Lipocine's LPCN 1144 Met Non-Alcoholic Steatohepatitis ("NASH") Resolution Regulatory Endpoint in Phase 2 LiFT Study

Histological Analysis Demonstrates Treatment Potential of LPCN 1144 in NASH
- Both LPCN 1144 treatment arms met with statistical significance the pre-specified histology based regulatory endpoint of NASH resolution with no worsening of fibrosis
- Treatment effect observed on fibrosis improvement needs confirmation in a larger study
- Changes in key liver enzymes and body composition support beneficial treatment effects of LPCN 1144
- LPCN 1144 was well tolerated with an overall safety profile comparable to placebo
- Positive topline results support LPCN 1144 development for regulatory approval
-- Conference Call Scheduled for 8:30 a.m. ET today

SALT LAKE CITY, Aug. 25, 2021 /PRNewswire/ -- Lipocine Inc. (NASDAQ: LPCN), a clinical-stage biopharmaceutical company focused on metabolic and endocrine disorders, today announced positive topline 36-week results from its Phase 2 proof of concept *LiFT* ("***Li***ver ***F***at intervention with oral ***T***estosterone") clinical study, NCT04134091, investigating LPCN 1144 in men with biopsy-confirmed NASH. Currently, there are no approved treatments for NASH, a leading cause of liver failure and liver transplantation globally. LPCN 1144 comprises an orally delivered prodrug of endogenous testosterone ("T").

The *LiFT* clinical study, a prospective, multi-center, randomized, double-blind, placebo-controlled, multi-arm, multi-site trial in the United States, enrolled biopsy-confirmed hypogonadal or eugonadal male NASH subjects with stage F1-F3 fibrosis and a NAFLD Activity Score ≥ 4 for a 36-week treatment period. Subjects with advanced fibrosis (F2-F3) and steatohepatitis (inflammation on liver biopsy) were also eligible. Subjects were randomized 1:1:1 to one of three arms (Treatment A, a twice daily oral dose of 142 mg testosterone equivalent; Treatment B, a twice daily oral dose of 142 mg testosterone equivalent formulated with 238 mg of d-alpha tocopherol equivalent; and the third arm, a twice daily matching placebo).

The primary endpoint of the *LiFT* clinical study was change in hepatic fat fraction via MRI-PDFF post 12 weeks of treatment. Additionally, key secondary endpoints post 36 weeks of treatment include assessment of histological change for NASH resolution and/or fibrosis improvement. The *LiFT* clinical study was not powered to assess statistical significance of any of the secondary endpoints.

At 12 weeks, treatments with LPCN 1144 resulted in statistically significant liver fat reduction, assessed by MRI-PDFF, meeting the pre-specific primary endpoint of the *LiFT* clinical study. Statistically significant reduction in liver fat was observed compared to placebo: up to a mean of 9.2% absolute reduction and a 46.8% relative reduction in liver fat.

Liver biopsies were performed at baseline ("BL") and after 36 weeks of treatment ("EOS"). Prespecified biopsy analyses include NASH Clinical Research Network ("CRN") scoring as well as a continuous paired ("Paired Technique") and digital technique ("Digital Technique-Fibronest"). All biopsy analyses were performed on the same slides and the reads for the three techniques were done independently. Analysis sets included the NASH Resolution Set (all subjects that have BL and EOS biopsy with NASH at BL [NAS ≥4 with lobular inflammation score ≥ 1 and hepatocyte ballooning score ≥1 at BL] (n=37)), the Biopsy Set (all subjects with baseline and EOS biopsies (n=44)), and the Safety Set (all randomized subjects (n=56)).

Both LPCN 1144 treatment arms met with statistical significance the pre-specified accelerated approval regulatory endpoint of NASH resolution with no worsening of fibrosis based on NASH CRN scoring. Additionally, both treatment arms showed substantial improvement of the observed NASH activity in steatosis, inflammation and ballooning.

Key results are presented in the following table:

-Histology NASH CRN Scoring Outcomes[1]			
	Placebo (n = 11)	Treatment A (n=13)	Treatment B (n=13)
NASH Resolution responders, n (%) [2]	1 (9%)	7 (54%)[3]	9, (69%)[4]
NASH Resolution with No Worsening of Fibrosis responders, n (%)	0 (0%)	6 (46%)[3]	9 (69%)[5]

[1] NASH Resolution Set

[2] Improvement in NASH defined as improvement in ballooning or inflammation, and no worsening of ballooning or inflammation

[3] $p < 0.05$ vs placebo

[4] $p < 0.01$ vs placebo

[5] $p < 0.001$ vs placebo

Both LPCN 1144 treatment arms showed significant improvement in NASH without worsening of fibrosis using Paired Technique, which concurred with the NASH CRN scoring findings (per Biopsy Set; NASH Improvement responders: Placebo – 13%, Treatment A – 60%, Treatment B – 57%; NASH Improvement with No Worsening of Fibrosis responders: Placebo – 13%, Treatment A – 60%, Treatment B – 57%).

The treatment effects on fibrosis improvement need confirmation in a larger study.

Key fibrosis improvement results are presented in the following table:

Histopathological Assessment Techniques[X]			
	Placebo (n = 15)	Treatment A (n=15)	Treatment B (n=14)
NASH CRN: Fibrosis Improvement ≥ 1 Stage with No Worsening of NASH, Responders, n (%)	6 (40%)[†]	4 (27%)	2 (14%)
Paired Technique: Fibrosis Improvement with No Worsening of NASH,[y] Responders, n (%)	3 (20%)	6 (40%)	8 (57%)
Digital Technique-FibroNest: Fibrosis Improvement,[z] Responders, n (%)	5 (33%)	12 (80%)	6 (43%)

[x] Biopsy Set

[y] Fibrosis improvement on paired reads defined as a score of improvement in fibrosis with a score of no worsening of ballooning, inflammation, or steatosis

[z] For Digital Reads (FibroNest - http://www.fibronest.com), improvement defined as a decrease in parenchymal tissue normalized phenotypic fibrosis composite score

[†] One subject in placebo is missing NASH CRN fibrosis score and is treated as a non-responder

In both treatment arms substantial reductions in markers of liver injury compared to placebo were observed post four weeks of treatment and were sustained through EOS. Using all available Safety Set data, alanine

aminotransferase ("ALT") decreased up to a mean of 23.4 U/L at EOS from all group mean baseline of 51.5 U/L and aspartate aminotransferase ("AST") decreased up to a mean of 13.3 U/L at EOS from all group mean baseline of 31.9 U/L.

Positive effects in appendicular lean mass and whole-body fat mass, an indicator overall tissue quality, based on dual-energy X-ray absorptiometry scans were noted in both LPCN 1144 treatment arms.

During the 36 weeks of treatment, LPCN 1144 was well tolerated with an overall safety profile comparable to placebo. Frequency and severity of treatment emergent adverse events, TEAEs, in both treatment arms were comparable to placebo. Study drug related TEAEs were mild to moderate. Four subjects discontinued due to TEAEs in the placebo arm vs one subject in total across the treatment arms. Cardiovascular events were balanced among groups with hematocrit increases averaging <2% in the treatment arms, no observed thromboembolic events, and comparable blood pressure changes in both treatment arms to placebo.

There were no reported cases of hepatocellular carcinoma or Drug Induced Liver Injury ("DILI"). Weight change from baseline, GI adverse events and PSA changes were small and comparable among groups. Additionally, no clinically meaningful changes in lipids in treatment groups were noted compared to placebo, and rates of pedal edema were low and similar in all arms.

Additionally, all subjects had the option to continue with LPCN 1144 treatment through an open label extension study (NCT04685993). The extension study will enable the collection of additional data on LPCN 1144 for up to a total of 72 weeks of therapy.

"The extent of the LPCN 1144 efficacy results in meeting the NASH resolution regulatory endpoint from the *LiFT* study are striking with no adverse safety signal. These data strongly support further development of this differentiated novel approach as a treatment of NASH," said Dr. Arun Sanyal, Professor in the Virginia Commonwealth University ("VCU") Department of Internal Medicine and Education Core Director in the VCU Center for Clinical and Translational Research.

"We are delighted by the remarkable efficacy results and the overall safety profile of LPCN 1144 in the *LiFT* study, which we believe demonstrate the potential for LPCN 1144 to be the "best in class" option for treating NASH with a discerning benefit to risk profile as required for a chronic therapy," said Dr. Mahesh Patel, Chairman, President and CEO of Lipocine Inc. "Additionally, the unique benefits of LPCN 1144 in improving body composition may fulfill an unmet medical need. We look forward to meeting with the FDA regarding the path forward for an accelerated approval and Phase 3 study requirements," said Dr. Patel.

Conference Call

Management will host a conference call and webcast today at 8:30 a.m. Eastern time to discuss LPCN 1144 Phase 2 *LiFT* clinical study key secondary endpoint topline results. To participate in the conference call, please dial 1-877-451-6152 from the U.S. or 1-201-389-0879 from outside the U.S. In addition, following the completion of the call, a telephone replay will be accessible until September 1, 2021, by dialing 1-844-512-2921 from the U.S. or 1-412-317-6671 from outside the U.S. and entering conference ID #13722634. Those interested in listening to the conference call live via the internet may do so by using the following link: http://public.viavid.com/index.php?id=146385. An archive of the webcast will also be available on the webcast page of the Company's website for 90 days.

About NASH

NASH is a more advanced state of non-alcoholic fatty liver disease ("NAFLD") and can progress to a cirrhotic liver and eventually hepatocellular carcinoma/liver cancer. Twenty-five to thirty percent of the U.S. population is estimated to suffer from NAFLD. NASH afflicts three to twelve percent of the U.S. population, which is a substantially large population that lacks effective therapy. Currently, there are no FDA approved

treatments for NASH. Approximately 50% of NASH patients are in adult males and the number of NASH cases is projected to increase 63% from 16.5 million cases in 2015 to 27.0 million cases in 2030. NAFLD/NASH is becoming more common due to its strong correlation with obesity and metabolic syndrome, including components of metabolic syndrome such as diabetes, cardiovascular disease and high blood pressure. In men, especially with comorbidities associated with NAFLD/NASH, testosterone deficiency has been associated with an increased accumulation of visceral adipose tissue and insulin resistance, which could be factors contributing to NAFLD/NASH.

About Lipocine

Lipocine Inc. is a clinical-stage biopharmaceutical company focused on metabolic and endocrine disorders using its proprietary drug delivery technologies. Lipocine's clinical development pipeline includes: TLANDO, LPCN 1144, TLANDO XR, LPCN 1148, LPCN 1154, and LPCN 1107. TLANDO, a novel oral prodrug of testosterone containing testosterone undecanoate, has received tentative approval from the FDA for conditions associated with a deficiency of endogenous testosterone, also known as hypogonadism, in adult males. LPCN 1144, an oral prodrug of bioidentical testosterone, recently completed a Phase 2 clinical study demonstrating the potential utility in the treatment of non-cirrhotic NASH. TLANDO XR, a novel oral prodrug of testosterone, originated and is being developed by Lipocine as a next-generation oral testosterone product with potential for once-daily dosing. In a phase 2 clinical evaluation when administered as once daily or twice daily TLANDO XR met the typical primary and secondary end points. LPCN 1148 is an oral prodrug of bioidentical testosterone targeted for the treatment of cirrhosis. LPCN 1107 is potentially the first oral hydroxyprogesterone caproate product candidate indicated for the prevention of recurrent preterm birth and has been granted orphan drug designation by the FDA. LPCN 1154 is an oral neuro-steroid targeted for the treatment of post-partum depression. For more information, please visit www.lipocine.com.

Cautionary and 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 Lipocine's product candidates and related clinical trials, the timing and completion of additional clinical trials and studies, the potential uses and benefits of LPCN 1144 for the treatment of NASH and fibrosis improvement, the timing of additional data, whether LPCN 1144 will be eligible for and receive accelerated approval from the FDA for LPCN 1144, and our product development efforts. Investors are cautioned that all such forward-looking statements involve risks and uncertainties, including, without limitation, the risk that 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, 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. There can be no assurance that we will choose, or have the ability, to conduct Phase 3 trials with respect to LPCN 1144 and, ultimately, apply for and receive approval from the FDA to market LPCN 1144 for the indications described in this press release. Lipocine assumes no obligation to update or revise publicly any forward-looking statements contained in this release, except as required by law.

SOURCE Lipocine Inc.

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