Lipocine Announces Continued Commercialization of TLANDO® through Verity Pharmaceuticals

SALT LAKE CITY, Feb. 2, 2024 /PRNewswire/ -- Lipocine Inc. (NASDAQ: LPCN), a biopharmaceutical company focused on treating Central Nervous System (CNS) disorders, today announced that commercialization of TLANDO® in the U.S. has been transitioned to its licensee Verity Pharma, effective February 1, 2024, enabling the continuity of patient access to TLANDO. TLANDO is the first and only oral testosterone replacement therapy (TRT) option approved by the US Food and Drug Administration (FDA) that does not require dose titration.

In January 2024, Lipocine and Gordon Silver Limited entered into an exclusive license agreement under which Verity Pharma will market TLANDO® in the United States and, if approved, in Canada. Under the terms of the license agreement, Lipocine has received the second tranche of the $11 million license fee, $5 million. In addition, per the license agreement, Gordon Silver Limited is to make license fee payments of $2.5 million and $1 million no later than January 1, 2025, and January 1, 2026, respectively.

About TLANDO

TLANDO is approved by the FDA as a testosterone replacement therapy ("TRT") in adult males indicated for conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired). TLANDO was developed using Lipocine's proprietary Lip'ral drug delivery technology platform.

For full prescribing information, please visit www.TLANDO.com.

IMPORTANT SAFETY INFORMATION

TLANDO (testosterone undecanoate) capsules, for oral use, CIII

Initial U.S. Approval: 1953

IMPORTANT SAFETY INFORMATION

WARNING: BLOOD PRESSURE INCREASES (See Boxed Warning on Product Label for more information)

TLANDO can cause blood pressure (BP) increases that can increase the risk of major adverse cardiovascular events (MACE), including non-fatal myocardial infarction, non-fatal stroke and cardiovascular death with greater risk in patients with established cardiovascular disease or risk factors for cardiovascular disease.

Before initiating TLANDO, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled.

Three weeks after initiating therapy monitor for and treat new-onset hypertension or exacerbations of pre-existing hypertension.

Re-evaluate whether the benefits of TLANDO outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease on treatment. Due to this risk, use TLANDO only for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies.

TLANDO INDICATIONS AND USAGE

TLANDO (testosterone undecanoate) is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired)

Hypogonadotropic hypogonadism (congenital or acquired)

LIMITATIONS OF USE

Safety and efficacy of TLANDO in males less than 18 years old have not been established.

CONTRAINDICATIONS

TLANDO is contraindicated in:

Patients with carcinoma of the breast or known or suspected carcinoma of the prostate.

Women who are pregnant. Testosterone can cause virilization of the female fetus when administered to a pregnant woman.

Known hypersensitivity to testosterone undecanoate or any of TLANDO's ingredients.

Men with hypogonadal conditions, such as "age-related hypogonadism", that are not associated with structural or genetic etiologies. The efficacy of TLANDO has not been established for these conditions, and TLANDO can increase BP that can increase the risk of MACE.

WARNINGS AND PRECAUTIONS

Increase in Blood Pressure: In Study 18-001, TLANDO increased systolic BP after 4 months of treatment by an average of 4.3 mmHg based on ambulatory blood pressure monitoring (ABPM) and 4.8 mmHg from baseline based on blood pressure cuff measurements [see Adverse Reactions (6.1)].

These BP increases can increase the risk of major adverse cardiovascular events (MACE), with greater risk in patients with established cardiovascular disease or risk factors for cardiovascular disease.

In some patients, the increase in BP with TLANDO may be too small to detect but can still increase the risk for MACE.

Before initiating TLANDO, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled. Check BP approximately 3 weeks after initiating TLANDO and periodically thereafter. Treat new-onset hypertension or exacerbations of pre-existing hypertension. Re-evaluate whether the benefits of continued treatment with TLANDO outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease.

Polycythemia: Increases in hematocrit levels, reflective of increases in red blood cell mass, may require discontinuation of TLANDO. Check hematocrit prior to initiating TLANDO. Evaluate hematocrit approximately every 3 months during the first year of treatment, and then every 6 months thereafter while the patient is taking TLANDO. If hematocrit becomes elevated, stop TLANDO until hematocrit decreases to an acceptable concentration. If TLANDO is restarted and again causes hematocrit to become elevated, stop TLANDO permanently. An increase in red blood cell mass may increase the risk of thromboembolic events.

Cardiovascular Risk: Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men.

TLANDO can cause BP increases that can increase the risk of MACE. Patients should be informed of this possible risk when deciding whether to use or to continue to use TLANDO.

Worsening of Benign Prostatic Hyperplasia (BPH) and Potential Risk of Prostate Cancer: Patients with BPH treated with androgens are at an increased risk for worsening of signs and symptoms of BPH. Monitor patients with BPH for worsening signs and symptoms. Patients treated with androgens may be at increased risk for prostate cancer. Evaluate patients for prostate cancer, including measurement of prostate specific antigen (PSA), prior to initiating and during treatment with androgens.

Venous Thromboembolism: There have been post marketing reports of venous thromboembolic events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients using testosterone replacement products such as TLANDO. Evaluate patients who report symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those who present with acute shortness of breath for PE. If a venous thromboembolic event is suspected, discontinue TLANDO and initiate appropriate workup and management.

Abuse of Testosterone and Monitoring of Serum Testosterone Concentrations: Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication and in combination with other anabolic androgenic steroids. Anabolic androgenic steroid abuse can lead to serious cardiovascular and psychiatric adverse reactions.

If testosterone abuse is suspected, check serum testosterone concentrations to ensure they are within therapeutic range. However, testosterone levels may be in the normal or subnormal range in men abusing

synthetic testosterone derivatives. Counsel patients concerning the serious adverse reactions associated with abuse of testosterone and anabolic androgenic steroids. Conversely, consider the possibility of testosterone and anabolic androgenic steroid abuse in suspected patients who present with serious cardiovascular or psychiatric adverse events.

Not for Use in Women: Due to lack of controlled studies in women and the potential for virilizing effects, TLANDO is not indicated for use in women. Potential for Adverse Effects on Spermatogenesis: With large doses of exogenous androgens, including TLANDO, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH) possibly leading to adverse effects on semen parameters including sperm count. Patients should be informed of this possible risk when deciding whether to use or to continue to use TLANDO.

Hepatic Adverse Effects: Prolonged use of high doses of orally active 17-alpha-alkyl androgens (e.g., methyltestosterone) has been associated with serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice). Peliosis hepatis can be a life-threatening or fatal complication. Long-term therapy with intramuscular testosterone enanthate has produced multiple hepatic adenomas. TLANDO is not a 17 alpha-alkyl androgen and is not known to produce hepatic adverse effects associated with 17-alpha-alkyl androgens.

Nonetheless, patients should be instructed to report any signs or symptoms of hepatic dysfunction (e.g., jaundice). If these occur, promptly discontinue TLANDO while the cause is evaluated.

Edema: Androgens, including TLANDO, may promote retention of sodium and water. Edema, with or without congestive heart failure, may be a serious complication in patients with preexisting cardiac, renal, or hepatic disease [see Adverse Reactions (6.1)]. In addition to discontinuation of the drug, appropriate work up and management of edema may be required.

Sleep Apnea: The treatment of hypogonadal men with testosterone products may potentiate sleep apnea in some patients, especially those with risk factors such as obesity or chronic lung diseases.

Gynecomastia: Gynecomastia may develop and persist in patients being treated for hypogonadism.

Lipid Changes: Changes in serum lipid profile may require dose adjustment of lipid lowering drugs or discontinuation of testosterone therapy. Monitor the lipid profile periodically after starting testosterone therapy.

Hypercalcemia: Androgens, including TLANDO, should be used with caution in cancer patients at risk of hypercalcemia (and associated hypercalciuria). Monitor serum calcium concentrations periodically in these patients.

Decreased Thyroxine-binding Globulin: Androgens, including TLANDO, may decrease concentrations of thyroxin-binding globulins, resulting in decreased total T4 serum concentrations and increased resin uptake of triiodothyronine (T3) and thyroxine (T4). Free thyroid hormone concentrations remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

Increases in Prolactin: Increases in serum prolactin have been reported in patients treated with TLANDO in clinical trials. Evaluate serum prolactin levels prior to initiating treatment with TLANDO. Re-evaluate serum prolactin levels 3 to 4 months after starting treatment. If serum prolactin remains elevated, discontinue TLANDO.

ADVERSE REACTIONS

The safety of TLANDO was evaluated in 2 clinical studies in a total of 233 men.

Study 18-001: 138 hypogonadal males were treated with TLANDO 225 mg twice daily with morning and evening meals for approximately 4 months.

Study 16-002: 95 hypogonadal males were treated with TLANDO 225 mg twice daily with morning and evening meals for approximately 24 days.

The most commonly reported adverse reactions (≥ 2%) were: increased blood prolactin, hypertension, increased hematocrit, upper respiratory tract infection, weight increased, headache, and musculoskeletal pain.

DRUG INTERACTIONS

Insulin: Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, insulin requirements.

Oral Anticoagulants: Changes in anticoagulant activity may be seen with androgens. Frequent monitoring of INR and prothrombin time may be necessary in patients taking anticoagulants, especially at the initiation and termination of androgen therapy.

Corticosteroids: The concurrent use of testosterone with corticosteroids may result in increased fluid retention and should be monitored cautiously, particularly in patients with cardiac, renal or hepatic disease.

Drugs that May Also Increase Blood Pressure: Some prescription drugs and nonprescription analgesic and cold medications can increase blood pressure. Concomitant administration of these medications with TLANDO may lead to additional increases in blood pressure.

USE IN SPECIFIC POPULATIONS

Pregnancy: TLANDO is contraindicated in pregnant women and not indicated for use in females. Testosterone is teratogenic and may cause fetal harm when administered to a pregnant woman based on data from animal studies (see Data) and its mechanism of action. Exposure of a female fetus to androgens may result in varying degrees of virilization. In animal developmental studies, exposure to testosterone in utero resulted in hormonal and behavioral changes in offspring and structural impairments of reproductive tissues in female and male offspring. These studies did not meet current standards for nonclinical development toxicity studies. Lactation: TLANDO is not indicated for use in females.

Females and Males of Reproductive Potential: During treatment with large doses of exogenous androgens, including TLANDO, spermatogenesis may be suppressed through feedback inhibition of the hypothalamic-pituitary-testicular axis. Reduced fertility is observed in some men taking testosterone replacement therapy. The impact on fertility may be irreversible. Testicular atrophy, subfertility, and infertility have also been reported in men who abuse anabolic androgenic steroids.

Pediatric Use: The safety and effectiveness of TLANDO in pediatric patients less than 18 years old have not been established. Improper use may result in acceleration of bone age and premature closure of epiphyses.

Geriatric Use: There have not been sufficient numbers of geriatric patients in controlled clinical studies with TLANDO to determine whether efficacy or safety in those over 65 years of age differs from younger subjects. Of the 95 patients enrolled in Study 16-002, the 24-day major safety and effectiveness study utilizing TLANDO, 16 (16.8%) were over 65 years of age. Additionally, there is insufficient long-term safety data in geriatric patients utilizing TLANDO to assess the potentially increased risk of cardiovascular disease and prostate cancer.

Geriatric patients treated with androgens may also be at risk for worsening of signs and symptoms of BPH and hypertension.

DRUG ABUSE AND DEPENDENCE

TLANDO contains testosterone undecanoate, a Schedule III controlled substance.

Abuse and misuse of testosterone are seen in male and female adults and adolescents. Testosterone, often in combination with other anabolic androgenic steroids may be abused by athletes and bodybuilders.

Serious adverse reactions have been reported in individuals who abuse anabolic androgenic steroids and include cardiac arrest, myocardial infarction, hypertrophic cardiomyopathy, congestive heart failure, cerebrovascular accident, hepatotoxicity, and serious psychiatric manifestations, including major depression, mania, paranoia, psychosis, delusions, hallucinations, hostility and aggression.

The following adverse reactions have also been reported in men: transient ischemic attacks, convulsions, hypomania, irritability, dyslipidemias, testicular atrophy, subfertility, and infertility.

The following additional adverse reactions have been reported in women: hirsutism, virilization, deepening of voice, clitoral enlargement, breast atrophy, male-pattern baldness, and menstrual irregularities.

The following adverse reactions have been reported in male and female adolescents: premature closure of bony epiphyses with termination of growth, and precocious puberty.

Withdrawal symptoms can be experienced upon abrupt discontinuation in patients with addiction. Withdrawal symptoms include depressed mood, major depression, fatigue, craving, restlessness, irritability, anorexia, insomnia, decreased libido, and hypogonadotropic hypogonadism. Drug dependence in individuals using approved doses for approved indications has not been documented.

For more information, call 1-844-996-7833.

Please see full Prescribing Information, including Boxed Warning and Medication Guide.

About TLANDO XR

TLANDO XR (also known as LPCN 1111) is a next-generation, novel ester prodrug of testosterone comprised of testosterone tridecanoate (TT) which uses Lipocine's proprietary delivery technology to enhance solubility and improve systemic absorption. Lipocine has successfully completed a Phase 2b dose finding study in hypogonadal men. Results suggested that the primary objectives were met, including identifying the dose expected to be tested in a planned Phase 3 study that would be required for FDA approval.

About Verity Pharma

Verity Pharma is a specialty pharmaceutical company focused on delivering meaningful solutions to healthcare professionals and their patients.

Verity Pharma works with best-in-class global pharmaceutical manufacturing partners to ensure that product quality and availability is a constant deliverable. The company is also committed to supporting programs, initiatives, and organizations that help improve health, expand research opportunities and promote education within the healthcare community. Learn more at www.veritypharma.com.

About Lipocine

Lipocine is a biopharmaceutical company leveraging its proprietary technology platform to augment therapeutics through effective oral delivery to develop differentiated 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, 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, LPCN1154, 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 Verity Pharma's development and commercialization of TLANDO and TLANDO XR, the amount of the license fee, milestone payments, and royalty payments we will ultimately receive, Verity Pharma's ability to grow the TLANDO franchise, our product development efforts, the application of our proprietary platform in developing new treatments for CNS disorders, our product candidates and related clinical trials, our development of and filing of a NDA with the FDA for LPCN 1148, 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 to treat CNS disorders, 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 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.

SOURCE Lipocine Inc.

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