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## **Antares Pharma Announces FDA Approval Of TLANDO™, an Oral Treatment for Testosterone Replacement Therapy**

**Commercial launch expected in 2Q 2022**

EWING, N.J., March 29, 2022 (GLOBE NEWSWIRE) -- Antares Pharma, Inc. (NASDAQ: ATRS) (the "Company"), a specialty pharmaceutical company, today announced that the U.S. Food and Drug Administration granted final approval for TLANDO™ (testosterone undecanoate), an oral treatment for testosterone replacement therapy ("TRT") indicated for conditions associated with a deficiency or absence of endogenous testosterone, or hypogonadism in adult males.

Robert F. Apple, President and Chief Executive Officer of Antares Pharma, commented, "The FDA approval of TLANDO brings to market an oral formulation of testosterone that we believe will prove beneficial to physicians and their patients. We have recently expanded our commercial organization to 108 sales representatives and expect to leverage our relationships with urologists and endocrinologists to drive adoption of TLANDO. This approval also reinforces the opportunity for Antares to continue to drive share gains in the TRT market with both TLANDO and XYOSTED and support our future growth with an expanded commercial portfolio. We look forward to launching TLANDO commercially, which will provide a complementary treatment option to patients and clinicians in the second quarter of this year."

"We are excited with the opportunity to commercialize TLANDO and reinforce our commitment to the TRT market. Our existing commercial capabilities and presence in the market with XYOSTED provide an important foundation for the potential commercial success of TLANDO. With an expanded commercial footprint, we expect to continue to foster our strong physician relationships to support their patient-centric care and preference for different treatment options. We believe TLANDO's oral formulation and convenient dosing, which requires no titration, differentiates it from other treatment options. As we prepare for the commercial launch, we look forward to our sales representatives detailing a differentiated portfolio of products consisting of XYOSTED, TLANDO and NOCDURNA that will continue to deliver solutions for improved patient care," added Joe Renda, Senior Vice President, Commercial of Antares Pharma.

For full prescribing information, please visit [www.antarespharma.com](http://www.antarespharma.com).

### **About Hypogonadism**

Male hypogonadism, also known as testosterone deficiency, is an endocrine disorder in which the body fails to produce enough of the hormone. Hypogonadism is a common condition in the male population, with a higher prevalence in older men, obese men, and men with type 2 diabetes. It is estimated that approximately 35% of men older than 45 years of age and 30-50% of men with obesity or type 2 diabetes have hypogonadism<sup>1</sup>. Hypogonadism can be treated with testosterone replacement therapy.

<sup>1</sup> Endocrine Society

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

Initial U.S. Approval: 1953

### **IMPORTANT SAFETY INFORMATION**

#### **WARNING: BLOOD PRESSURE INCREASES**

- 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.

- Before initiating TLANDO, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled.
- Periodically monitor for and treat new-onset hypertension or exacerbations of pre-existing hypertension and 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.

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. 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 thyroxine-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 ( $\geq 2\%$ ) 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 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 have not been documented.

## **About Antares Pharma**

Antares Pharma, Inc. is a specialty pharmaceutical company focused primarily on the development and commercialization of pharmaceutical products and technologies that address patient needs in targeted therapeutic areas. The Company develops, manufactures and commercializes, for itself or with partners, novel therapeutic products using its advanced drug delivery systems that are designed to provide commercial or functional advantages such as improved safety and efficacy, convenience, improved tolerability, and enhanced patient comfort and adherence. The Company has a portfolio of proprietary and partnered commercial products and ongoing product development programs in various stages of development. The Company has formed partnership arrangements with several different industry leading pharmaceutical companies.

## **SAFE HARBOR STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995**

This press release contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are subject to certain risks and uncertainties that can cause actual results to differ materially from those described. Factors that may cause such differences include, but are not limited to: successful commercial launch, market acceptance, payor coverage and future prescriptions and revenue for TLANDO™; the Company's ability to achieve the 2022 revenue guidance; the uncertainty regarding the ongoing COVID-19 pandemic, including new strains of the virus, and the mitigation measures and other restrictions implemented in response to the same and the impact on demand for our products, new patients and prescriptions, future revenue, product supply, clinical trials, and our overall business, operating results and financial condition; the timing and results of the Company's or its partners' research projects or clinical trials of product candidates in development; actions by the FDA or other regulatory agencies with respect to the Company's products or product candidates of its partners; commercial success of the Company's products or partner products and continued growth in product, development, licensing and royalty revenue; the Company's ability to obtain financial and other resources for its research, development, clinical, and commercial activities and other statements regarding matters that are not historical facts, and involve predictions. These statements involve known and unknown risks, uncertainties and other factors that may cause actual results, performance, achievements or prospects to be materially different from any future results, performance, achievements or prospects expressed in or implied by such forward-looking statements. In some cases you can identify forward-looking statements by terminology such as "may", "will", "should", "would", "expect", "intend", "plan", "anticipate", "believe", "estimate", "predict", "potential", "seem", "seek", "future", "continue", or "appear" or the negative of these terms or similar expressions, although not all forward-looking statements contain these identifying words. Additional information concerning these and other factors that may cause actual results to differ materially from those anticipated in the forward-looking statements is contained in the "Risk Factors" section of the Company's Annual Report on Form 10-K, and in the Company's other periodic reports and filings with the Securities and Exchange Commission. The Company cautions investors not to place undue reliance on the forward-looking statements contained in this press release. All forward-looking statements are based on information currently available to the Company on the date hereof, and the Company undertakes no obligation to revise or update these forward-looking statements to reflect events or circumstances after the date of this press release, except as required by law.

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