

# LPCN 1148

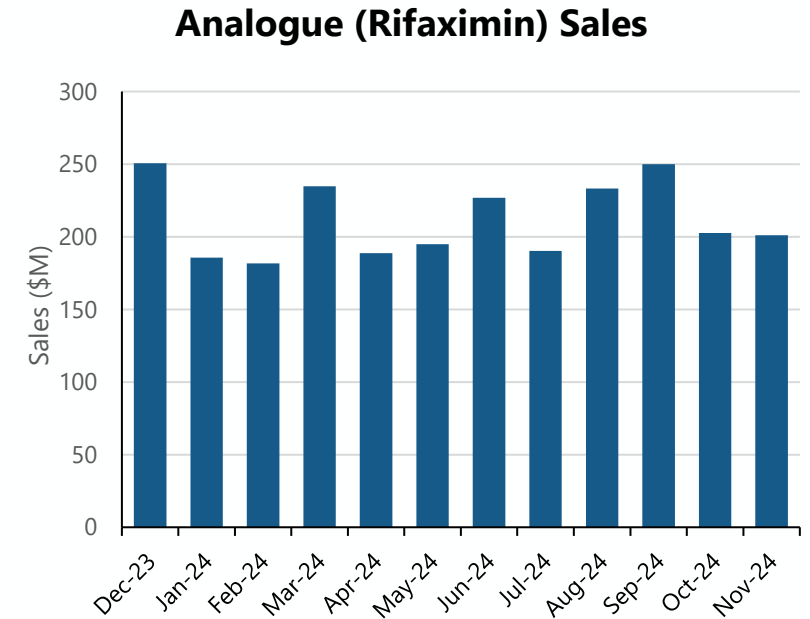
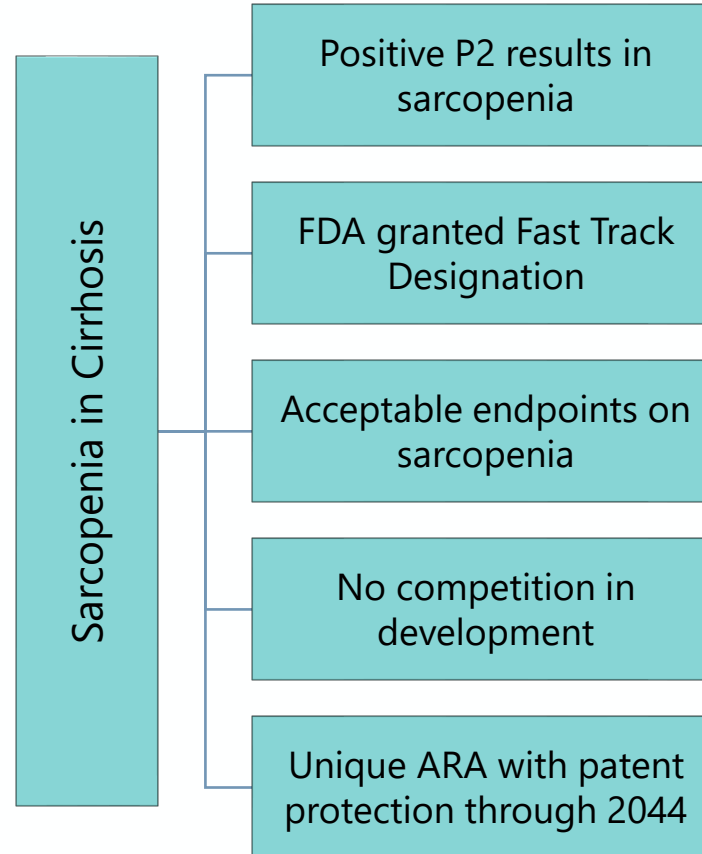
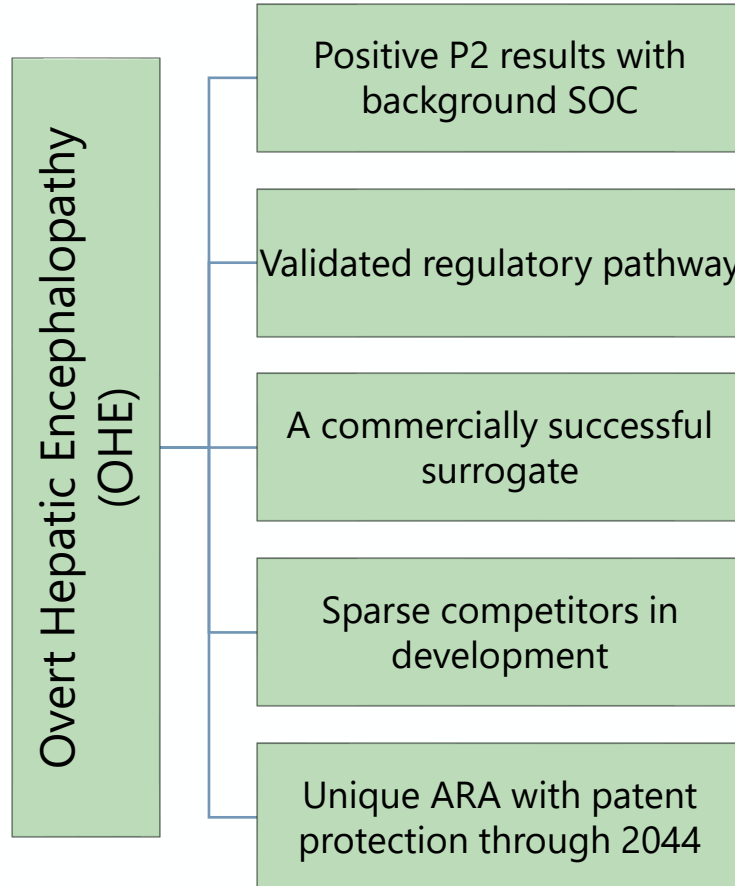
## Management of Liver Cirrhosis

- Overt Hepatic Encephalopathy (OHE)
- Sarcopenia in Decompensated Cirrhosis (Fast Track Designation)



# LPCN 1148 - Unique Opportunity Addressing Two Distinct Liver Disease Markets

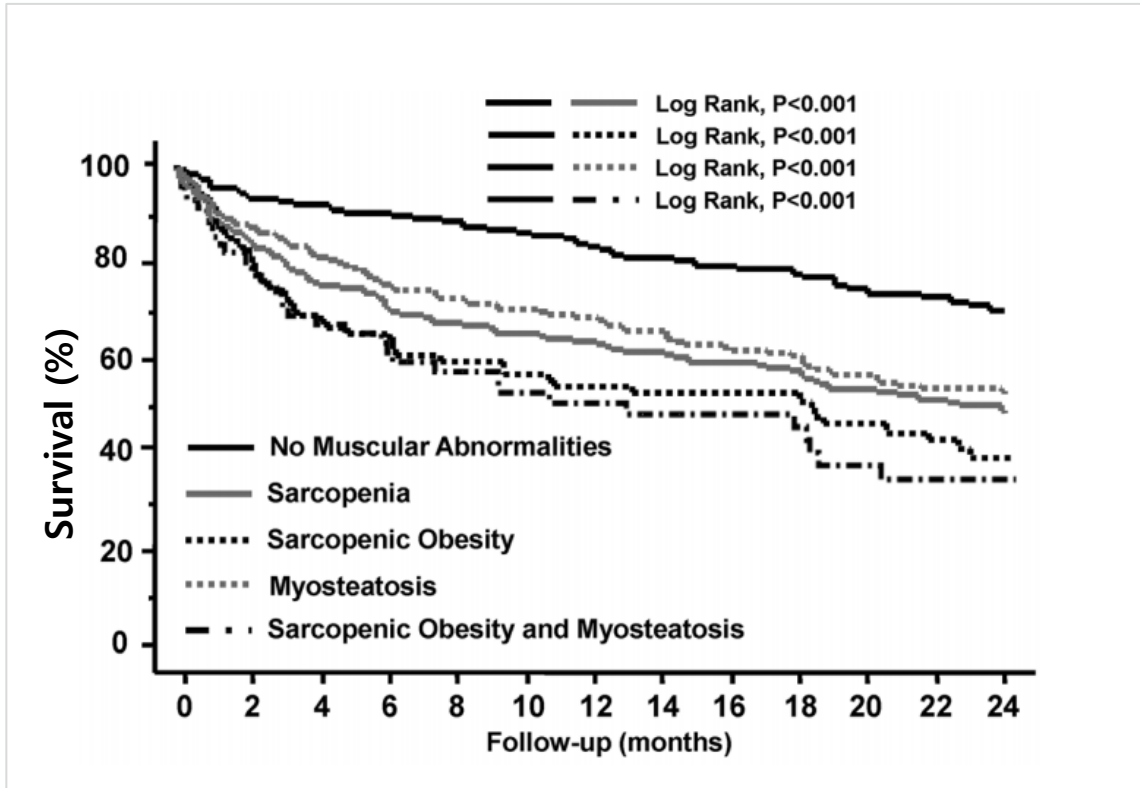
Positive POC Phase 2 results in treatment of sarcopenia and OHE in cirrhosis



BofA Global Research, Pharmaceutical Scripts/Sales Data Report 21 January 2025

# Sarcopenia in Cirrhosis

## A serious comorbidity



**Low muscle mass (sarcopenia) and quality (myosteatorsis) are associated with worse overall survival <sup>1</sup>**

Sarcopenia is a predictor for increased morbidity and mortality in cirrhosis<sup>2</sup>

- 3-fold higher mortality rate compared to no sarcopenia<sup>2</sup>

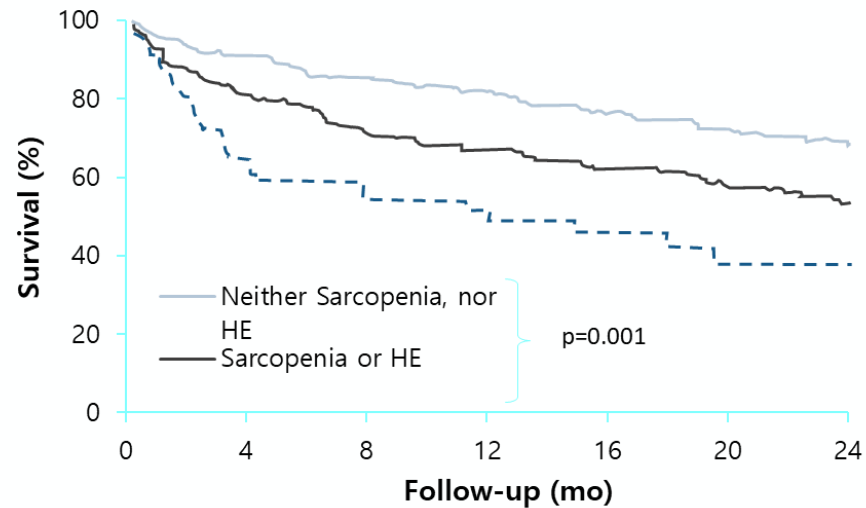
Sarcopenia in cirrhosis correlates with decompensation events, particularly hepatic encephalopathy (HE)<sup>3</sup>

- Presence of sarcopenia increases the risk of overt HE ~2 fold<sup>3</sup>
- Primary pathophysiology associated with sarcopenia and decompensated cirrhosis include a catabolic state, progressive immobility, imbalance between muscle breakdown and formation, and hormonal changes<sup>3</sup>

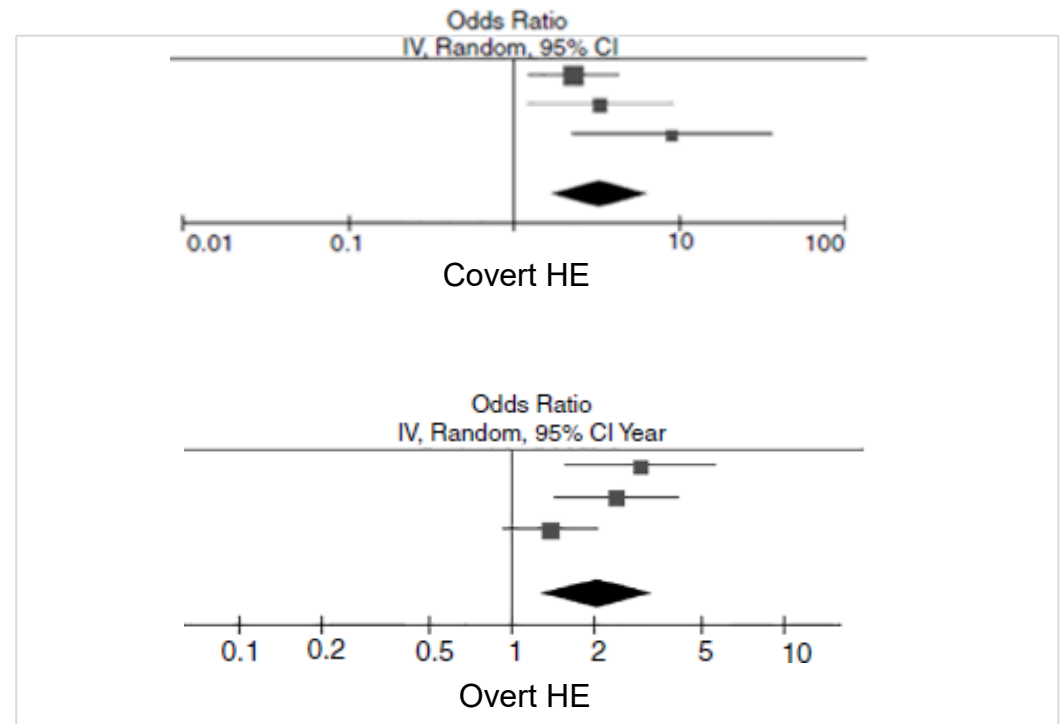
# Overt Hepatic Encephalopathy (OHE) in Cirrhosis

Presence of both sarcopenia and HE further increases risk of mortality<sup>5</sup>

**Survival Rate of Patients with Cirrhosis<sup>1</sup>**



Pt Followed (no.)	0	4	8	12	16	20	24
— (Neither Sarcopenia, nor HE)	348	256	210	183	153	135	117
— (Sarcopenia or HE)	254	166	125	99	81	71	58
- - -	75	29	21	18	12	8	8



**Sarcopenia and myosteatosis are associated with increased risk of hepatic encephalopathy<sup>1,2</sup>**

# LPCN 1148 for the Management of Cirrhosis

## Product Candidate Attributes

Oral androgen receptor agonist; dosage form comprising testosterone dodecanoate, a unique prodrug of an endogenous hormone

## Targeted Mechanism of Action

### Anabolic<sup>1</sup>

Stimulates muscle satellite activator, FGF2<sup>2</sup>, inhibit myostatin<sup>3</sup>, increase muscle mass and strength<sup>4</sup>, and reduce fat mass<sup>5</sup>

### Androgenic

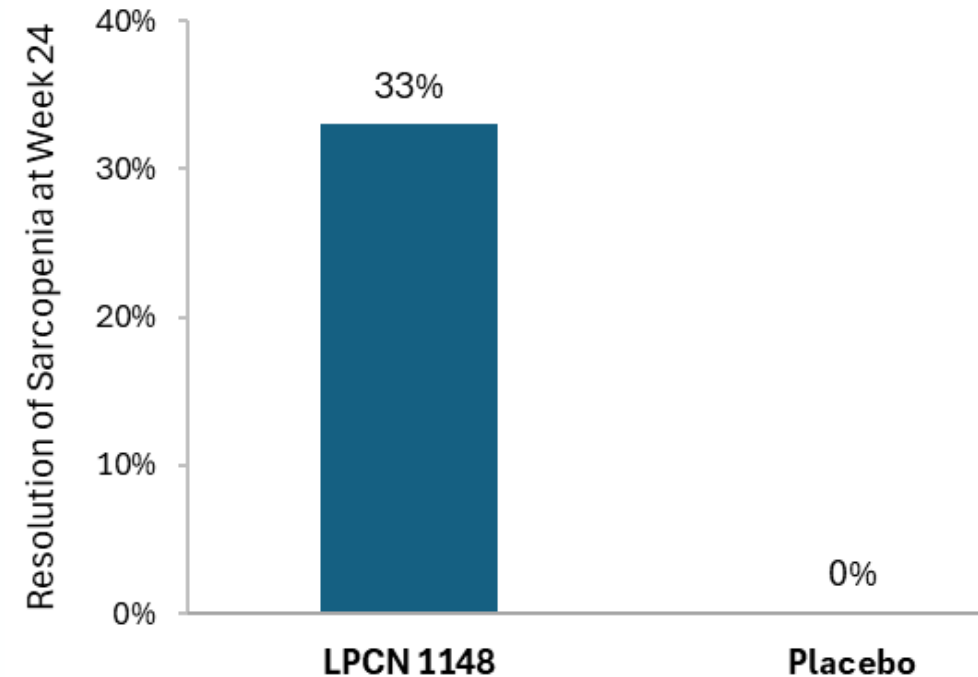
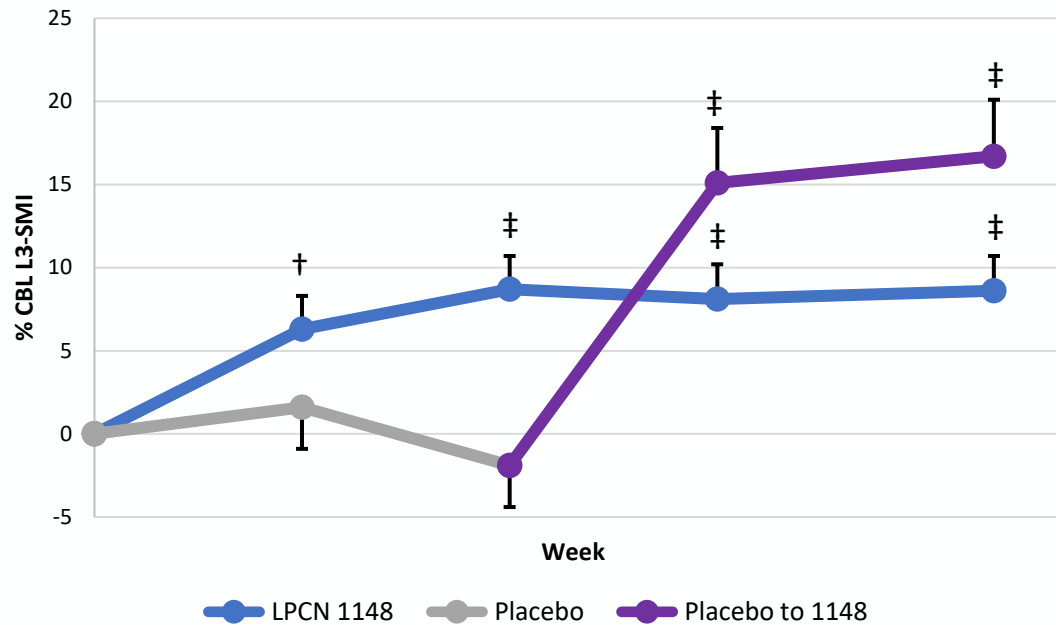
Induce hematopoiesis<sup>9</sup>; improve endocrine/sexual dysfunction<sup>10</sup>

### Ammonia Lowering

Via improved liver health<sup>6</sup> and improved muscle health<sup>7</sup>; antibacterial<sup>8</sup>

# LPCN 1148 Phase 2 Results – Sarcopenia Primary Endpoint Met

Resolution for sarcopenia and significantly increased skeletal muscle mass index (SMI)



- ~9% increase in L3-SMI at week 24

- 33% of patients had resolution of sarcopenia\* at week 24

# LPCN 1148 Phase 2 Results – HE Endpoint Met

Fewer overt hepatic encephalopathy events

Parameter	Through Week 24		Week 24 to EOS	
	Placebo N=14	LPCN 1148 N=15	LPCN 1148 N=11	LPCN 1148 switch from placebo N=8
History of HE prior to randomization (n)	11 (79%)	11 (73%)	7 (64%)	6 (75%)
Recurrent Overt HE (events)	6	1*	1	1
Time to first recurrent event (days)	35	114	294	140

# LPCN 1148 Phase 2 Results Safety Data

## Overall LPCN 1148 was well tolerated

- Rates and severities of AEs similar to those in Stage 1 with placebo
- Fewer participants experienced severe AEs when switched from placebo to LPCN 1148

Parameter	Placebo (Through Week 24) N=14	LPCN 1148 (Through Week 24) N=15	LPCN 1148 (Week 24 to EOS) N=11	LPCN 1148 switch from placebo (Week 24 to EOS) N=8
Total AEs	9 (64%)	9 (60%)	7 (64%)	7 (88%)
Serious AEs	5 (36%)	5 (33%)	5 (45%)	1 (13%)
Severe AEs	4 (29%)	4 (27%)	3 (27%)	1 (13%)
Deaths	2 (14%)	0	1 (9%)	0

Safety set; includes all participants who received study drug in a given stage. Post-transplant AEs excluded. Severe AEs: CTCAE severity  $\geq$  Grade 3



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