

# LIPOCINE®

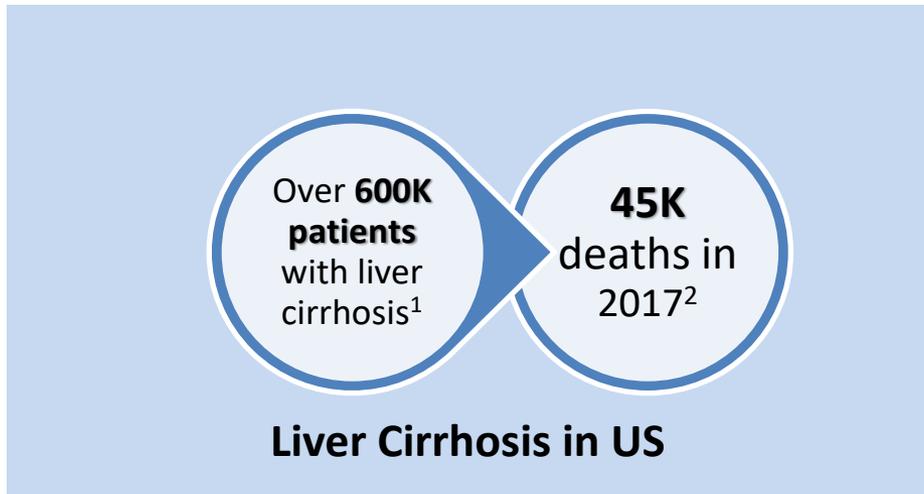
ENHANCING HEALTH

Enabling Oral Drug Delivery to Improve Patient Compliance

**LPCN 1148**  
(Oral Testosterone)  
for Liver Cirrhosis



# LPCN 1148: Oral T for Cirrhosis



## Common Causes<sup>3</sup>

Alcoholic liver disease

Nonalcoholic Fatty Liver Disease (NAFLD)

Chronic hepatitis B

Chronic hepatitis C

Cryptogenic

1. Scaglione et al. J Clin Gastroenterol, 2015; 2.Yoon and Chen, National Institute on Alcohol Abuse and Alcoholism; Surveillance Report #114, 2019

3. <https://www.niddk.nih.gov/health-information/liver-disease/cirrhosis/symptoms-causes>

# Complications of Cirrhotic Patients

## Portal hypertension

- Varices in esophagus, stomach, or intestines leading to internal bleeding
- Edema
- Ascites
- Hepatic encephalopathy

## Infections

## Cachexia, malnutrition, and weight loss

## Sarcopenia, loss muscle mass and function

## Frailty with compromised energetics

## Bone diseases (e.g., osteoporosis)

## Liver cancer

## Insulin resistance and type 2 diabetes

# High Economic Burden of a Liver Transplant

## Transplant Only Cure for Liver Cirrhosis

### **Estimated Total of \$812,500/ Transplant in U.S.**

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30 Days Pre-Transplant: \$41,400

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Procurement: \$94,000

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Hospital Transplant Admission: \$463,200

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Physician during Transplant Admission: \$56,000

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180 Days Post-Transplant Discharge: \$126,900

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Op Immunosuppressants & Other Rx: \$30,800

# Unmet Need in Liver Cirrhosis



Improvement in survival rate



Improvement in quality of life



Stay on transplant list

Sarcopenia is a leading contributory cause of removal from the waitlist

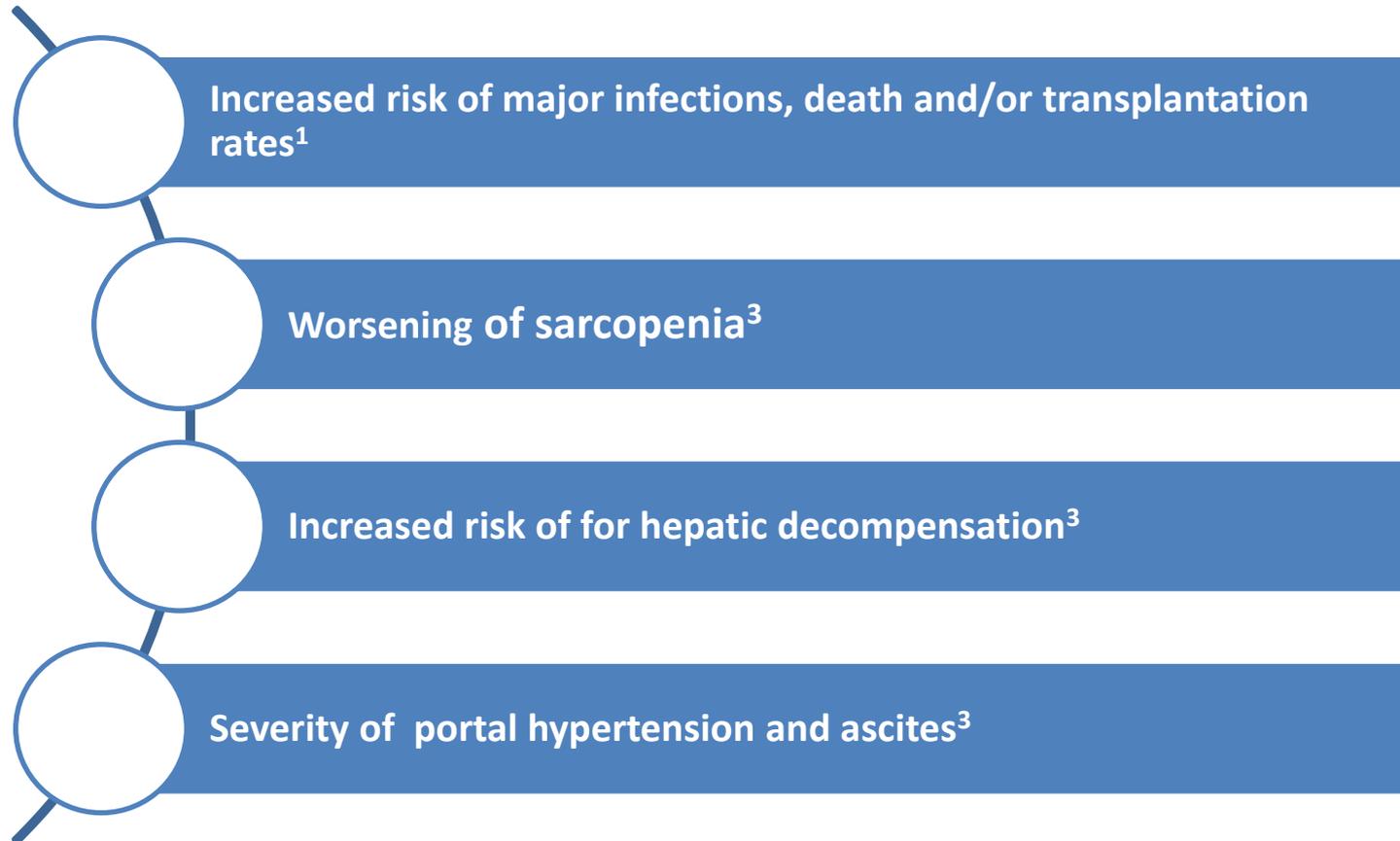
- 40 -70% of cirrhotic patients are sarcopenic



Improvement of post transplant survival/outcomes

# Reduced Testosterone\* – Cirrhosis Association

## Progressive Drop in T Level with Increasing Disease Severity<sup>1</sup>



**\*Most cirrhotic male patients have low T<sup>2</sup>**

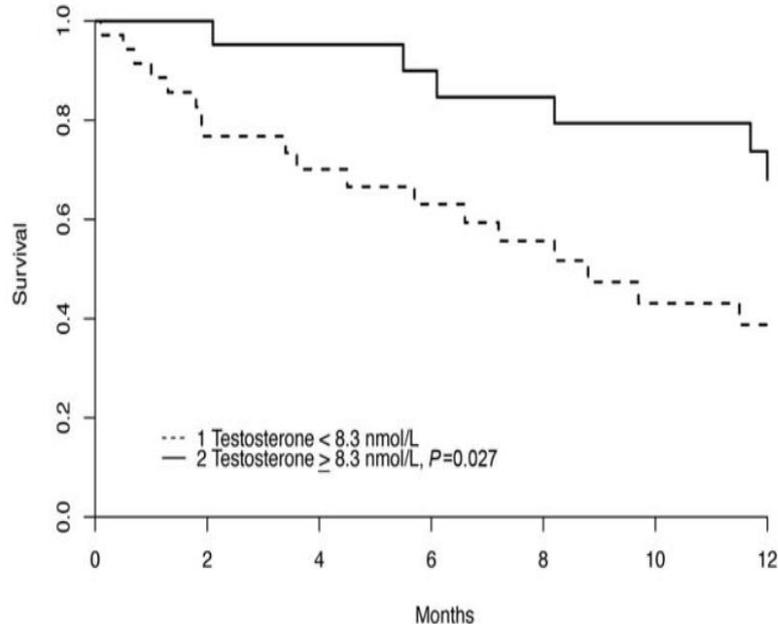
1. Sinclair et al., Liver Transplantation, 2016; 2. Sinclair et al., J Gastroenterol Hepatol. 2016;

3.. Paternostro et al, Hepatol Res 2019

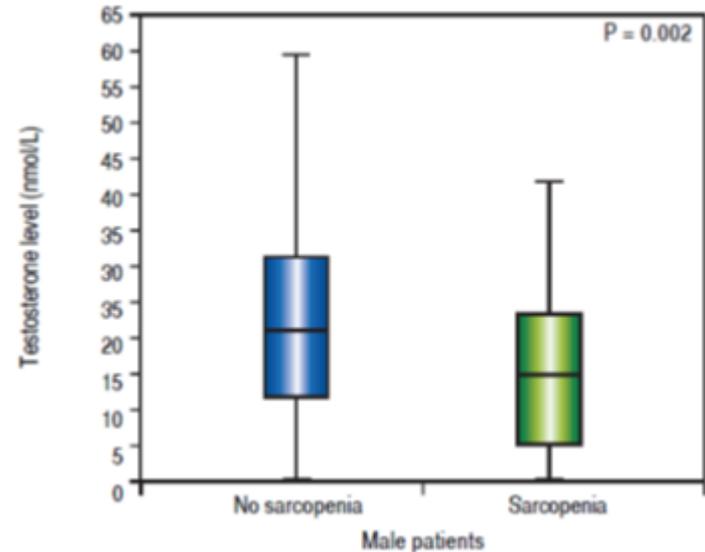
MELD Score: Model For End-Stage Liver Disease Score; Child-Pugh Score for Cirrhosis Mortality

# Testosterone (T)

## An Independent Predictor of Mortality in Late Stage Cirrhosis<sup>1</sup>



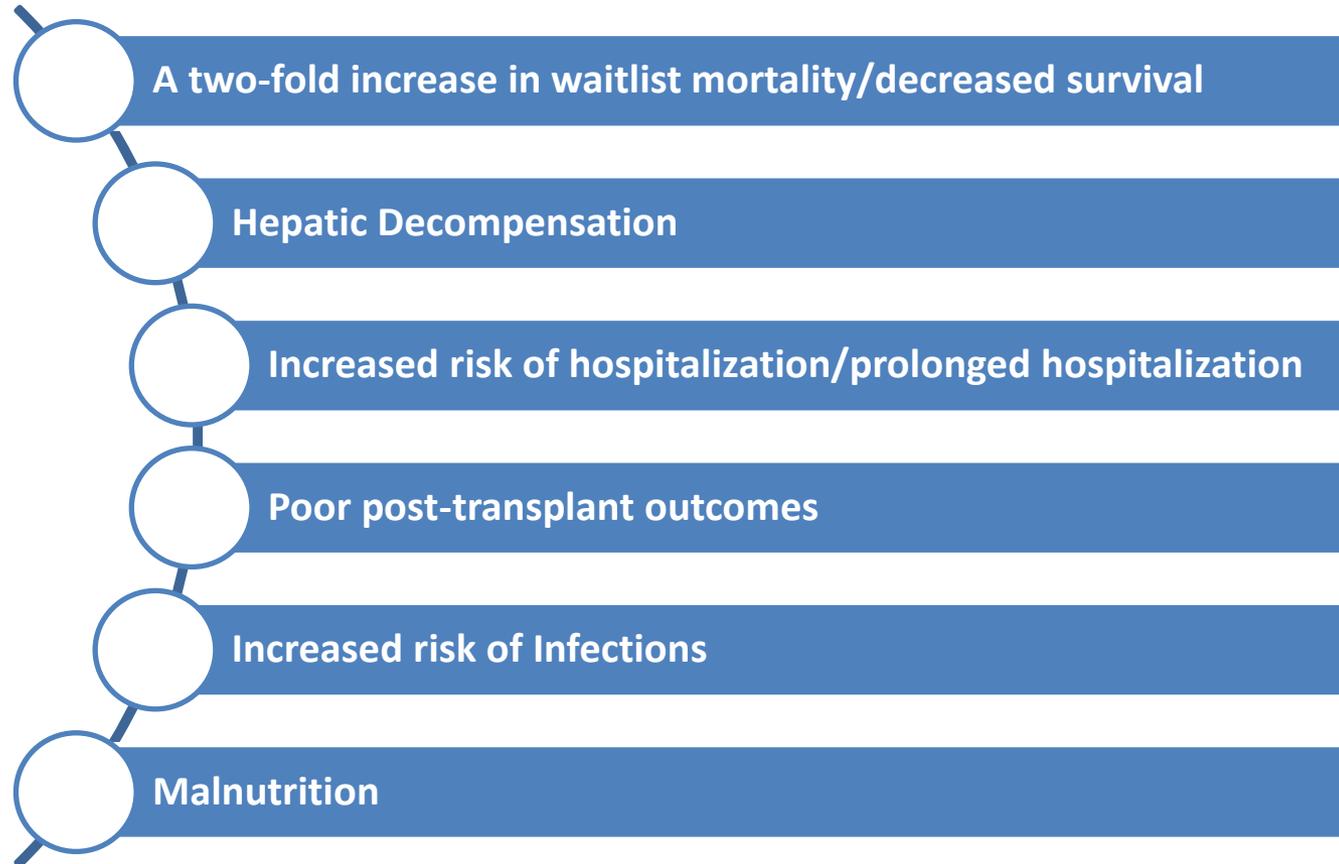
❑ Low T (<8.3 nmol/L) associated with increased risk of major infections, death and/or transplantation rates<sup>1</sup>



❑ A significant association between testosterone levels and sarcopenia in male patients<sup>2</sup>

# Sarcopenia in Liver Cirrhosis

Equivalent to Adding 10 Points to the MELD Score



References: Kim and J.W. Jang, World Journal of Gastroenterology, 2015; Sinclair et al., Journal of Gastroenterology and Hepatology (Australia), 2016; Moctezuma-Velazquez et al., Clinical Nutrition, 2018.; Sinclair et al., World Journal of Gastroenterology, 2017. Montano-Loza et al., Clinical and Translational Gastroenterology, 2015; Lai, J.C., et al., Hepatology, 2017; Englesbe et al., J Am Coll Surg, 2010.

# Potential Key Effects of LPCN 1148 in Cirrhotic Patients

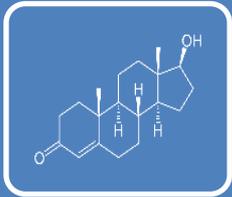
Anabolic	Androgenic	Anti-Inflammatory	Improve immunodysregulation	SHBG lowering
<ul style="list-style-type: none"><li>• Increase muscle mass and strength</li><li>• Reduce fat mass</li><li>• Increase bone density</li><li>• Inhibit myostatin</li><li>• Improve nutritional status*</li></ul>	<ul style="list-style-type: none"><li>• Induce hematopoiesis</li><li>• Improve sexual dysfunction</li></ul>	<ul style="list-style-type: none"><li>• Reduce IL-1, IL-6, and TNF-<math>\alpha</math></li></ul>	<ul style="list-style-type: none"><li>• Lower infection rate</li></ul>	<ul style="list-style-type: none"><li>• Increase free T</li></ul>

References: Trivedi and Tapper, Gastroenterol Rep (Oxf), 2018; Berzigotti et al., Hepatology, 2017; Chen and Dunn, Clin Liver Dis (Hoboken), 2018; Sinclair et al., Liver international, 2016; Neff et al., Digestive Diseases and Sciences, 2004; Puliyl et al., Australian and New Zealand Journal of Medicine, 1977; Brown et al., Cleve Clin Q, 1960; Girolami M, Am Geriatr Soc, 1958; Neff et al., Transplant Proc, 2004; Wells R., The Lancet, 1960; Yurci et al., Clinics and Research in Hepatology and Gastroenterology, 2011; Muting D., Verh Dtsch Ges Inn Med, 1969; Gluud C., Liver, 1984.

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

# LPCN 1148: Oral Testosterone Therapy

## Comprising Testosterone Tridecanoate



**Prodrug of endogenous testosterone (non-methylated)**



**Known anabolic and androgenic agent**



**Preferred route for self-administration**

# Phase 2: Proof of Concept Study

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- A Phase 2, randomized double-blind, placebo-controlled, multi-center study to assess the efficacy, safety, and tolerability of a 52-week treatment period of oral LPCN 1148 in male subjects with cirrhosis of the liver and sarcopenia (with interim results at 24 weeks)