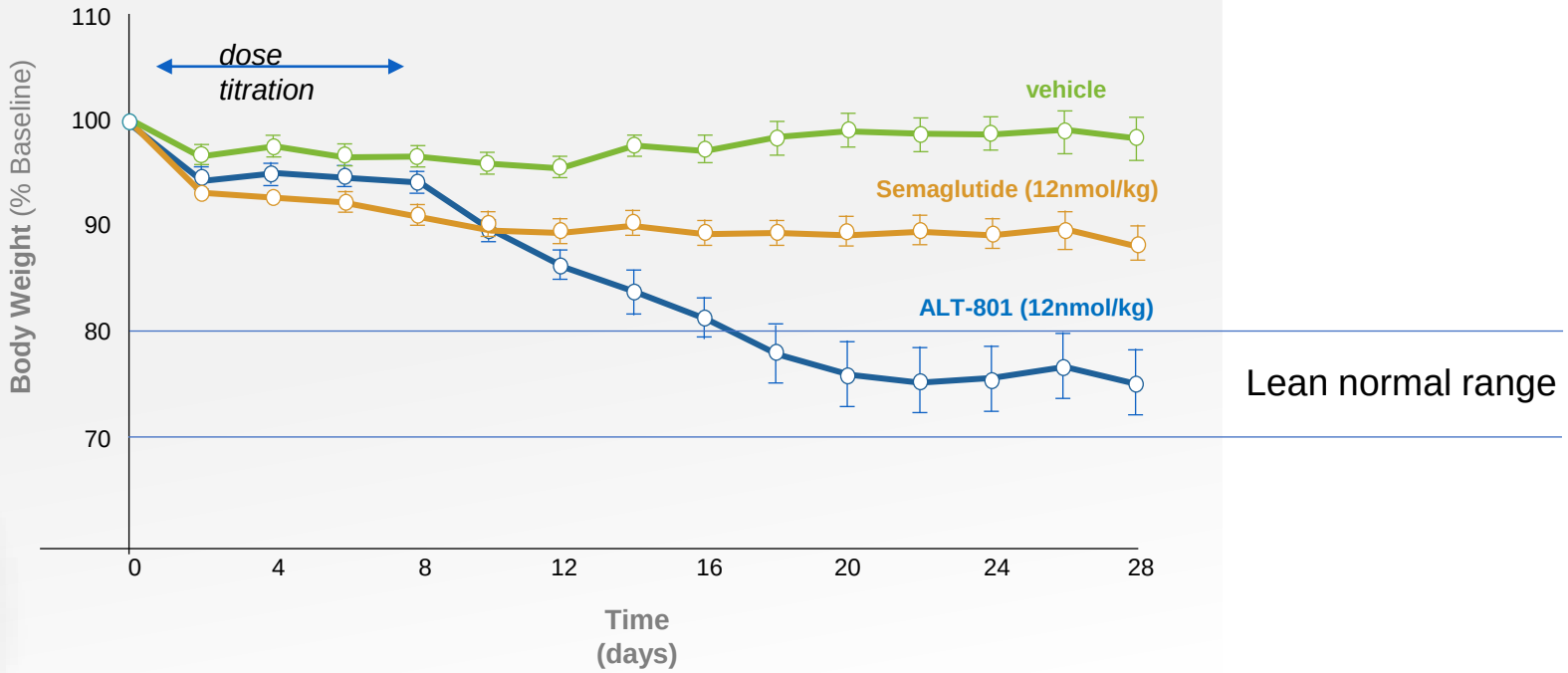
PEMVIDUTIDE (ALT-801) IN MOUSE DIET-INDUCED OBESITY (DIO) MODEL

2-FOLD GREATER WEIGHT REDUCTION THAN GLP-1 MONOTHERAPY AND TO LEAN NORMAL RANGE

Mouse DIO Model After 4 Weeks of Treatment



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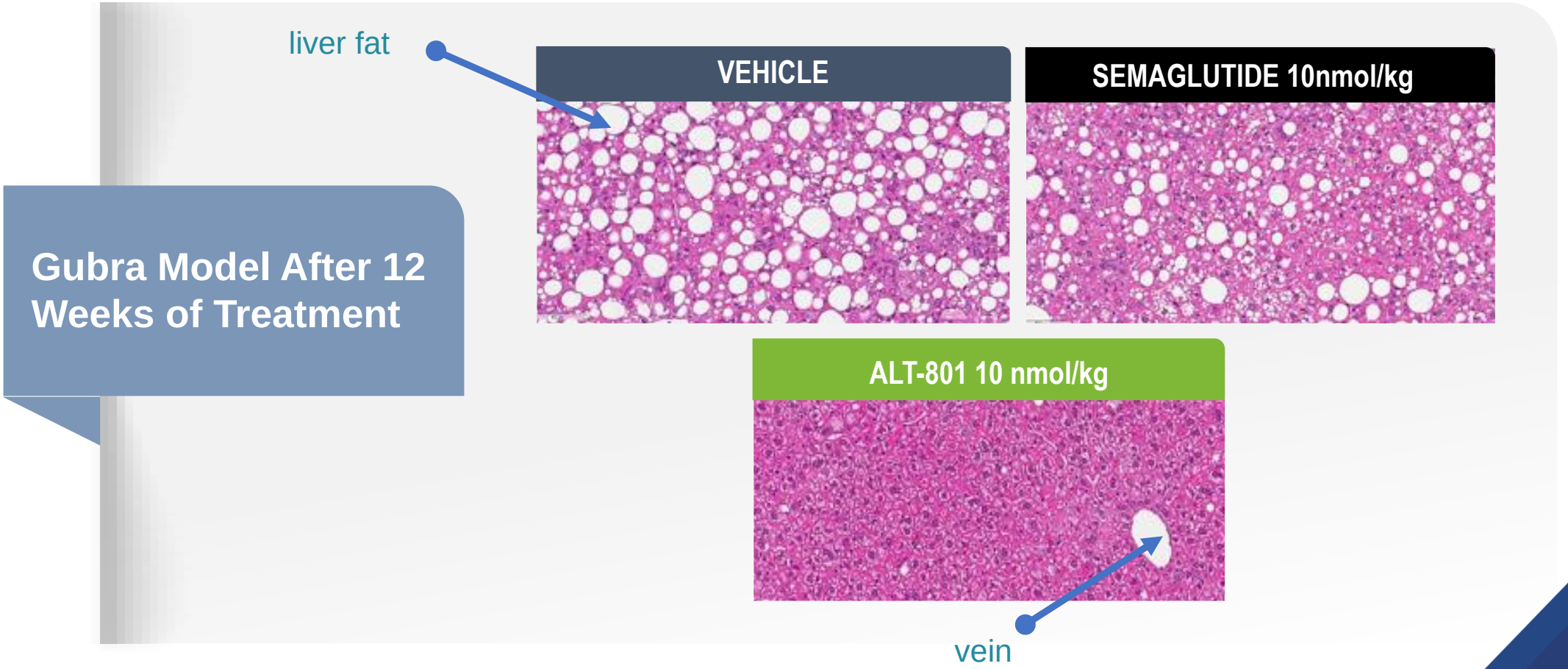
PEMVIDUTIDE (ALT-801) IN GUBRA MOUSE MODEL OF NASH

SUPERIOR EFFECTS VS GLP-1 MONOTHERAPY—LIVER FAT REDUCED TO ALMOST UNDETECTABLE LEVELS

Gubra Model After 12 Weeks of Treatment



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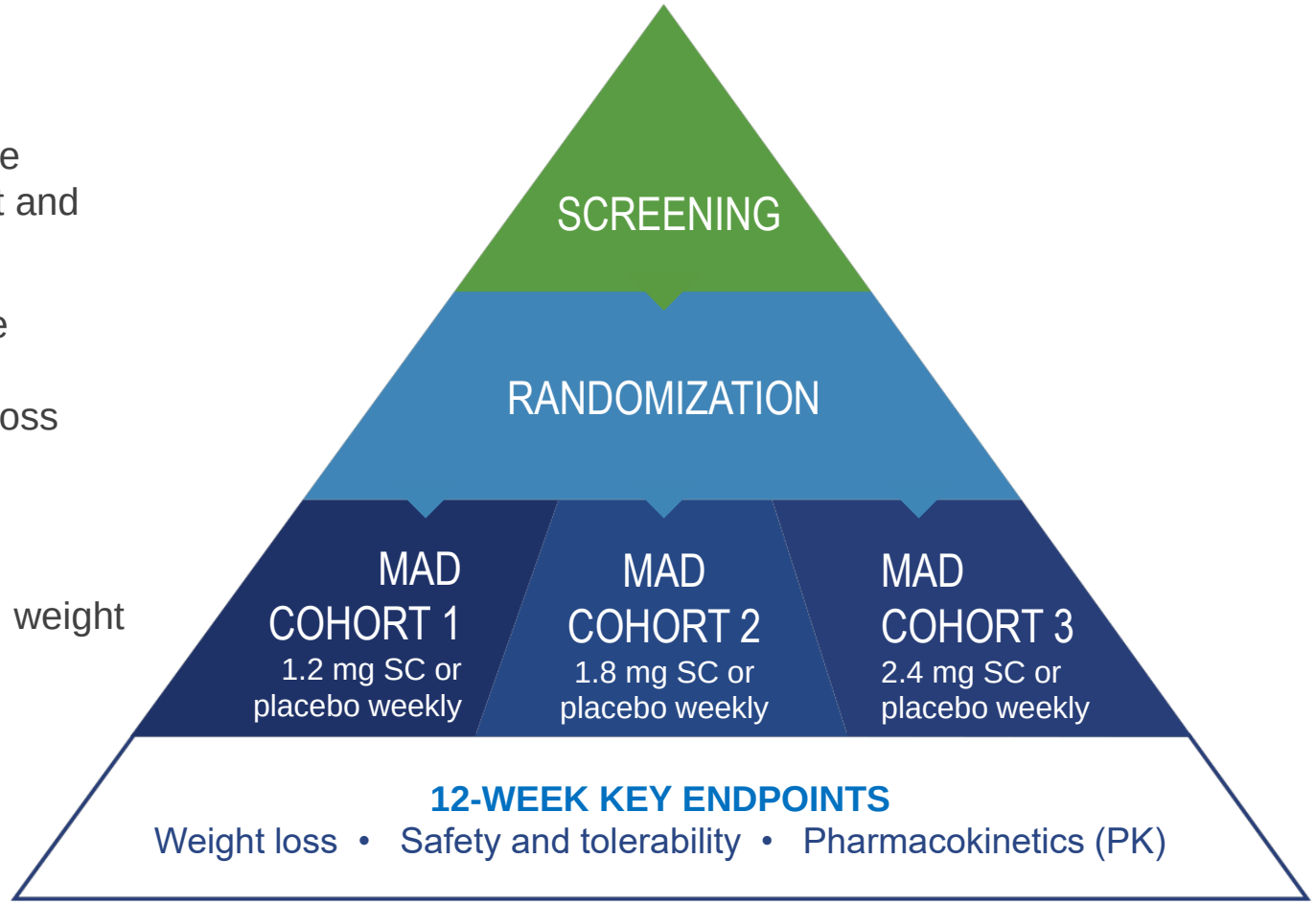
PEMVIDUTIDE PHASE 1— MAD TRIAL DESIGN

- Phase 1, first-in-human, placebo-controlled, multiple ascending dose (MAD) study in healthy overweight and obese volunteers
- Within MAD cohorts, patients were randomized 4:1 to pemvidutide or placebo, with placebos pooled across cohorts
- **No dose titration**
- No calorie restriction or behavioral weight loss programs



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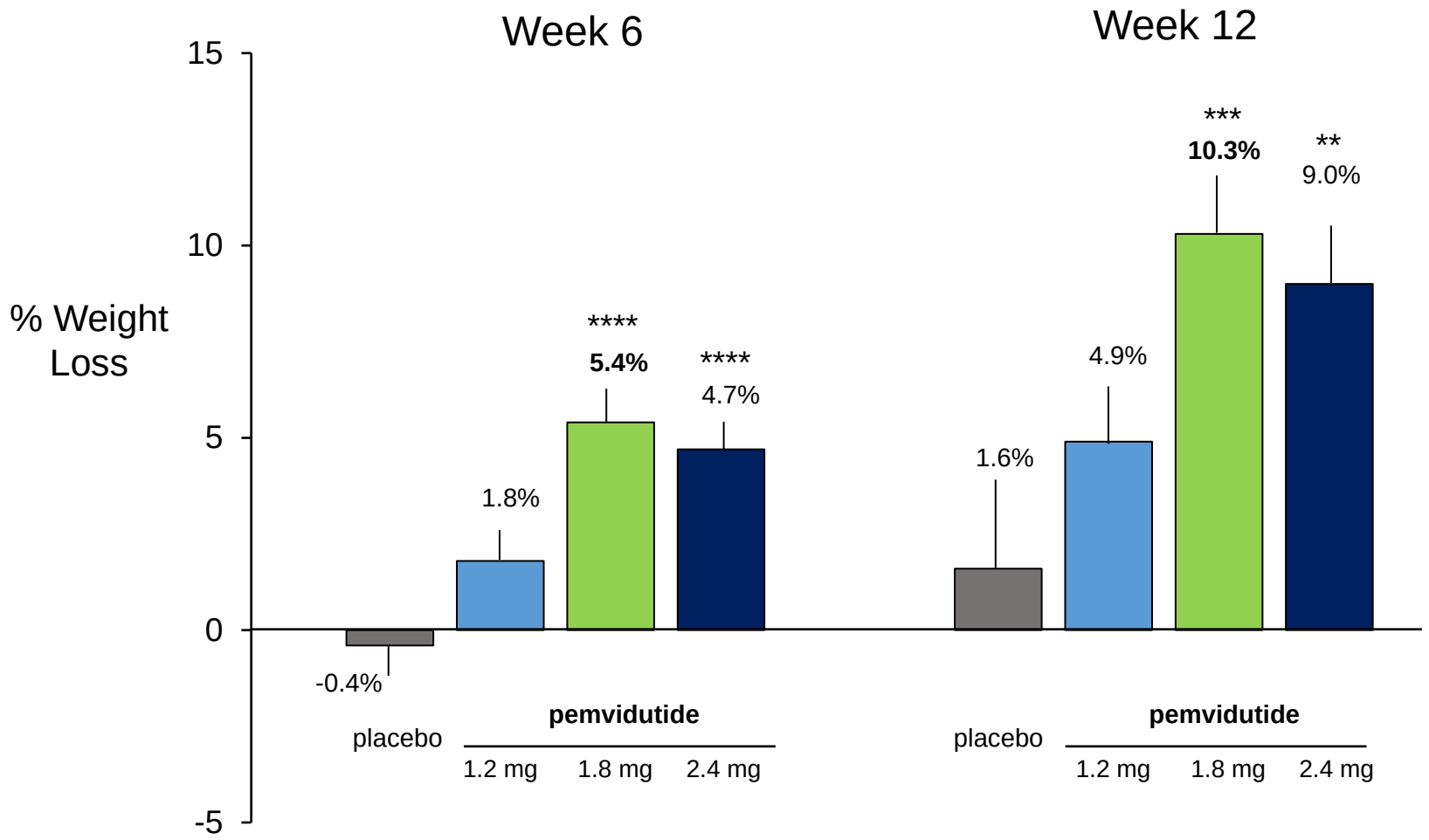
SUBSTANTIAL WEIGHT LOSS AT WEEK 12

10.3% MEAN WEIGHT LOSS ACHIEVED AT 1.8 MG DOSE



*** p < .01, ***p < .005, ****p < .001; compared to placebo*

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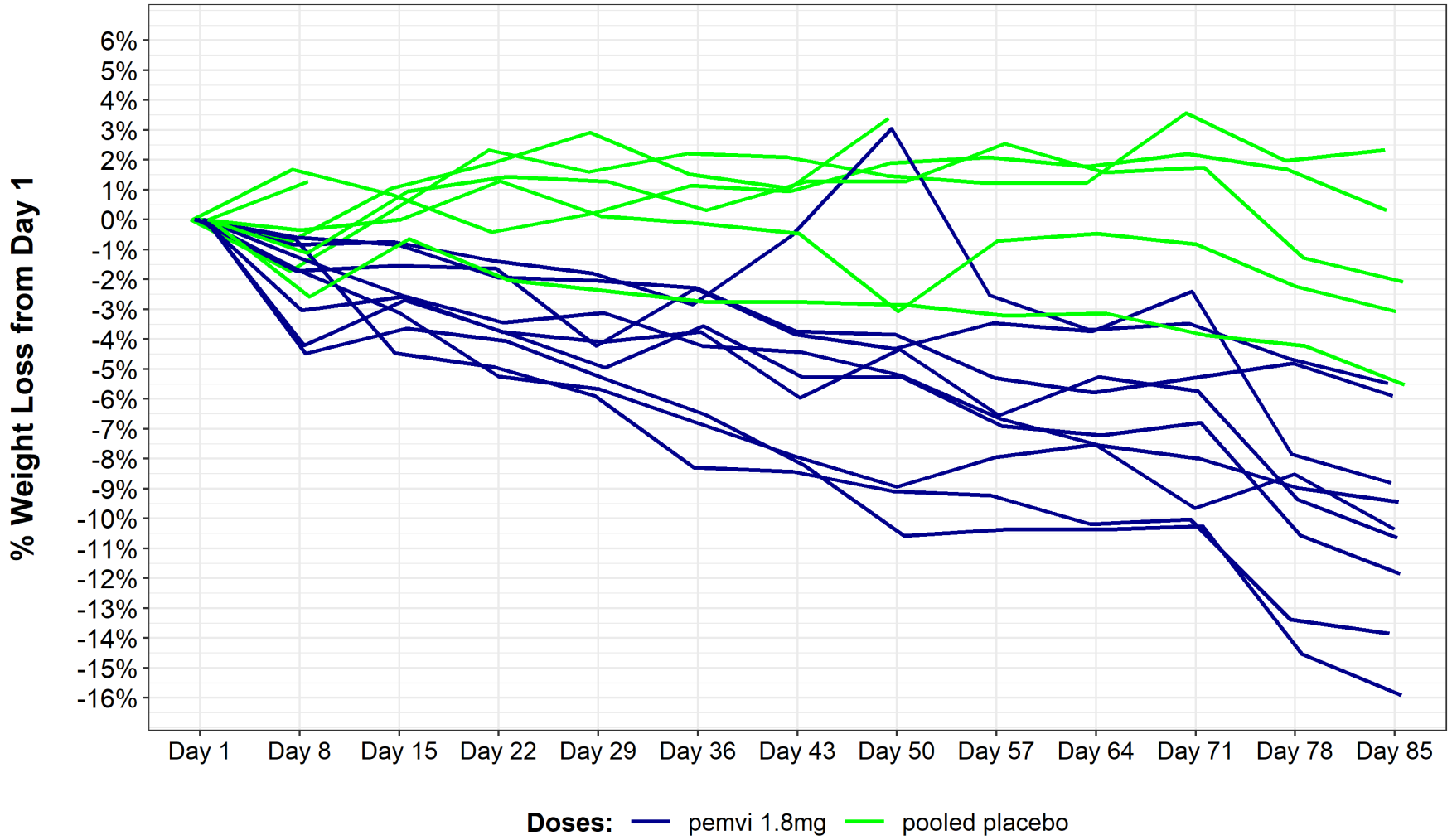
MAJORITY OF SUBJECTS AT 1.8 MG DOSE ACHIEVED 10% OR MORE WEIGHT LOSS AT WEEK 12



- 55% of subjects achieved 10% or more weight loss by Week 12
- 100% of subjects achieved 5% or more weight loss by Week 12

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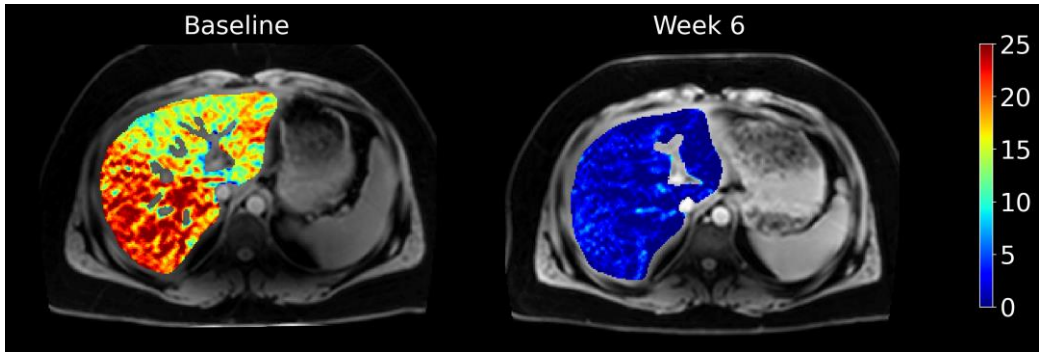
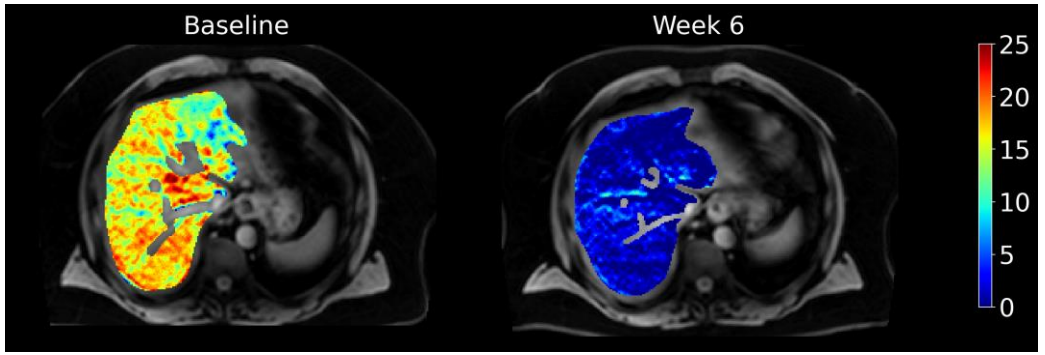
GREATER THAN 90% REDUCTION IN LIVER FAT BY MRI-PDFF IN 6 WEEKS

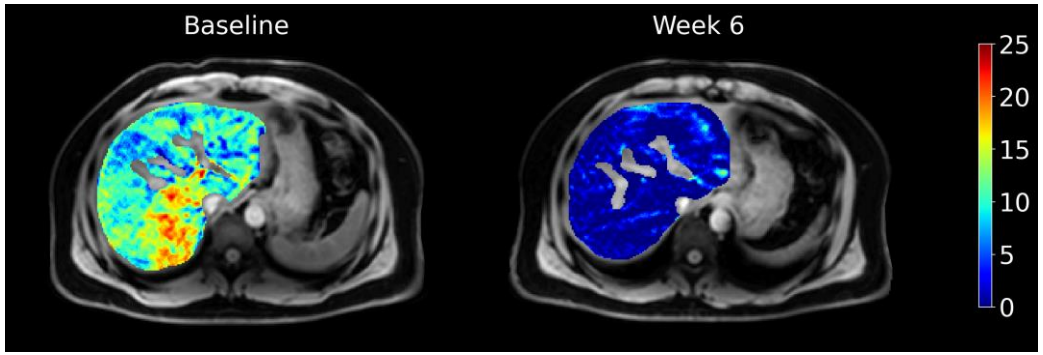
PEMVIDUTIDE DECREASED LFC TO UNDETECTABLE LEVELS AT THE 1.8 MG AND 2.4 MG DOSES



19.5% **Below LOD**



17.0% **Below LOD**



12.5% **Below LOD**

Exploratory analysis of subjects with baseline LFC ≥ 5%

- All subjects receiving pemvidutide 1.8 or 2.4 mg achieved undetectable levels of liver fat by MRI-PDFF at Week 6 – a greater than 90% reduction
- Potentially a new standard in NASH treatment for the speed and magnitude of liver fat effects

LFC, liver fat content; LOD, Limit of Detection

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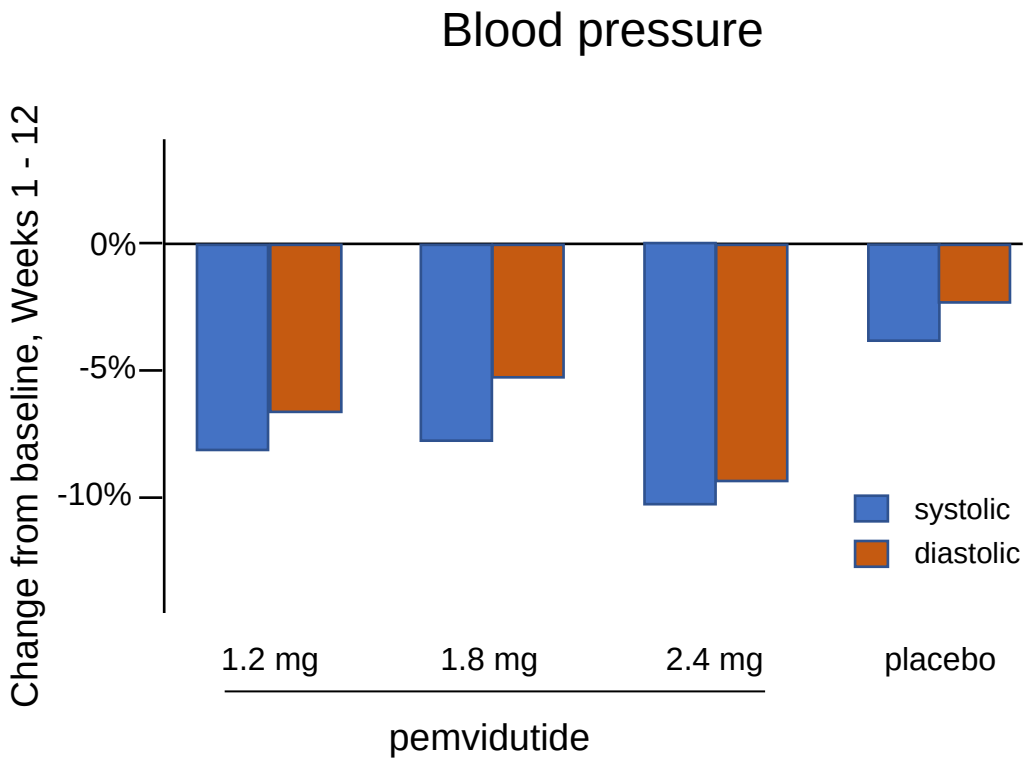
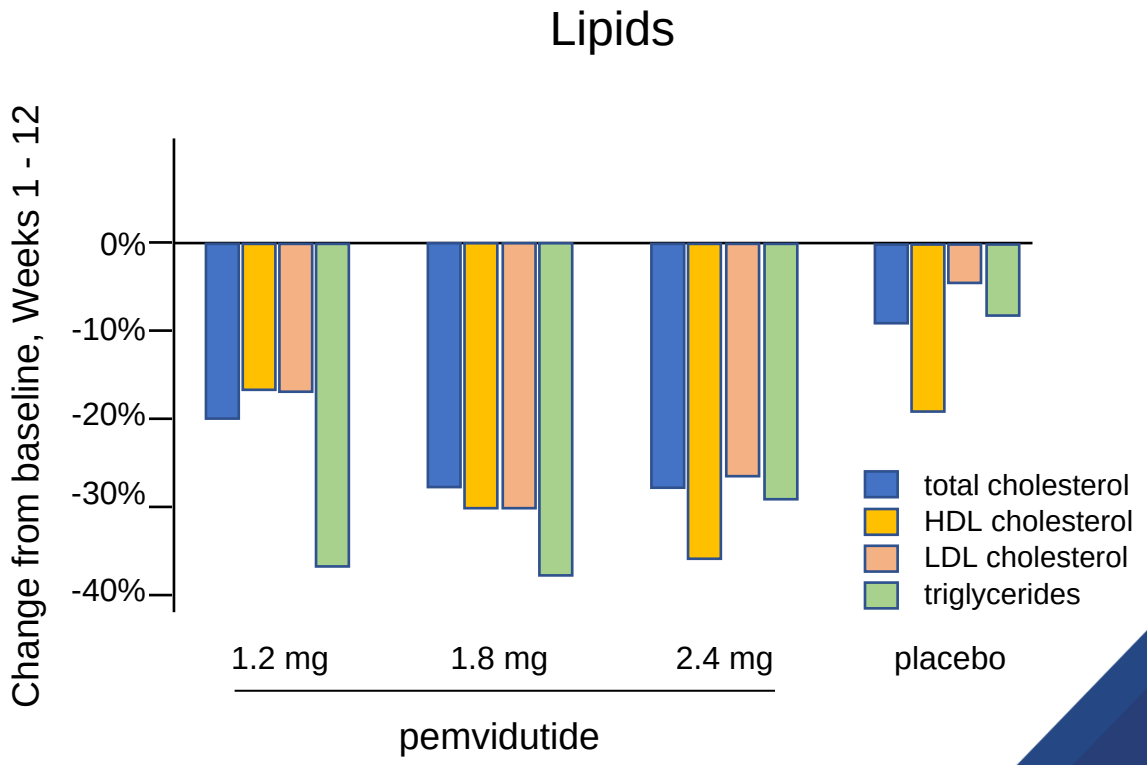
REDUCTIONS IN CARDIOVASCULAR RISK

REDUCTIONS IN BLOOD PRESSURE AND LIPIDS, WEEKS 1-12





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SAFETY OVERVIEW

NO STUDY DISCONTINUATIONS DUE TO ADVERSE EVENTS

Characteristic		Treatment			
		1.2 mg	1.8 mg	2.4 mg	Pooled placebo
AEs leading to discontinuation	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
Serious or severe AEs	**n (%)**	**0 (%)**	**0 (%)**	**0 (%)**	**0 (%)**
Nausea					
Mild	n (%)	1 (14.3%)	5 (55.6%)	5 (45.5%)	1 (14.3%)
Moderate	n (%)	1 (14.3%)	1 (11.1%)	5 (45.5%)	0 (0.0%)
Vomiting					
Mild	n (%)	1 (14.3%)	1 (11.1%)	5 (45.5%)	1 (14.3%)
Moderate	n (%)	0 (0.0%)	1 (11.1%)	3 (27.3%)	0 (0.0%)
Diarrhea					
Mild	n (%)	0 (0.0%)	0 (0.0%)	2 (18.2%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation					
Mild	n (%)	0 (0.0%)	1 (11.1%)	2 (18.2%)	0 (0.0%)
Moderate	n (%)	0 (0.0%)	1 (11.1%)	1 (9.1%)	0 (0.0%)
Hyperglycemia	n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

1 subject receiving 1.8 mg dose and 1 subject receiving placebo experienced 3-5X alanine aminotransferase (ALT) elevations during treatment

Gastrointestinal Adverse Events

- Most frequently mild at 1.8 mg dose with on-drug resolution and not requiring treatment
- No study discontinuations due to AEs

No significant effects on

- Blood glucose control by fasting serum glucose and HbA1c
- Mean heart rate at Week 6 and Week 12

SUMMARY

- NASH and obesity are significant problems in the US
- Weight loss medications are needed that deliver the effects of bariatric surgery
- Pemvidutide is a promising new agent for the treatment of these conditions

THANK YOU

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NASDAQ: ALT