Lipocine Announces LPCN 1154 Meets Bioequivalence with IV Brexanolone in Pivotal Study

- **Met standard bioequivalence (BE) criteria C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$**
- **C_{trough} criterion was met**
- **LPCN 1154 was well tolerated with no sedation or somnolence events observed**
- **On track for NDA filing, targeted by end of Q4 2024**

SALT LAKE CITY, June 25, 2024 /PRNewswire/ -- Lipocine Inc. (NASDAQ: LPCN), a biopharmaceutical company leveraging its proprietary technology platform to augment therapeutics through effective oral delivery, today announced positive topline study results demonstrating bioequivalence of LPCN 1154 to IV brexanolone in an NDA enabling pivotal pharmacokinetic (PK) study. Lipocine is developing LPCN 1154, oral brexanolone, for the treatment of postpartum depression (PPD). The U.S. Food & Drug Administration (FDA) has agreed with Lipocine's proposal for a 505(b)(2) NDA filing based on a single pivotal PK bridging study comparing exposure of LPCN 1154 with the approved IV infusion of brexanolone. Intravenous brexanolone is approved based on evidence demonstrating efficacy and safety with two dosing regimens with different maximum infusion rates of either 60 µg/kg/hr (IV60) or 90 µg/kg/hr (IV90). Lipocine is targeting NDA submission by the end of the fourth quarter of 2024.

"I'm pleased with the positive outcome of this pivotal study which brings us a step closer to potentially offering a differentiated preferred treatment option for PPD patients in need," said Dr. Mahesh Patel, President and CEO of Lipocine. "PPD is a serious and potentially life-threatening condition. LPCN 1154 is targeted to be a highly effective, oral, fast-acting and short duration treatment option. We believe a 48-hour oral dosing duration with fast onset of efficacy would be an important solution for patients and caregivers."

Per published FDA bioequivalence guidance[1], the criteria to establish bioequivalence are that Geometric Mean Ratios (GMR) and corresponding 90% confidence intervals (CIs) for AUC_{0-t}, $AUC_{0-\infty}$, and C_{max} (key measures of drug exposure) fall within 80% to 125% for test vs reference products.

The pivotal PK study was an open label, randomized, crossover study in 24 healthy postmenopausal women utilizing the "to be marketed" formulation and oral dosing regimen of LPCN 1154 and the commercial IV brexanolone formulation using the approved high dose infusion regimen (IV90). The primary objective of the study is to compare the PK of a multi-dose regimen of oral LPCN 1154 (test product) to IV infusion brexanolone (reference product).

Twenty-four post-menopausal women were randomized (safety set), and all completed dosing in both study periods. The PK analysis data set includes 23 participants; data from one participant meeting outlier criteria was excluded.

PK Comparisons of LPCN 1154 vs. IV90 Brexanolone

LPCN 1154 and IV90 brexanolone were bioequivalent based on GMRs and 90% CIs for C_{max}, $AUC_{0-\infty}$, and AUC_{0-t} meeting established criteria. As targeted, C_{trough} of LPCN 1154 geometric mean was higher than the trough of IV brexanolone (geometric lower 90% CI).

PK Parameter	GMR (%) Test vs. Reference	90% CI LB Test vs. Reference	90% CI UB Test vs. Reference
C_{max}	105	92	120
$AUC_{0-\infty}$	97	88	107
AUC_{0-t}	88	80	99

n=23; Outlier participant presented PK results for the IV administration period greater than 70 standard deviations away from the PK data set mean for all PK parameters included above; LB = lower bound, UB = upper bound, t = 100 hours for AUC0-t

LPCN 1154 treatment was well tolerated with no sedation nor somnolence events observed. All events were mild to moderate, and no severe or serious adverse events occurred. Reported study related events were venipuncture site reaction, headache, arthralgia, fatigue, dizziness, low back pain, and pelvic pain and no event was reported by more than two participants.

PPD is a major depressive disorder with onset either during pregnancy or within four weeks of delivery, with symptoms persisting for up to 12 months after childbirth. There is an unmet need for an oral fast-acting product with an improved efficacy and safety profile to treat PPD. Oral LPCN 1154 comprising a bioidentical neuroactive steroid is designed to provide rapid relief with robust efficacy and 48-hour outpatient dosing.

Recent reports suggest that the market size for PPD is larger than previously estimated. Approximately 500,000 women are

affected by PPD annually in the United States and, according to the CDC, an estimated 175,000 women suffer from moderate to severe PPD. Increasing awareness of PPD among physicians and patients is expected to result in higher diagnosis rates and greater numbers of patients seeking treatment.

About LPCN 1154

LPCN 1154 is an oral formulation of brexanolone in development targeted for administration resulting in rapid relief of PPD. Brexanolone is a bioidentical to naturally occurring neuroactive steroid, allopregnanolone, a positive allosteric modulator of y-aminobutyric acid (GABA) receptor. LPCN 1154 is expected to have characteristics that could be particularly appealing to patients with severe PPD, acutely elevated suicide risk, and in whom rapid improvement is a priority while presenting no significant risk of adverse reactions to breastfed infants from exposure to brexanolone.

About Postpartum Depression and Unmet Needs

PPD is a major depressive disorder with onset either during pregnancy or within four weeks of delivery, with symptoms persisting up to 12 months after childbirth. Hormonal changes leading to GABA dysfunction are common in depression and pregnancy. Symptoms of PPD include hallmarks of major depression, including, but not limited to, sadness, depressed mood, loss of interest, change in appetite, insomnia, sleeping too much, fatigue, difficulty thinking/concentrating, excessive crying, fear of harming the baby/oneself, and/or thoughts of death or suicide. Results from a recent survey (Truist Securities Research, January 2024) show that obstetricians believe approximately 20-40% of their patients may suffer from PPD. Further, obstetricians are comfortable making a diagnosis and prescribing antidepressants for PPD. Traditional antidepressants, not approved for PPD, have slow onset of action, side effects such as weight gain, and do not demonstrate adequate remission post-acute treatment.

About Lipocine

Lipocine is a biopharmaceutical company leveraging its proprietary technology platform to augment therapeutics through effective oral delivery to develop differentiated products. 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, LPCN 2203 an oral candidate targeted for the management of essential tremor, LPCN 2401 an oral proprietary combination of anabolic androgen receptor agonist and α-tocopherol, an antioxidant, as an adjunct therapy to incretin mimetics, as an aid for improved body composition in chronic weight management and LPCN 1148, a novel androgen receptor agonist prodrug for oral administration 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 1154, for rapid relief of postpartum depression, LPCN 1148, for the management of decompensated cirrhosis, and LPCN 1144, our candidate for treatment of non-cirrhotic NASH. 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, the application of our proprietary platform in developing new treatments, our product candidates and related clinical trials, the timing and outcome of product studies, our development of and filing of a NDA with the FDA for LPCN 1154, and the potential uses and benefits of our product candidates. 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, we may not have sufficient capital to complete the development processes for our product candidates, 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 risk that we do not ultimately receive FDA approval for LPCN 1154, the results and timing of clinical trials, patient acceptance of Lipocine's products, risks related to 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.

[1]FDA Guidance, Statistical Approaches to Establishing Bioequivalence December 2022

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