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ENHANCING HEALTH

LPCN 1148

A Novel Approach for the Management of Liver Cirrhosis

Phase 2 Study Week 24 Topline Results

July 27, 2023

Enabling Effective Oral Drug Delivery

Forward-Looking Statements

This presentation contains “forward-looking statements” that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and include statements that are not historical facts regarding our product development efforts, our product candidates and related clinical trials, our strategic plans for developing products to treat CNS disorders, our ability to monetize non-core product candidates, including through entering into partnering arrangements, the application of our proprietary platform in developing new treatments for CNS disorders, the timing and completion of regulatory reviews, outcomes of clinical trials of our product candidates, the potential uses and benefits of our product candidates, the potential uses and benefits of LPCN 1148, the timing of and our ability to make any NDA filing relating to LPCN 1148, . Investors are cautioned that all such forward-looking statements involve risks and uncertainties, including, without limitation, the risks that we may not be successful in developing product candidates to treat CNS disorders, we may not be able to enter into partnerships or other strategic relationships to monetize our non-core assets, the FDA will not approve any of our products, risks related to our products, expected product benefits not being realized, clinical and regulatory expectations and plans not being realized, new regulatory developments and requirements, risks related to the FDA approval process including the receipt of regulatory approvals and our ability to utilize a streamlined approval pathway for LPCN 1154, the results and timing of clinical trials, patient acceptance of Lipocine's products, the manufacturing and commercialization of Lipocine's products, and other risks detailed in Lipocine's filings with the SEC, including, without limitation, its Form 10-K and other reports on Forms 8-K and 10-Q, all of which can be obtained on the SEC website at www.sec.gov. Lipocine assumes no obligation to update or revise publicly any forward-looking statements contained in this release, except as required by law.

Liver Cirrhosis

Cirrhosis is scarring of the liver, when scar tissue replaces healthy tissue, causing damage and reducing liver function

Globally, 10.6M cases of decomp. cirrhosis 2017[1*]

Globally, 1.32M deaths in 2017[1]

In the US, 62,493 deaths in 2017[1]

Common Causes[2]

- Alcoholic Liver Disease
- Nonalcoholic Fatty Liver Disease (NAFLD)
- Chronic Hepatitis B, C
- Primary Biliary Cholangitis
- Primary Sclerosing Cholangitis

In 2021 there were 9,236 liver transplants in US[3]

62% of the liver transplant (LT) waitlist are males[4]

1. Lancet Gastroenterol Hepatol. 2020 Mar; 5(3): 245–266.
2. https://www.niddk.nih.gov/health-information/liver-disease/cirrhosis/symptoms-causes
3. United Network for Organ Sharing (UNOS)
4.. Sarkar et al. J Hepatol. 2015
* Collectively referred as cirrhosis and other chronic liver diseases

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Cirrhosis: Complications and Recent Trends

Complications

- **Decompensation** events - hepatic encephalopathy, varices, ascites, etc.
- Compromised **liver** function, immunity, and protein synthesis
- **Muscle** & bone disorders including sarcopenia
- Cachexia, malnutrition, and weight loss
- Symptoms of hypogonadism
- Increased inflammation
- Portal hypertension

Recent Trends

- Occurrence of cirrhosis and related deaths are on the rise
- In the US between 1999 and 2019, greater than three-fold increase in deaths from alcoholic cirrhosis was observed[1]
- Hepatitis C virus (HCV) infection remains the leading cause of global deaths related to cirrhosis, followed by alcohol-associated liver disease [2]
- In the Americas, the dominant cause of cirrhosis is shifting from viral hepatitis to NAFLD and alcohol-associated liver disease[2]
- The global burden of cirrhosis associated with non-alcoholic fatty liver disease (NAFLD) has increased substantially in the past decade[2]
- There are more people who need a liver than the supply available[3]

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1. Termeie et al, The American Journal of Medicine, May 2022.
2. Huang et. al, Natures reviews gastroenterology and hepatology, March 2023
3. American Liver Foundation.

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Product Candidate Attributes

Oral androgen receptor agonist

Dosage form comprising testosterone dodecanoate, a unique prodrug of an endogenous hormone

Targeted Mechanism of Action

Anabolic[1]

Increase muscle mass and strength[2]; Reduce fat mass[3]; Increase bone density[4]; Inhibit myostatin[5]; Improve appetite and nutritional status*

Ammonia Lowering

Via Improved liver health[6] and muscle disorders[7]; Antibacterial[8]

Androgenic

Induce hematopoiesis[9]; Improve endocrine/sexual dysfunction[10]

1. Gentile MA et al., J Mol Endocrine, 2010
2. Sinclair et al., J Gastroenterol Hepatol 2016
3. Shalender Bhasin, Clin Infect Dis. 2003;37 Suppl 2:S142-9
4. Snyder et al. JAMA Intern Med. 2017 Apr 1;177(4):471-479
5. Dasarathy and Merli, J Hepatol. 2016
6. SS Fiati Kenston et al., (2018) J. of Gastroenterology and Hepatology
7. Simone Di Cola et al, J Clin Med. 2022 Feb; 11(3): 611.
8. Jin et al, J Microbiol Biotechnol. (2021) Jan 28; 31(1): 130–136
9. Basaria, S., Dobs, A.S. (2003). Androgens and the Hematopoietic System. In: Bagatell, C.J.,Bremner, W.J. (eds) Androgens in Health and Disease.
10. Rizk et al., Curr Opin Urol 2017

*individual's health condition as it is influenced by the intake and utilization of nutrients

Sarcopenia in Cirrhosis Patients: Disease Overview

A prevalent and serious comorbidity

- Sarcopenia is a condition characterized by severe muscle depletion and observed in ~60% of patients with cirrhosis[1-2, 4]
- Sarcopenia is a predictor for increased morbidity and mortality in cirrhosis[1]
  - 3-fold higher mortality rate compared to no sarcopenia[1]
- Primary pathophysiology associated with sarcopenia and decompensated cirrhosis include a catabolic state, progressive immobility, imbalance between muscle breakdown and formation, and hormonal changes[3]
- Sarcopenia in cirrhosis correlates with decompensation events, particularly hepatic encephalopathy (HE)[3]
  - Presence of sarcopenia increases the risk of overt HE ~2 fold [3]
- Presence of both sarcopenia and HE further increases risk of mortality[5]

1. Kim. PLoS One. 2017 2. Tandon. Clin Gastroenterol Hepatol. 2016 3. Tandon. J Hepatol. 2021
4. Jindal Clin Mol Hepatol 2019 5. Bhanji et al. Hepatology International 2018.

Current Standard of Care And Key Unmet Needs

Options are limited, resulting in significant enduring medical need

Current Standard of Care

Decompensated Liver Cirrhosis

- Management of Etiology
  - Alcohol cessation, antiviral treatment
- Management of Decompensation
  - Treat complications
- Liver Transplantation
  - Only curative therapy for decompensated cirrhosis

Sarcopenia

- Nutrition and Exercise

Key Unmet Needs

Significant Mortality

Limited Therapeutic Options

Liver Transplant Limitations

Decompensated cirrhosis patients with sarcopenia exhibit significantly shorter overall survival

No therapies are specifically approved for sarcopenia or decompensated cirrhosis

The only curative therapy for decompensated cirrhosis is liver transplant

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Hepatic Encephalopathy in Cirrhosis Patients

Up to 50% of cirrhosis patients will experience an overt HE episode in their lifetime[1]

- Overt HE is a debilitating, episodic, neurological disorder with a high recurrence rate
- HE is a major complication of advanced liver disease. Patients exhibit global neurological, psychiatric, and musculoskeletal deficits
- HE has a complex pathophysiology that includes impairment of ammonia clearance and increased inflammatory cytokines
- HE recurrence is common, despite use of standard-of-care therapies
- Complications of overt HE include a need for transplantation, progression to coma, and mortality[2]
- 1-year survival for persons with HE is ~50%[3]

1 Leise. Mayo Clin Proc. 2014. 2. Bajaj. Clin Gastroenterol Hepatol. 2017 3. Tapper Ailment Pharmacol Ther 2020

Current Standard of Care And Key Unmet Needs in HE

Options are limited, resulting in significant enduring medical need

Current Standard of Care

Overt HE[1]

- First Line: Lactulose or Lactitol
- Refractory Patients: IV or Oral Amino Acids
- Alternative/Add On: Antibiotics

Prevention of Overt HE Recurrence[1]

- First Line: Lactulose or Lactitol
- Add On to 1st Line: Rifaxamin
- Transplantation

Key Unmet Needs

Significant Mortality

High Recurrence Rate

Low Tolerability

Overt HE patients have significant near-term morbidity and mortality[2]

Lactulose/lactitol and rifaximin are used in the secondary prevention of overt HE, however many patients have recurrent episodes on these therapies[3]

Adherence to lactulose / lactitol is thought to be hindered by its tolerability profile, which can include nausea, vomiting, and gastrointestinal adverse events [4,5]

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1. Vilstrup. Hepatology. 2014 2.Bajaj. Clin Gastroenterol Hepatol. 2017. 3. Hudson. Eur J Gastroenterol Hepatol. 2019
4. Lactulose Package Insert, 5. Lactitol Package Insert

LPCN 1148: Proof of Concept Study

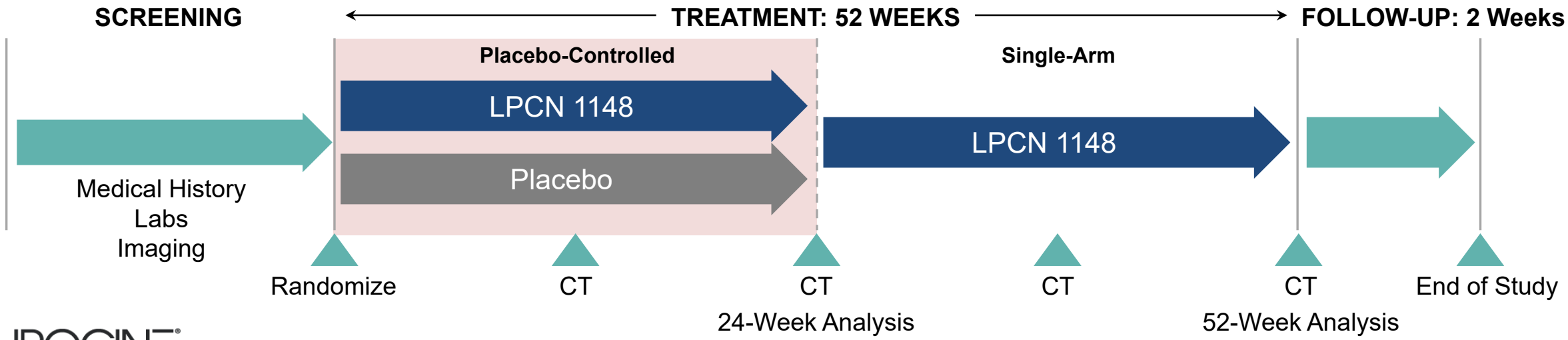
Phase 2, multicenter, double-blinded, placebo-controlled study

Study Design:

- Male subjects with liver cirrhosis and sarcopenia on the liver transplant waitlist
- Two-arm (1:1 randomization, N=29)
  - Oral LPCN 1148, T dodecanoate, vs. Placebo
  - Standard of care treatments/therapies allowed
- 24-week placebo-controlled
  - Followed by 28-week open-label extension (OLE)
  - All subjects receive LPCN 1148 during OLE

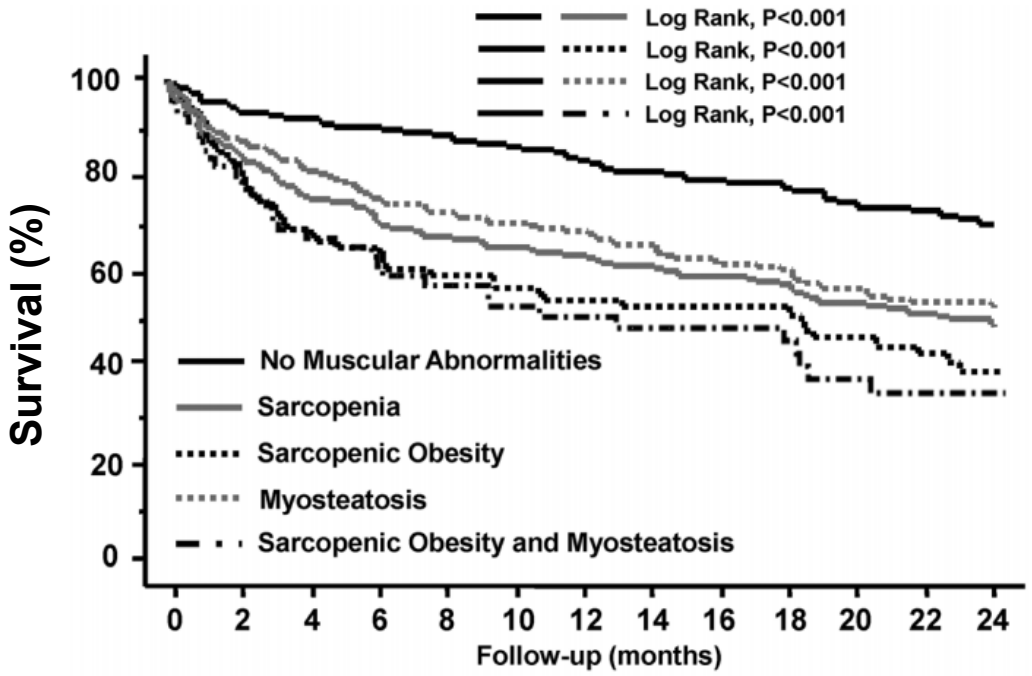
Endpoints:

- Primary: Change in Skeletal Muscle Index (L3 region, L3-SMI) at Week 24 in LPCN 1148 treated participants compared to placebo
- Other Endpoints:
  - Major decompensation events including HE, Patient Reported Outcomes (PROs), Anemia, Functional tests, Muscle quality (myosteatosis)

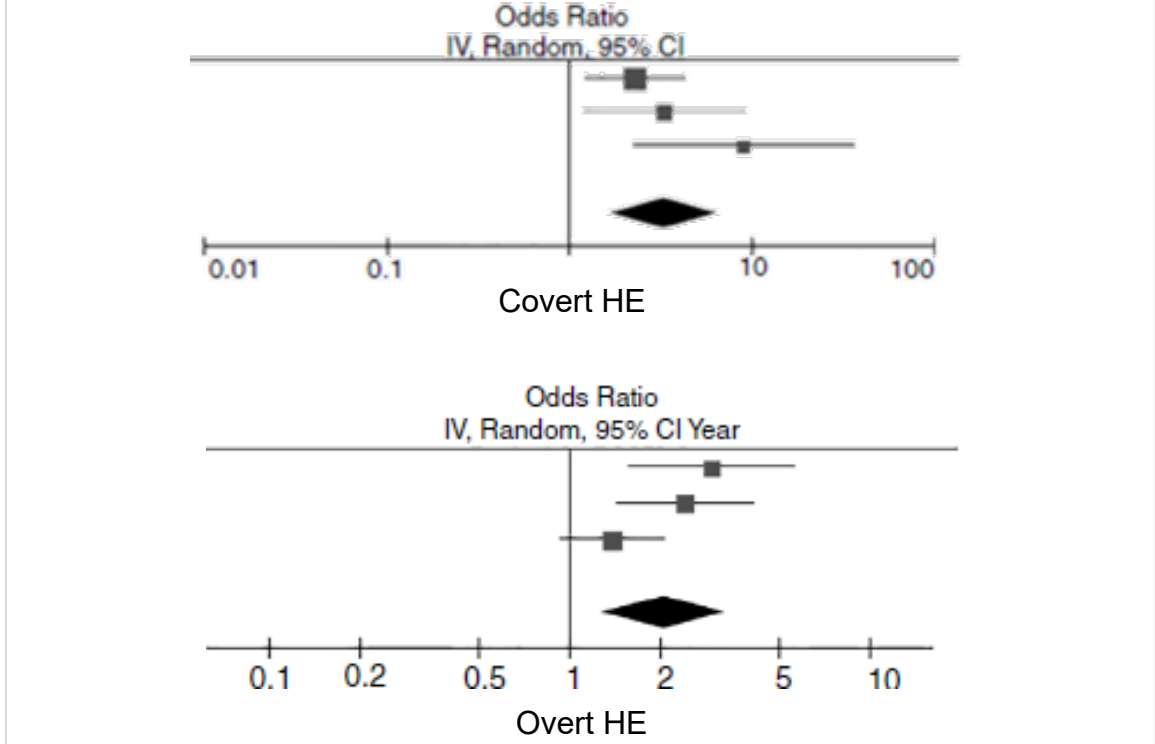


Presence of Sarcopenia is Linked with Worse Clinical Outcomes

Higher rates of death and hepatic encephalopathy



Low muscle mass (sarcopenia) and quality (myosteatosis) are associated with worse overall survival [1]



Sarcopenia and myosteatosis are associated with increased risk of hepatic encephalopathy [2, 3]

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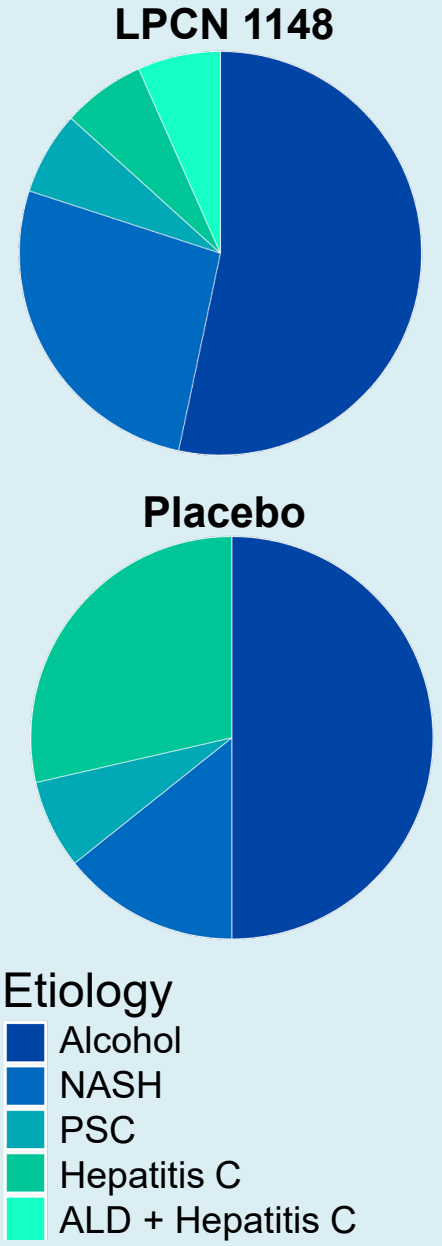
1. Montano-Loza, J Cach, Sarco, and Musc, 2016. 2. Wijarnpreecha. Ann Hep, 2020. 3. Bhanji, Hep Int, 2018.

Baseline Characteristics

Generally well-balanced between treatment arms

	LPCN 1148 (N=15)	Placebo (N=14)
Age (years)	58.3 ± 7.5	58.8 ± 9.5
BMI (kg/m^2)	29.2 ± 5.3	29.0 ± 8.6
L3-SMI (cm^2/m^2)	47.8 ±7.0	44.8 ± 8.5
MELD Score	15.9 ± 3.7	18.1 ± 4.6
Medical History		
≥ 1 Decompensation Event#	14 (93%)	14 (100%)
≥ 2 Decompensation Event	13 (87%)	12 (86%)
Hepatic Encephalopathy (HE)	11 (73%)	11 (79%)
Ascites	11 (73%)	10 (71%)
Esophageal Varices	8 (53%)	8 (57%)
Medical Therapy for HE*	12 (80%)	11 (79%)



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Safety set
Decompensation events include esophageal varices, ascites, hepatic encephalopathy, portal hypertension, and spontaneous bacterial peritonitis
*Medical therapy for HE includes lactulose and/or rifaximin. MELD: Model for End-Stage Liver Disease

Analysis Datasets and Subject Disposition

Analysis Datasets	LPCN 1148 (N=15)	Placebo (N=14)
Safety set*	15	14
Modified Intent to Treat (mITT)**	15	10
No post-baseline CT scan	0	3
Low compliance	0	1

Subject Disposition	LPCN 1148 (N=15)	Placebo (N=14)
Completed Week 24	15	10
Withdrawal of informed consent post liver transplant	0	2
Death	0	1
Hospitalized	0	1

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*Randomized and received study drug
**Subjects were eligible for mITT with at least one evaluable post-baseline CT

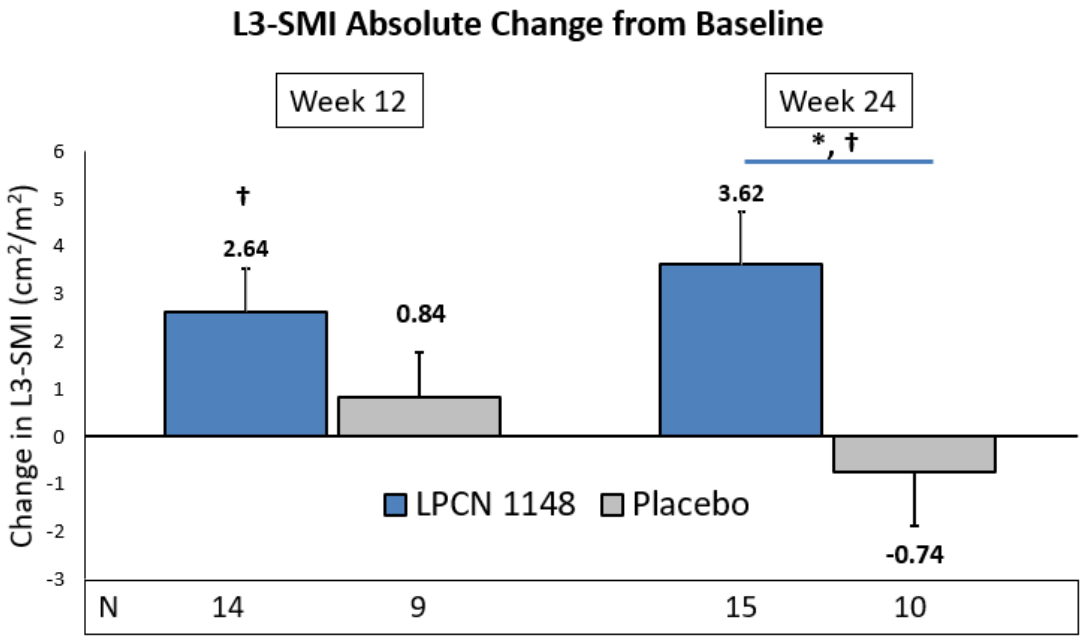
Primary Endpoint Met

LPCN 1148 therapy resulted in a significant increase in L3-SMI at Week 24

L3-SMI Change from Baseline

Timepoint	LPCN 1148 **(N=15)**	Placebo **(N=10)**	P-value	
			1148 CFB	1148 vs. Placebo
Baseline (cm^2/m^2)	47.8 (1.8)	45.8 (2.3)	N/A	NS
Week 24 CFB (cm^2/m^2)	3.62 (0.93)	- 0.74 (1.14)	<0.001	0.007

LS mean (SE). CFB – Change from baseline



LS mean (SE), †P<0.05 for change from baseline; * P=0.007 vs. placebo

LPCN 1148 Therapy Resulted in Significantly Fewer HE > Grade 1 Events

Positive clinical outcome achieved

Parameter	LPCN 1148 (N=15)	Placebo (N=14)	Total (N=29)
Total decompensation events	7	10	17
Total decompensation events > Grade 1	6	10	16
Hepatic Encephalopathy	3	6	9
HE > Grade 1*	2	6	8
Recurrence of HE > Grade 1*	1	6	7
Time to first recurrence of HE > Grade 1 (days)	115	39**	54**

*P<0.05 vs. placebo. **Mean value

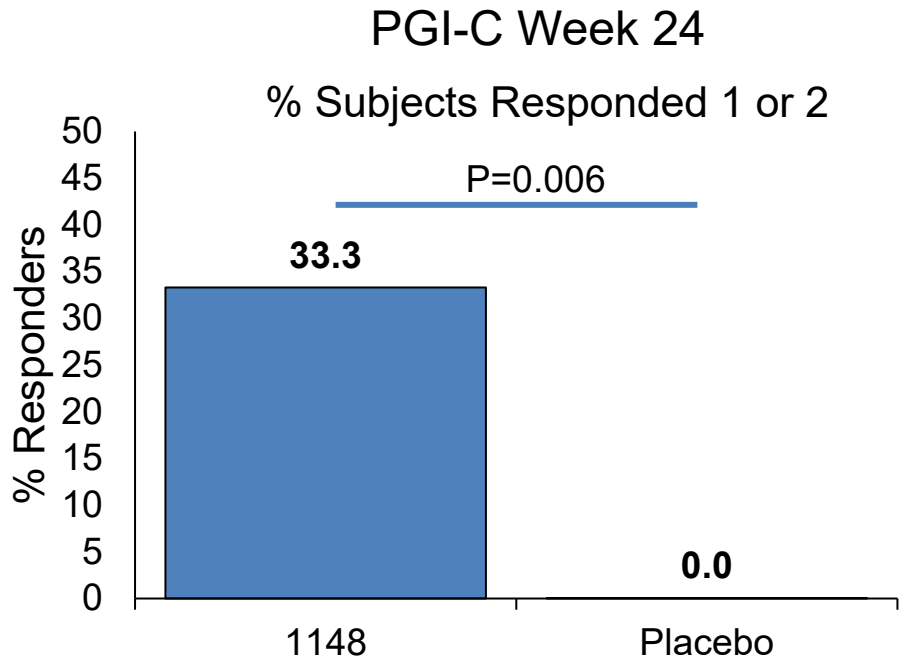
LPCN 1148-treated Participants Reported Significant Symptom Improvement

As assessed by PGI-C

Patient Global Impression of Change (PGI-C) Scale

Please choose the response below that best describes the overall change in your symptoms since you started using the study treatment.

1) Very much better
2) Moderately better
3) A little better
4) No change
5) A little worse
6) Moderately worse
7) Very much worse



- Significantly more 1148-treated subjects reported feeling ‘very much’ or ‘moderately’ better
  - No 1148-treated subjects reported symptom worsening (>4) at Week 24
- Mean PGI-C score was significantly lower with 1148-treatment at Week 24
- Significant symptom improvement was noted as early as Week 4

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Safety set, LOCF. n=15 for LPCN 1148, n=13 for placebo. PGI-C: Patient Global Impression of Change Scale

Observed Hematologic Benefits

LPCN 1148 therapy resulted in significant increase in hemoglobin

Hemoglobin **Timepoint**	**LPCN 1148 (N=15)**	**Placebo (N=14)**	P-value	
			Change from Baseline	Vs. Placebo
Baseline (g/dL)	11.39 (0.75)	13.04 (0.8)	N/A	NS
Week 24 CFB (g/dL)	1.20 (0.33)	-0.05 (0.35)	0.001	0.02

LS Mean (SE)

Anemia Status	**LPCN 1148 (N=15)**	**Placebo (N=14)**
Anemic at baseline	11 (73%)	7 (50%)
Anemic at W24	7 (47%)	7 (54%)
Resolution	4 (36%)	1 (14%)
New onset	0 (0%)	1 (14%)

More subjects had resolution of anemia* at Week 24

*Anemia defined as hemoglobin < 13g/dL. Safety set, LOCF One placebo subject had no post-baseline data (liver transplant)

LPCN 1148 Safety

Overall LPCN 1148 was well tolerated

Parameter	LPCN 1148 (N=15)		Placebo (N=14)	
	#	n	#	n
Total AE events	33	8	36	10
Serious AE events	15	5	16	5
Severe AE events	6	4	10	4
Total Hospital Days	54	5	117	5

- Administration of LPCN 1148 was well tolerated in this end-stage population, with rates and severities of adverse events (AEs) similar to those within the placebo group
- Fewer days in the hospital with 1148 therapy
- No cases of drug-induced liver injury

Study Conclusions

Positive Week 24 results support benefits of 1148 for men with cirrhosis and sarcopenia

- LPCN 1148 met the primary endpoint - resulted in significantly increased skeletal muscle index
  - Superior to placebo at Week 24
  - Significant improvement from baseline as early as Week 12
- Fewer decompensation events with 1148 treatment
  - LPCN 1148 therapy resulted in significantly fewer HE > Grade 1 Events
- LPCN 1148-treated participants reported significant symptom improvement
- LPCN 1148 treatment improved anemia status and significantly increased hemoglobin
- Trends towards improvements across numerous other domains
- LPCN 1148 was well-tolerated, with AE rates and severity similar to that of placebo

LPCN 1148: Target Product Differentiation

- Novel multimodal MOA
  - Effects not limited to GI tract
- Potential to improve sarcopenia and reduce recurrence of HE
  - Improved efficacy in conjunction with background HE therapies
- Attractive benefit to risk profile
  - Endogenous hormone with favorable safety and tolerability profile
  - Improved quality of life
  - Address comorbidities

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