LPCN 1148 Phase 2 Study Meets Primary Endpoint in Patients with Cirrhosis

- Met primary endpoint: treatment with LPCN 1148 increased L3 skeletal muscle index (L3-SMI) relative to placebo (P <0.01)
- Fewer hepatic encephalopathy (HE) events of grade >1 in the LPCN 1148 treatment arm relative to placebo (P < 0.05)
- More patients on LPCN 1148 reported symptom improvement compared to placebo (P < 0.05)
- LPCN 1148 was well-tolerated, with AE rates and severities similar to placebo
- Conference call and webcast today at 8:30am ET

SALT LAKE CITY, July 27, 2023 /PRNewswire/ -- Lipocine Inc. (NASDAQ: LPCN), a biopharmaceutical company focused on treating Central Nervous System (CNS) disorders by leveraging its proprietary platform to develop differentiated products, today announced positive topline results from a Phase 2 clinical study of LPCN 1148. LPCN 1148 is an oral candidate under development for the clinical management of cirrhosis. Lipocine plans to meet with the FDA to discuss a development path to NDA filing.

"We are delighted with the positive results from our Phase 2 study," said Dr. Mahesh Patel, President and CEO of Lipocine Inc. "Managing cirrhosis is a significant unmet medical need with a strong pharmaco-economic rationale. We believe LPCN 1148 is a compelling development opportunity; if approved, we believe it has potential to be the standard of care in managing advanced cirrhosis."

This Phase 2 proof of concept study is an ongoing randomized placebo-controlled study in sarcopenic male patients with cirrhosis on the liver transplant waitlist. Twenty-nine patients were randomized 1:1 to receive either LPCN 1148 or matching placebo for 24 weeks. At Week 24, the open-label extension stage of the study begins; during this stage all patients receive LPCN 1148. The study's primary endpoint was a change in L3-SMI at week 24. L3-SMI estimates whole body skeletal muscle mass and is the standard for sarcopenia assessment in cirrhosis. Secondary endpoints included rates of decompensation events including hepatic encephalopathy, and participant-reported change in symptoms using the PGI-C scale.

All LPCN 1148-treated patients completed Week 24 (n=15), whereas ten of fourteen placebo patients completed Week 24. All LPCN 1148-treated patients had at least one evaluable post-baseline CT scan and are therefore part of the modified intent to treat (mITT) analysis; ten placebo-treated patients had an evaluable post-baseline CT. As prespecified, L3-SMI analysis was performed on the mITT population (n=25), with the last evaluable post-baseline observation carried forward (LOCF).

Results

Primary endpoint: LPCN 1148 treatment resulted in a significant increase in L3-SMI at Week 24 compared to placebo, as shown in Table 1 below.

Table 1. Change in L3-SMI at Week 24

Timepoint	LPCN 1148 (n=15)	Placebo (n=10)	P-value	
			Change from Baseline	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

Data are LS mean (SE). CFB, Change from Baseline

Clinical Decompensation Events: 1148-treated patients experienced significantly fewer cases of hepatic encephalopathy > Grade 1 compared to placebo, despite the two treatment groups having similar number of patients with a medical history of hepatic encephalopathy.

Table 2: Major Decompensation Events During the First 24 Weeks of the Study

	LPCN 1148 (n=15)	Placebo (n=14)
Total decompensation events	7	10
Total decompensation events > Grade 1	6	10
Hepatic Encephalopathy	3	6
HE > Grade 1 *	2	6

Recurrence of HE > Grade 1	1	6
Time to first recurrence of HE > Grade 1 (days)	115	39**

Decompensation events include HE, ascites, variceal bleeding, spontaneous bacterial peritonitis
Recurrence of HE: Medical history of HE + HE events during the study
*P < 0.05 vs placebo
** Mean value

Consistent with the American Association for the Study of Liver Disease (AASLD) statement, if a patient recovers a significant amount of liver function and muscle mass from the time they had bouts of HE, the patient may be able to stop standard HE therapy. Our study results support the concept that improvement in sarcopenia improves clinical outcomes.

As assessed by PGI-C, patients who received active treatment reported significant improvement in symptoms as early as Week 4, which persisted through Week 24. LPCN 1148 patients showed a significant increase in hemoglobin and trended towards resolution of anemia, improvement of ascites, and reduced total number of days hospitalized. CT scans also suggest improved muscle quality and reduced visceral and subcutaneous fat with LPCN 1148 therapy.

LPCN 1148 was well-tolerated, with adverse event (AE) rates and severities similar to placebo; no mortality was noted in the LPCN 1148 treatment group. Rates of diarrhea and nausea were low and similar in both groups. There were no cases of drug-induced liver injury.

Dr. Arun J. Sanyal, MD**,** Interim Chair, Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University, commented, "Sarcopenia and frailty are major markers of poor outcomes for patients with end-stage liver disease. It is very exciting to see proof of concept that correction of sarcopenia by LPCN 1148 safely improved muscle mass, functional status and quality of life as well as reduced days in the hospital compared to placebo. This demonstrates for the first time that correcting sarcopenia improves many clinically significant issues for this very sick population and could provide a better bridge to transplant and quality of life for those who are not transplant candidates. I look forward to larger studies to further confirm the efficacy and safety of LPCN 1148 that was observed in this study."

Dr. Jennifer Lai, MD, MBA, study principal investigator, Professor of Medicine, UCSF, and a practicing general/transplant hepatologist and board-certified Physician Nutrition Specialist, added, "All of these patients had advanced liver disease awaiting liver transplant which predisposes them to losing muscle mass. The fact that those who received LPCN 1148 gained muscle mass in a relatively short time is remarkable. The signals toward improved clinical outcomes, such as hospitalized days and rates of hepatic encephalopathy, are scientifically plausible effects of having higher muscle mass and are quite promising."

Cirrhosis is an end stage liver disease of varying etiologies such as alcoholic liver disease, chronic hepatitis, nonalcoholic fatty liver disease and primary cholangitis. Complications of cirrhosis include decompensation events such as hepatic encephalopathy due to systemic ammonia buildup, variceal bleeding, and ascites, which require frequent hospitalizations. Poor Quality of Life (QOL) is common while waiting for a liver transplant. Although there is a limited supply of donor livers, transplant is the only cure for end-stage cirrhosis. Hepatic encephalopathy (HE) is a frequent complication and one of the most debilitating manifestations of liver disease, severely affecting the lives of patients and their caregivers. Furthermore, cognitive impairment associated with cirrhosis results in utilization of more health care resources in adults than other manifestations of liver disease. LPCN 1148 comprises testosterone dodecanoate, a unique androgen receptor agonist. It is targeted as a differentiated intervention option with a novel multimodal mechanism of action to elicit potential benefits in management of cirrhosis and associated comorbidities of cirrhosis.

About the Phase 2 study
This multi-center study enrolled and dosed a total of 29 patients across 8 centers in the US. The primary objective was to evaluate the efficacy of 24 weeks of LPCN 1148 treatment in cirrhotic men with sarcopenia. The secondary objective was to evaluate the safety and tolerability of LPCN 1148. Baseline characteristics, including age, disease etiology baseline L3-SMI, and other comorbidities were generally well-balanced between groups. Overall, the average baseline Model for End-Stage Liver Disease (MELD) score was 16.8, and 97% of patients had previously experienced at least one clinical decompensation event. Sarcopenia, or low muscle mass, was assessed by computed tomography (CT) scan; total skeletal muscle area was measured by CT scan at the third lumbar vertebra and normalized by subject height (L3-SMI, L3-skeletal muscle index). Patients had study visits every four weeks, with CTs performed at Week 12 and Week 24. Patients with a variety of cirrhosis etiologies were eligible. During the study there were no restrictions on standard of care medications,

procedures, or other interventions. Further details on the study design, including inclusion and exclusion criteria, can be found on Clinicaltrials.gov (NCT04874350).

Conference Call and Webcast
Lipocine management will host a conference call and webcast with slides beginning at 8:30 a.m. Eastern Time today to discuss the Phase 2 clinical study results and answer questions. To participate via telephone, please dial 1-877-451-6152 or 1-201-389-0879 (ex-U.S. toll dial-in number) using the conference ID 13740396. Participants can also click the Call me™ link, https://callme.viavid.com/viavid/?callme=true&passcode=13738729&h=true&info=company&r=true&B=6, for instant telephone access to the event. The Call me™ link will be made active 15 minutes prior to scheduled start time. The webcast is available to view here and also at www.lipocine.com. It will be available for replay for 180 days.

About Lipocine
Lipocine is a biopharmaceutical company leveraging its proprietary technology platform to augment therapeutics through effective oral delivery to develop products for CNS disorders. Lipocine has drug candidates in development as well as drug candidates for which we are exploring partnering. Our drug candidates represent enablement of differentiated, patient friendly oral delivery options for favorable benefit to risk profile which target large addressable markets with significant unmet medical needs.

Lipocine's clinical development candidates include: LPCN 1154, oral brexanolone, for the potential treatment of postpartum depression, LPCN 2101 for the potential treatment of epilepsy and LPCN 1148, an oral prodrug of bioidentical testosterone targeted for the management of symptoms associated with liver cirrhosis. Lipocine is exploring partnering opportunities for LPCN 1107, our candidate for prevention of preterm birth, LPCN 1148, for the management of decompensated cirrhosis, LPCN 1144, our candidate for treatment of non-cirrhotic NASH, and LPCN 1111, a once-a-day therapy candidate for testosterone replacement therapy (TRT). TLANDO, a novel oral prodrug of testosterone containing testosterone undecanoate developed by Lipocine, is approved by the FDA for conditions associated with a deficiency of endogenous testosterone, also known as hypogonadism, in adult males. For more information, please visit www.lipocine.com.

Forward-Looking Statements

This release 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.

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