Efficacy and Safety of Pemvidutide in the Treatment of Adults with Alcohol Use Disorder: Results from RECLAIM, a 24-Week Phase 2 Randomized Double-Blind Placebo-Controlled Trial

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Disclosures

Dr. Kranzler's Disclosures:

Dr. Kranzler serves on advisory boards for Altimmune, Inc. and Clearmind Medicine; consults for Altimmune, Inc., Eli Lilly and Company, Sobrera Pharmaceuticals, Ribocure and Boehringer Ingelheim; and receives research support from Alkermes, Altimmune, and Eli Lilly and Company

Disclaimer:

This presentation discusses pemvidutide, an investigational product candidate that has not been approved by the FDA or any other regulatory authority. Its safety and efficacy have not been established. The statements about pemvidutide are based on current expectations and are subject to risks and uncertainties that could cause actual results to differ materially. For additional information regarding these risks and uncertainties, please refer to the Company's filings with the U.S. Securities and Exchange Commission, including the most recent Form 10-K and Form 10-Q. This study was sponsored by Altimmune, Inc.

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Alcohol Use Disorder (AUD) Causes Severe Clinical Complications with Substantial Gaps in Current Care

Epidemiological Burden



57.9M Engage in binge drinking monthly

28.1M U.S. adults affected by AUD

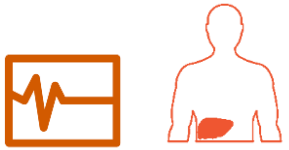
Healthcare Burden



~2M Adult hospitalizations annually

<2% Patients treated with FDA-approved AUD medications

Clinical Burden



~178,000 Deaths annually due to excessive alcohol use

51% Alcohol-associated liver disease

Leading indication for liver transplantation

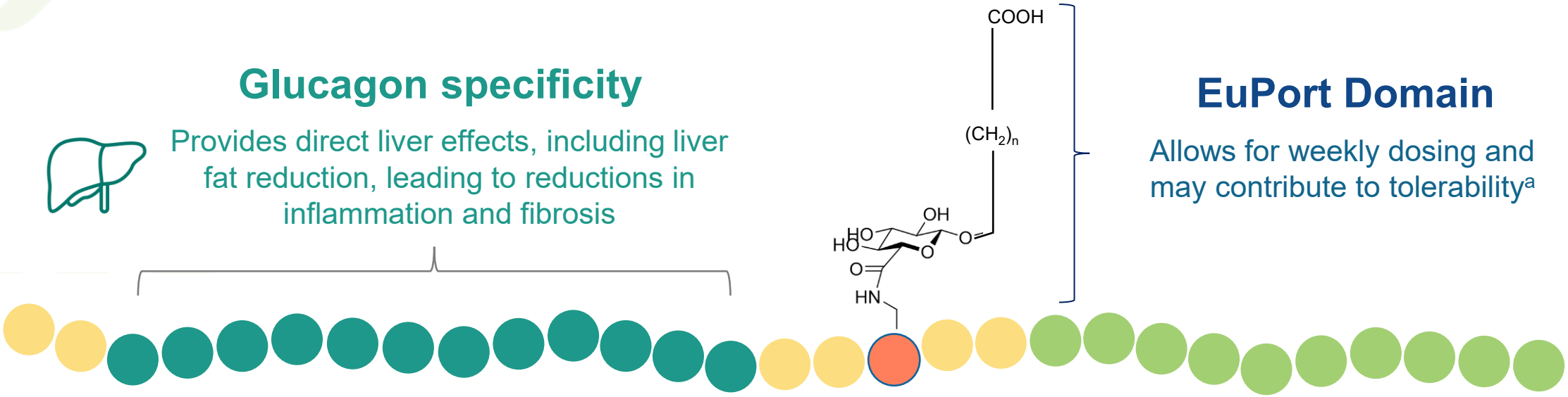
Hadland et al. *NEJM Evid*. 2026;5(8):EVIDra2500065; SAMHSA, National Survey on Drug Use and Health (NSDUH) 2024; CDC, Facts About U.S. Deaths from Excessive Alcohol Use; NIAAA, Alcohol Use Disorder: From Risk to Diagnosis to Recovery; Amonker et al. *Hepatol Commun*. 2023;7(5):e0133; Sacks et al. *Am J Prev Med*. 2015;49(5):e73–e9; Han et al. *JAMA Psychiatry* 2021;78(8):922-4. FDA: Food and Drug Administration

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Pemvidutide is a Balanced 1:1 Glucagon/GLP-1 Dual Receptor Agonist

Glucagon specificity

Provides direct liver effects, including liver fat reduction, leading to reductions in inflammation and fibrosis



EuPort Domain

Allows for weekly dosing and may contribute to tolerability[a]

GLP-1 specificity

Mediates metabolic effects such as appetite suppression, decreased alcohol cravings and consumption, and drives weight loss

[a] Nestor et al. *Sci Rep*. 2022 Apr 23;12(1):6666. ALD: Alcohol-associated liver disease; AUD: Alcohol use disorder; GLP-1: Glucagon-like peptide 1.

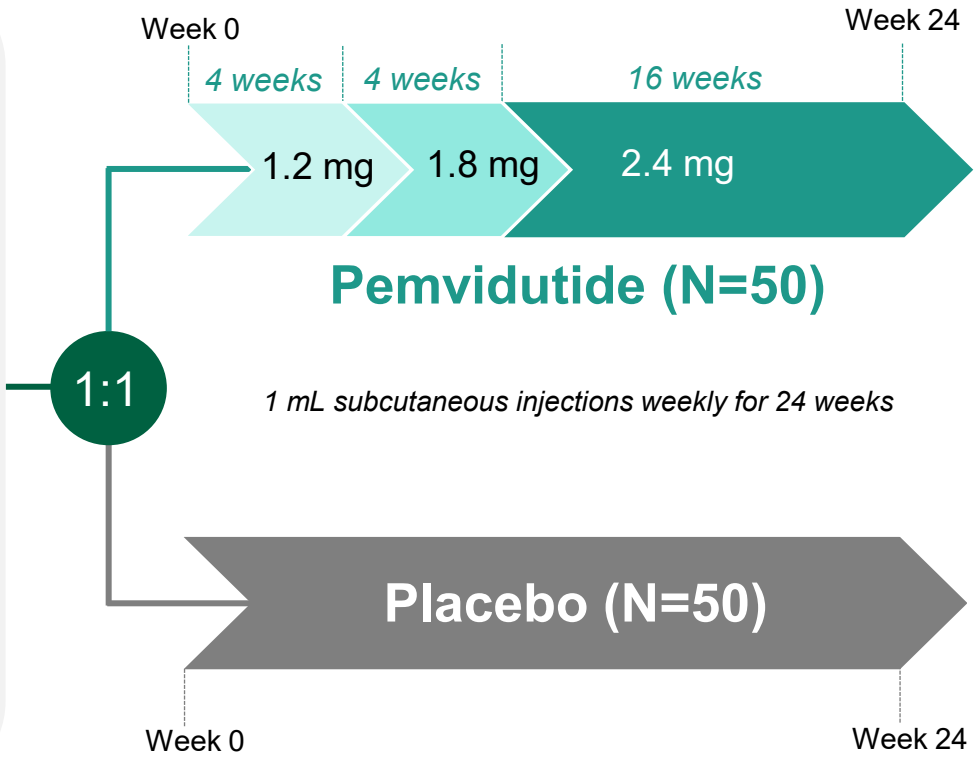
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RECLAIM Phase 2 AUD Trial Design

A Phase 2, multicenter, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of pemvidutide in AUD (NCT06987513)

Adult Patient Population

- Moderate-to-severe AUD by DSM-5
- Heavy drinking[a]
- AUD treatment-seeking (reduce/stop drinking)
- BMI ≥ 25.0 kg/m^2



All patients viewed a monthly computer-based behavioral video (Take Control[c]) on alcohol misuse

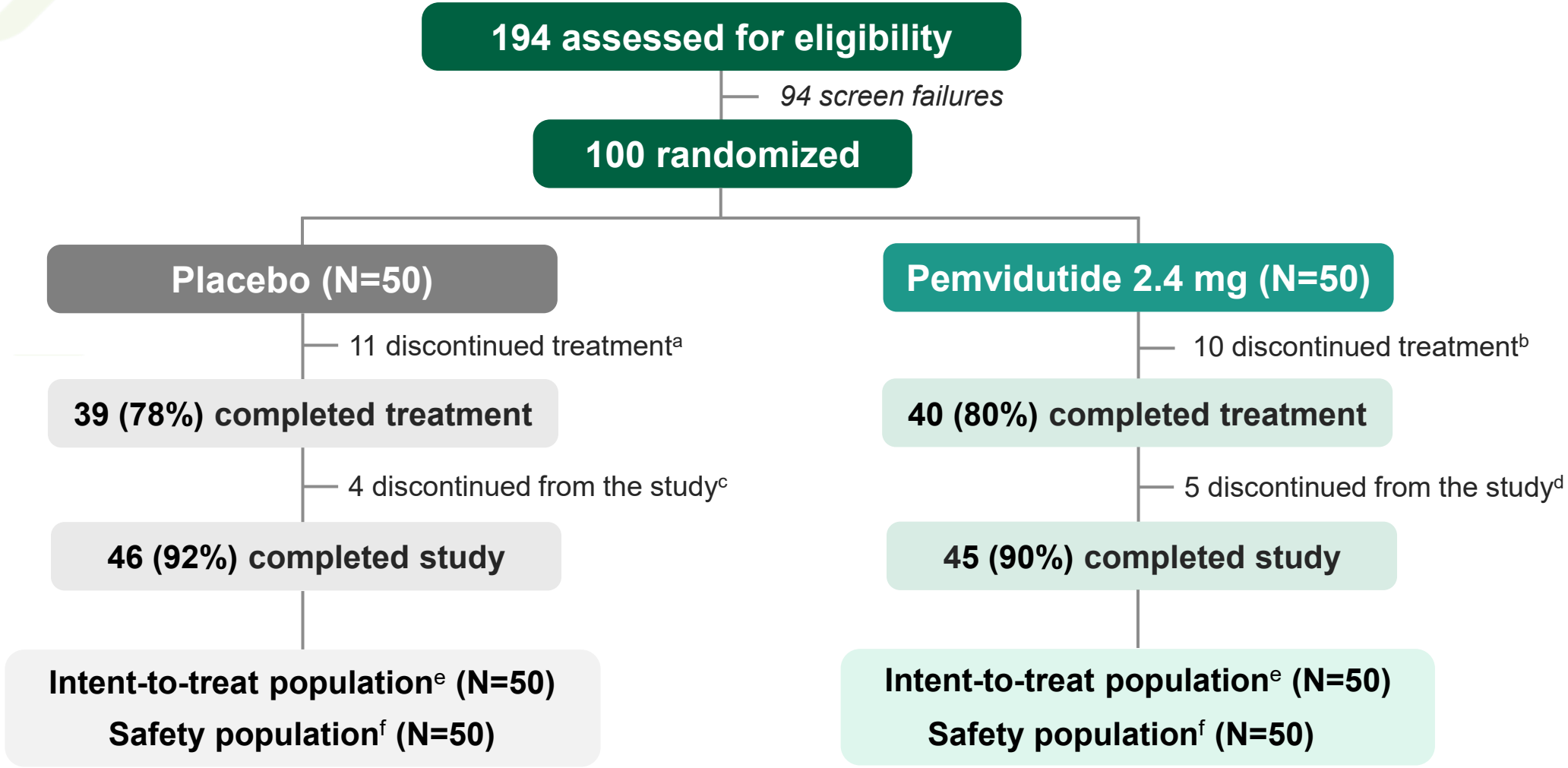
Week 24 Endpoints

- Primary endpoint
  - Heavy drinking days (HDDs)/week - TLFB[b]
- Secondary endpoints
  - ≥2-level reduction in WHO Risk Drinking levels (WHO-RDL) - TLFB[b]
  - Zero HDDs - TLFB
  - Percent days abstinent (PDA) - TLFB
  - Drinks per drinking day (DDD) - TLFB
  - Serum phosphatidylethanol (PEth)
  - Body weight
- Exploratory endpoints
  - Change in percentage of HDDs (PHDDs) - TLFB
  - Fibrosis-4 index (among patients with elevated baseline values)
- Safety endpoints

[a] 28 (men)/21(women) drinks/week with at least 3 heavy drinking days (HDDs)/week (≥5 drinks/day for men, ≥4 drinks/day for women) by TLFB over 28 days prior to screening. [b] TLFB, Timeline follow-back; Under pre-specified multiplicity testing strategy. [c] Devine et al. *Contemp Clin Trials.* 2016;50:178-85. AUD: Alcohol use disorder; BMI: Body mass index; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

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High Overall Retention (91%) with Similar Treatment Discontinuation Across Groups



[a] AE/SAE: n=0, Others: n=11. [b] AE/SAE: n=6, Others: n=4. [c] AE/SAE: n=0, Others: n=4. [d] AE/SAE: n=2, Others: n=3. [e] The intent-to-treat (ITT) population includes all subjects who were randomized, regardless of whether they received investigational product (IP) or completed post-baseline assessments. [f] The safety population includes all randomized subjects who received at least 1 dose of IP.
AE: adverse event; AUD: Alcohol use disorder; IP: Investigational product; SAE, Serious adverse event.

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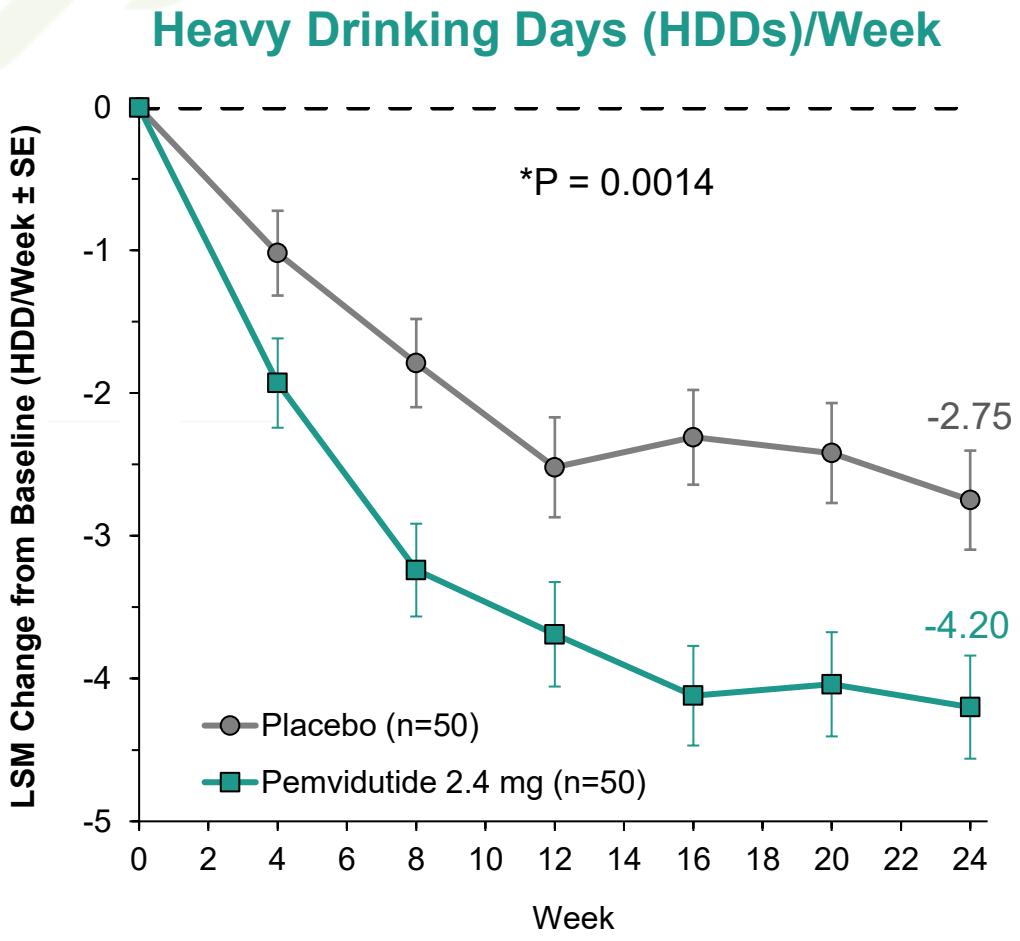
Demographic and Baseline Clinical Characteristics Similar Across Groups

Characteristic	Placebo (N=50)	Pemvidutide 2.4 mg (N=50)
Age, years (SD)	50.0 (10.0)	50.8 (11.9)
Female sex, n (%)	26 (52)	26 (52)
Body weight, kg (SD)	96.0 (21.4)	92.0 (19.1)
BMI, kg/m^2 (SD)	32.5 (6.6)	32.3 (5.8)
AUD by DSM-5, n (%)		
Moderate (4–5 symptoms)	12 (24)	13 (26)
Severe (>5 symptoms)	38 (76)	37 (74)
Heavy Drinking Days per week (SD)	5.6 (1.5)	5.9 (1.3)
WHO Risk Drinking Level, n (%)		
Moderate	2 (4)	1 (2)
High	15 (30)	15 (30)
Very high	33 (66)	34 (68)
Percent days abstinent (SD)	12.2 (15.2)	8.2 (13.4)
Drinks per drinking day (SD)	9.9 (6.7)	8.5 (5.2)
Total alcohol consumption, g/28 days (SD)	3310.2 (2166.2)	3047.8 (2049.5)
PEth, ng/mL (SD)	374.6 (307.9)	406.2 (356.9)
FIB-4 (SD)	1.1 (0.6)	1.1 (0.4)
FIB-4 ≥ 1.3[a], n (%)	15 (30)	10 (20)

[a] Suggestive of intermediate-to-high risk of significant fibrosis (cut-off value reported by Angulo et al. Gastroenterology 2013;145(4):782-9 e4). AUD: Alcohol use disorder; BMI, body mass index; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; FIB-4, Fibrosis-4 index; Peth: Phosphatidylethanol; SD: Standard deviation; WHO: World Health Organization.

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Pemvidutide Achieved Significantly Greater Reduction in Heavy Drinking Days/Week than Placebo (Primary Endpoint)



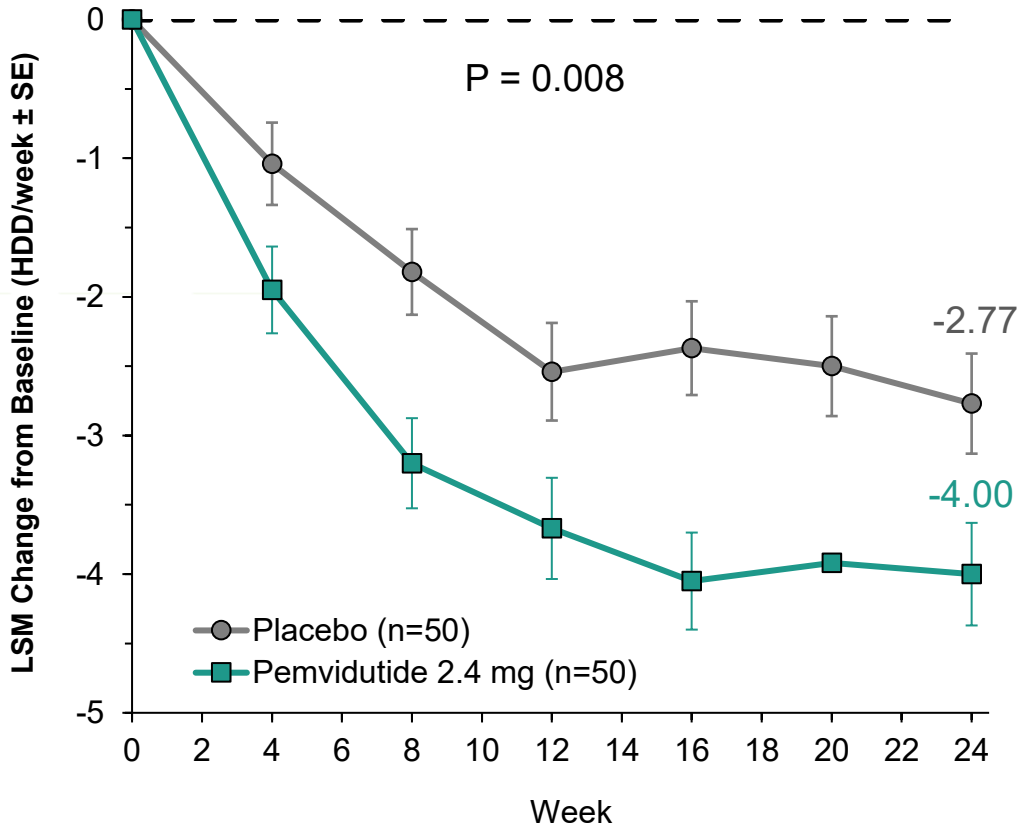
- **Pemvidutide met the trial's primary endpoint at week 24 (reduction in HDDs/week)**
  - Treatment difference: -1.45 HDDs/week [95% CI, -2.32 to -0.58]
- **Pemvidutide also achieved a greater reduction in percentage of HDDs than placebo at week 24**
  - Treatment difference: -20.69 percentage points [95% CI, -33.15 to -8.23]; p=0.0014

Change in Heavy Drinking Days (HDDs; primary outcome) and percentage of HDDs (PHDDs) per week from baseline, measured every 4 weeks using the Timeline Follow-back (TLFB) method. Data were analyzed using a mixed model for repeated measures (MMRM) analysis showing least-squares mean (LSM) change from baseline. *Multiplicity was addressed with a hierarchical fixed-sequence testing procedure for the primary endpoint followed by WHO-RDL. CI: Confidence interval; SE: Standard error.

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Pemvidutide Maintained Reduction in HDDs/Week (Primary Endpoint) in Sensitivity Analysis

Sensitivity Analysis[a] for Heavy Drinking Days (HDDs)/Week



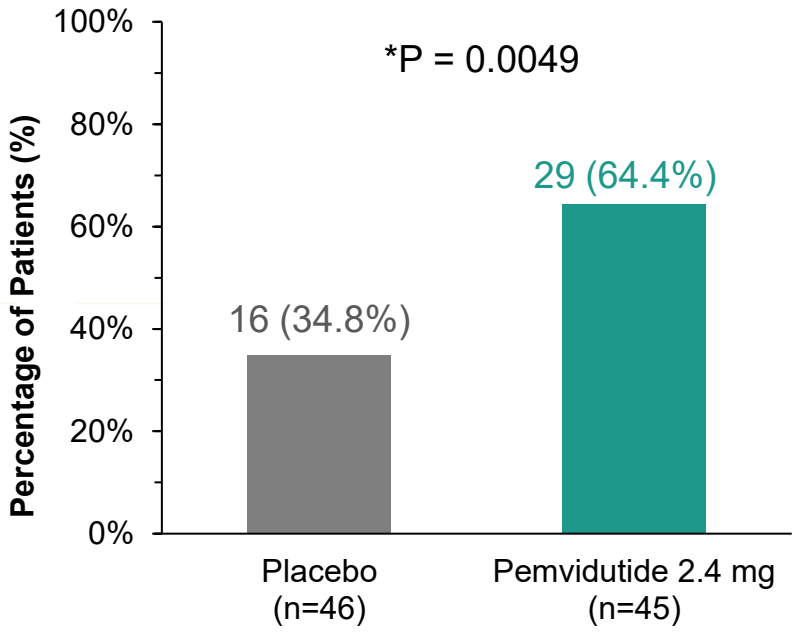
- **The treatment effect on the primary endpoint at week 24 (reduction in HDDs/week) remained consistent in the sensitivity analysis accounting for intercurrent events[a]**
  - Treatment difference: -1.24 HDDs/week [95% CI, -2.15 to -0.33]

[a] Sensitivity analysis for HDDs/week was assessed using an alternative handling of intercurrent events (ICEs). In this analysis, all TLFB observations that occurred following an ICE-1 (treatment discontinuation), ICE-2 (initiation of non-study AUD treatment), or ICE-4 (use of prohibited substances/medications that may affect alcohol consumption outcomes) were considered missing. ICE-3 (death) did not occur. Changes in HDDs/Week was measured every 4 weeks using the Timeline Follow-back (TLFB) method and analyzed using a mixed model for repeated measures (MMRM) analysis showing least-squares mean (LSM) change from baseline. CI: Confidence interval; LSM: Least-squares mean; SE: Standard error.

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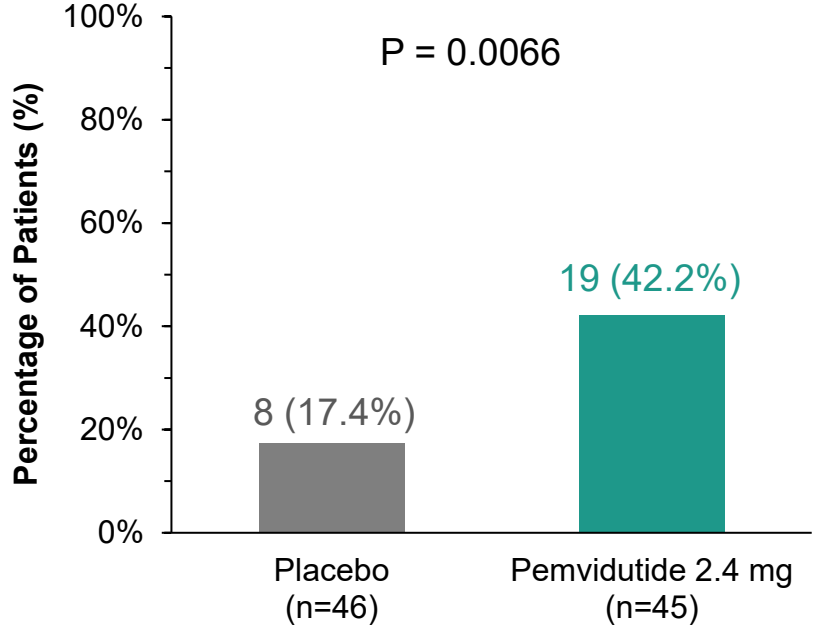
Pemvidutide Achieved Higher Rates of a ≥2-level WHO-RDL Reduction and Zero HDDs (FDA Registrational Endpoints)

≥2-level World Health Organization Risk Drinking Level (WHO-RDL)



Treatment difference at week 24: OR = 3.3 [95% CI, 1.4 to 7.7]

Zero Heavy Drinking Days



Treatment difference at week 24: OR = 3.8 [95% CI, 1.4 to 10.4]

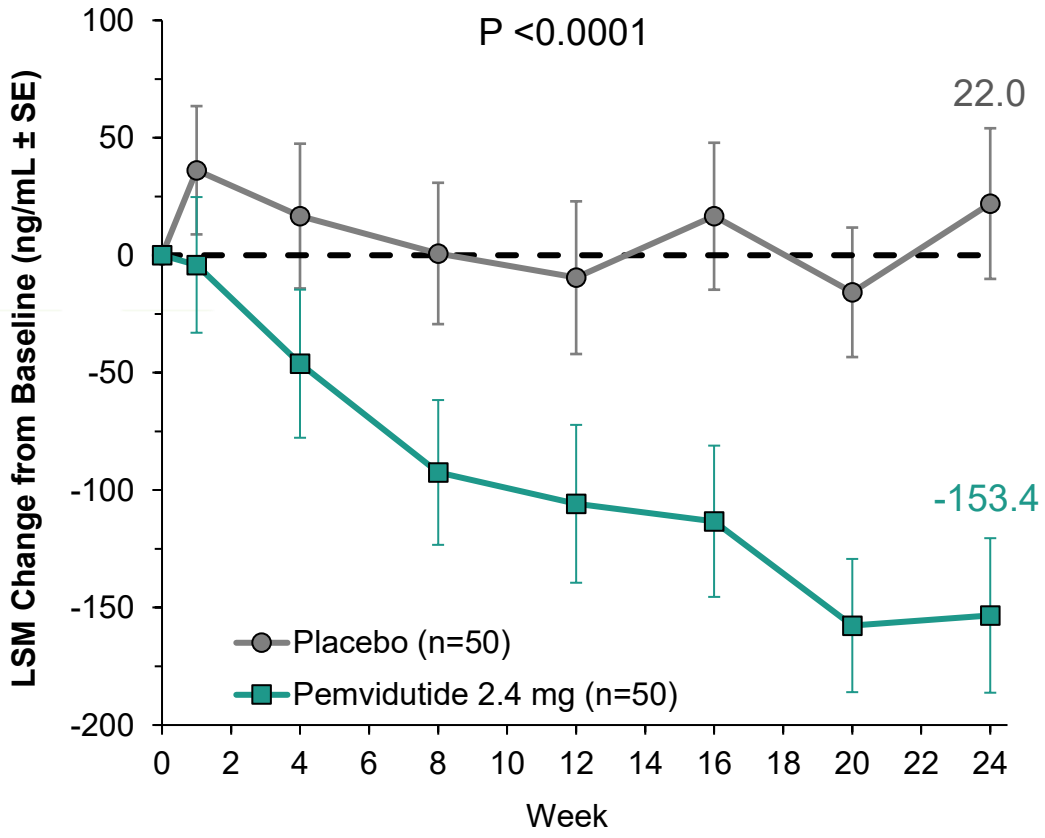
In the pemvidutide group, nearly 2/3 of patients achieved a ≥2-level WHO-RDL reduction (vs. ~1/3 on placebo), and over double the proportion achieved zero HDDs vs. placebo

WHO-RDL and zero HDDs were measured using the Timeline Follow-back (TLFB) method. Data were analyzed using the Cochran-Mantel-Haenszel (CMH) test. Denominator for the proportion is the number of subjects who have non-missing outcome data. *Multiplicity was addressed with a hierarchical fixed-sequence testing procedure for the primary endpoint followed by WHO-RDL. CI: Confidence interval; FDA: Food and Drug Administration; HDDs: Heavy drinking days; OR: Odds ratio.

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Pemvidutide Showed a Reduction in Serum PEth Levels
(Sensitive and Specific Biomarker of Alcohol Consumption)

Serum Phosphatidylethanol (PEth)



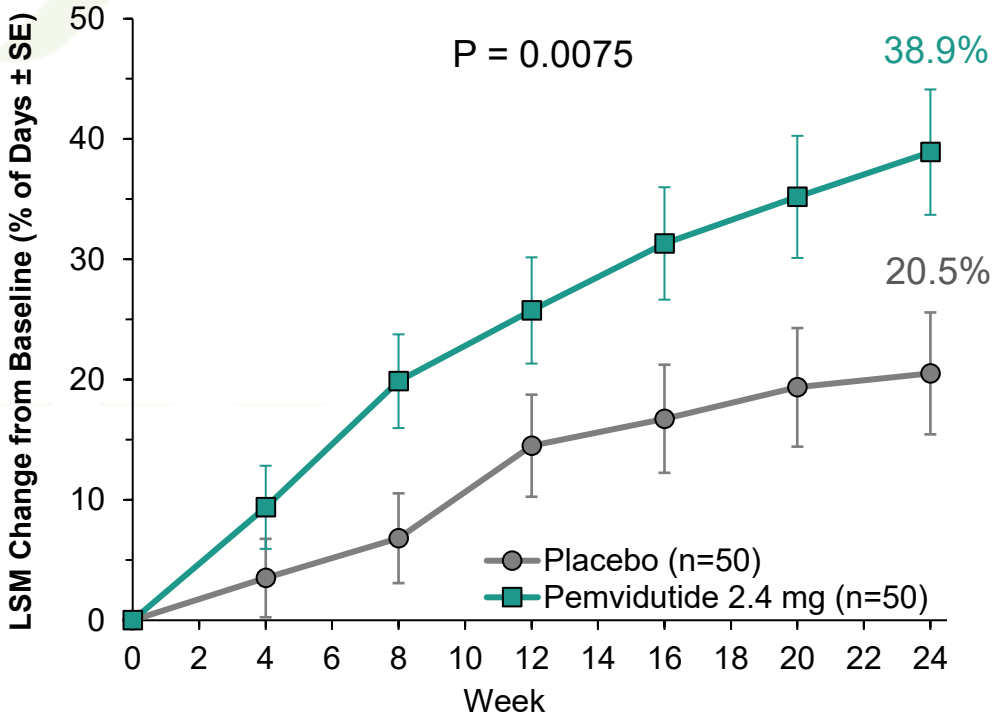
- **Self-reported drinking outcomes were corroborated by reductions in objective PEth concentrations in the pemvidutide group**
  - Treatment difference at week 24: -175.4 ng/mL [95% CI, -259.6 to -91.1]

Change in serum PEth concentration (ng/mL) from baseline was measured every 4 weeks (in addition to week 1) using a mixed model for repeated measures (MMRM) analysis showing least-squares mean (LSM) change from baseline. CI: Confidence interval; SE: Standard error.

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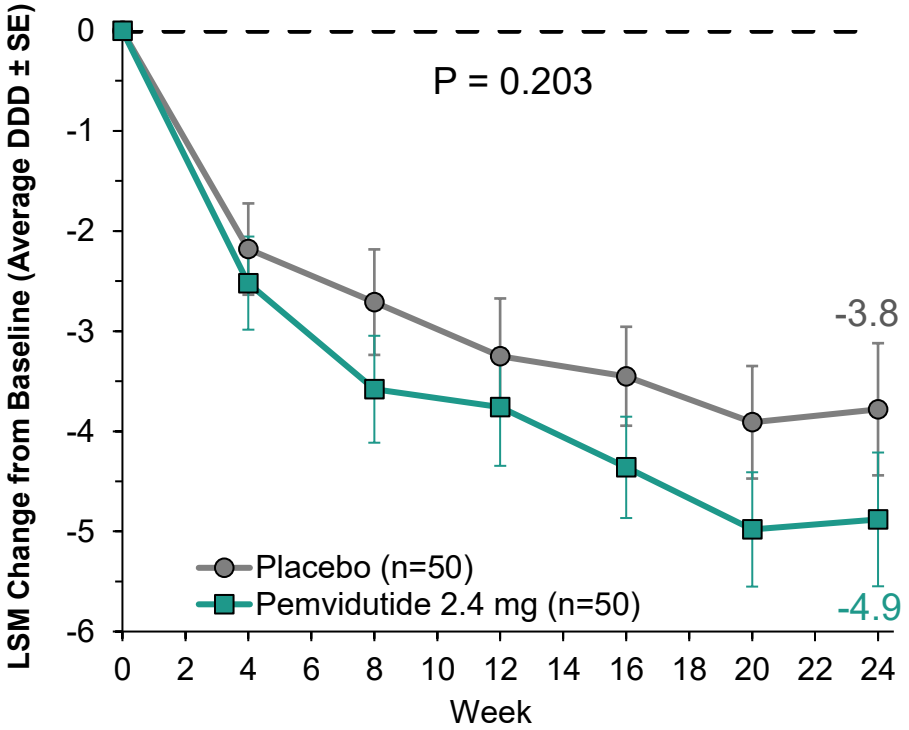
Pemvidutide Showed an Increase in Percent Days Abstinent

Percent Days Abstinent (PDA)



Treatment difference at week 24: 18.4% [95% CI, 5.0 to 31.8]

Drinks Per Drinking Day[a] (DDD)



Treatment difference at week 24: -1.1 [95% CI, -2.8 to 0.6]

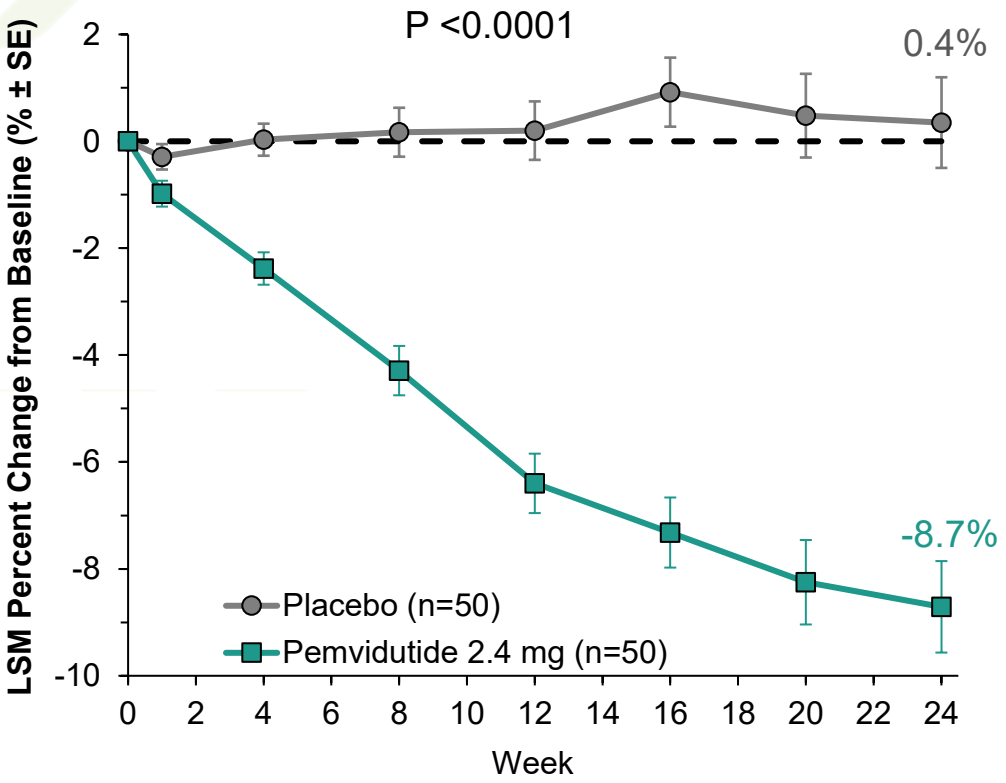
Pemvidutide nearly doubled the increase in percent of days with abstinence and numerically reduced drinks per drinking day vs. placebo at week 24

[a] Subjects who were completely abstinent were assigned with a 0 value. Changes in PDA and DDD from baseline were measured every 4 weeks using the Timeline Follow-back (TLFB) method and analyzed using a mixed model for repeated measures (MMRM) analysis showing least-squares mean (LSM) change from baseline. CI: Confidence interval; LSM: Least-squares mean; SE: Standard error.

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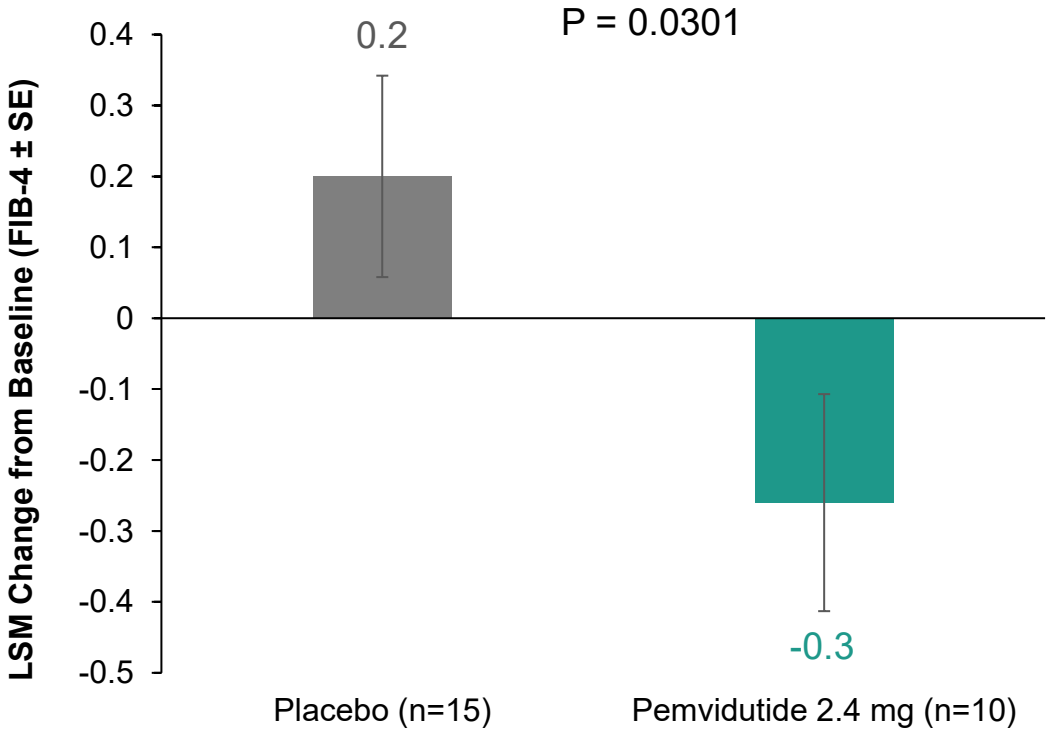
Pemvidutide Showed Progressive Decrease in Body Weight and Reduced FIB-4 Scores

Percent Change in Body Weight



Treatment difference at week 24: -9.1% (-11.4 to -6.7)

Change in FIB-4 Score At Week 24 Among Patients with Baseline FIB-4 ≥1.3[a] (n=25)



Treatment difference at week 24: -0.5 [95% CI, -0.9 to -0.1]

Treatment with pemvidutide led to reductions in body weight and FIB-4 score compared with placebo

[a]Suggestive of intermediate-to-high risk of significant fibrosis (cut-off value reported by Angulo et al. Gastroenterology 2013;145(4):782-9 e4). Changes in body weight and FIB-4 scores were analyzed using a mixed model for repeated measures (MMRM) analysis showing least-squares mean (LSM) change from baseline. CI: Confidence interval; FIB-4, Fibrosis-4 index; LSM: Least-squares mean; SE: Standard error.

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Adverse Events Were Predominantly Mild or Moderate

Event, n (%)	Placebo (N=50)	Pemvidutide 2.4 mg (N=50)
Serious adverse events	1 (2.0)[a]	2 (4.0)[b]
Serious adverse events related to trial drug	0 (0.0)	1 (2.0)
Severe adverse events	3 (6.0)	6 (12.0)
Severe adverse events related to trial drug	0 (0.0)	3 (6.0)[c]
Adverse events of special interest related to trial drug	0 (0.0)	0 (0.0)
Study drug-related adverse events leading to treatment discontinuation	0 (0.0)	5 (10.0)[d]
Gastrointestinal disorders	17 (34.0)	31 (62.0)
Nausea	12 (24.0)	22 (44.0)
Constipation	3 (6.0)	13 (26.0)
Diarrhea	5 (10.0)	10 (20.0)
Vomiting	3 (6.0)	9 (18.0)
Upper abdominal pain	3 (6.0)	4 (8.0)
Dry mouth	0 (0.0)	5 (10.0)
Gastroesophageal reflux disease	2 (4.0)	3 (6.0)
Dyspepsia	0 (0.0)	4 (8.0)

Overall, pemvidutide was generally well-tolerated; mild-to-moderate gastrointestinal events were the most frequent adverse events

[a] Spinal stenosis; [b] 1 subject with hyponatremia possibly related to trial drug, 1 subject with breast cancer; [c] 1 subject with hyponatremia (same as serious AE), 1 subject with migraine, 1 subject with fatigue, night sweats, nausea and gastroesophageal reflux disease; [d] 2 vomiting, 1 constipation, 1 fatigue, 1 exacerbation of hemorrhoids.

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Summary

- The RECLAIM trial met its primary endpoint, with pemvidutide demonstrating a significantly greater reduction in HDDs/week than placebo among patients with moderate-to-severe AUD
- Patients treated with pemvidutide showed consistent improvements in other measures of self-reported alcohol consumption, body weight, and hepatic fibrosis risk (FIB-4)
- Pemvidutide-associated declines in HDDs/week were corroborated by objective measures of PEth concentration
- Given the well-documented hepatic burden of chronic alcohol use, the previously demonstrated glucagon-mediated hepatic lipid clearance by pemvidutide may offer an additional therapeutic benefit over GLP-1 receptor agonism alone
- These findings in a multi-site, placebo-controlled randomized trial may represent an important step forward in developing new potential treatments for AUD

Future Directions

- The significant effects by pemvidutide on both alcohol consumption and the potential for liver damage, together with its generally favorable safety profile, support further evaluation of pemvidutide in a Phase 3 trial for AUD

AUD: Alcohol use disorder; GLP-1: Glucagon-like peptide; HDDs: Heavy drinking days; PEth: Phosphatidylethanol

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