

# Titan Pharmaceuticals Announces First Patients Treated With Probuphine(R) for Opioid Dependence

# More Than 1,000 Health Care Professionals Are Now Certified to Provide Probuphine

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 06/20/16 -- <u>Titan Pharmaceuticals, Inc.</u> (NASDAQ: TTNP) today announced that 10 patients received treatment last week with the Probuphine (buprenorphine) implant, making them the first patients in the United States to receive the medication since it was approved by the U.S. Food and Drug Administration (FDA) on May 26, 2016 for the maintenance treatment of opioid dependence. Probuphine was developed using Titan's long-term, continuous drug delivery platform ProNeura.

To date, more than 1,000 health care providers in 44 states have been trained and certified to provide Probuphine. More than 5,000 health care providers have requested additional information on Probuphine training and will have the opportunity to participate in one of 252 training sessions in 55 U.S. cities this summer, potentially bringing the total number of certified health care providers to more than 2,000 by the end of July and a total of more than 4,000 by the end of 2016.

According to Titan's development and commercialization partner, Braeburn Pharmaceuticals, insurance companies have also expressed strong interest in discussing how they would provide coverage for Probuphine. Several Blue Cross Blue Shield Plans, as well as United Healthcare, have been among those that approved reimbursement for the first patients implanted.

Titan granted exclusive commercialization rights to Probuphine in the U.S. and Canada to Braeburn in 2012 and is currently exploring licensing opportunities in other countries where buprenorphine treatment is part of the opioid addiction treatment practice.

## **About Opioid Addiction**

According to recent estimates, there are 2.5 million people with opioid addiction in the U.S. Approximately 20 percent of this population is addicted to illicit opioids, such as heroin, and the other 80 percent to prescription opioids, such as oxycodone, hydrocodone, methadone, hydromorphone and codeine. Before the year 2000, medication-assisted therapies for opioid dependence had been sanctioned to a limited number of facilities in the U.S. The Drug Addiction Treatment Act of 2000 (DATA 2000) allowed medical office-based treatment of opioid dependence and greatly expanded patient access to medication-assisted treatments (MAT). In 2015, the U.S. Health and Human Services Department announced it would move to expand access to medication-assisted-treatment even further by revising regulations that cap the number of patients who can be treated with buprenorphine products by physicians.

The HHS revision to the regulation will be developed to provide a balance between expanding the supply of buprenorphine-based treatment, encouraging use of evidence-based MAT, and minimizing the risk of drug diversion. Sales of buprenorphine drug products for treatment of opioid addiction in 2014 were approximately \$1.75 billion in the United States.

# About Probuphine®

Probuphine is a subdermal implant designed to deliver buprenorphine continuously for six months following a single treatment, and to promote patient compliance and retention. Buprenorphine, which is the active ingredient in multiple FDA-approved drug products for the treatment of opioid dependence, is currently available in tablet and film formulations that require self-administration by patients on a daily basis.

Probuphine was developed using ProNeura<sup>™</sup>, Titan's continuous drug delivery system that consists of a small, solid implant made from a mixture of ethylene-vinyl acetate (EVA) and a drug substance. The resulting construct is a solid matrix that is placed subdermally, normally in the upper arm in an outpatient office procedure, and removed in a similar manner at the end of the treatment period. The efficacy and safety of Probuphine have previously been studied in several clinical trials, including a 163-patient, placebo-controlled study over a 24-week period (published in the Journal of the American Medical Association (JAMA)), and a follow on study of 287 patients (published in the journal Addiction).

WARNING: IMPLANT MIGRATION, PROTRUSION, EXPULSION and NERVE DAMAGE ASSOCIATED WITH INSERTION and REMOVAL

# Risk Associated with Insertion and Removal

Insertion and removal of PROBUPHINE are associated with the risk of implant migration, protrusion, expulsion resulting from the procedure. Rare but serious complications including nerve damage and migration resulting in embolism and death may result from improper insertion of drug implants inserted in the upper arm. Additional complications may include local migration, protrusion and expulsion. Incomplete insertions or infections may lead to protrusion or expulsion.

Because of the risks associated with insertion and removal, PROBUPHINE is available only through a restricted program called the PROBUPHINE REMS Program. All Healthcare Providers must successfully complete a live training program on the insertion and removal procedures and become certified, prior to performing insertions or prescribing PROBUPHINE implants. Patients must be monitored to ensure that PROBUPHINE is removed by a healthcare provider certified to perform insertions.

Please see additional Important Safety Information in the Package Insert that can be found at probuphine.com or by following this link <a href="http://probuphinerems.com/wp-content/uploads/2016/02/final-approved-pi.pdf">http://probuphinerems.com/wp-content/uploads/2016/02/final-approved-pi.pdf</a>.

## About Titan Pharmaceuticals

Titan Pharmaceuticals Inc. (NASDAQ: TTNP), based in South San Francisco, CA, is a specialty pharmaceutical company developing proprietary therapeutics primarily for the treatment of serious medical disorders. The company's lead product is Probuphine®, a novel and long-acting formulation of buprenorphine for the long-term maintenance treatment of opioid dependence. Probuphine employs Titan's proprietary drug delivery system

ProNeura<sup>™</sup>, which is capable of delivering sustained, consistent levels of medication for three months or longer. Titan has granted U.S. and Canadian commercial rights for Probuphine to Braeburn Pharmaceuticals. Probuphine is the first and only commercialized treatment of opioid dependence to provide continuous, around-the-clock blood levels of buprenorphine for six months following a single procedure. The ProNeura technology has the potential to be used in developing products for treating other chronic conditions, such as Parkinson's disease, where maintaining consistent blood levels of a therapeutic agent may benefit the patient and improve medical outcomes. For more information about Titan, please visit <a href="https://www.titanpharm.com">www.titanpharm.com</a>.

This press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Such statements include, but are not limited to, any statements relating to our product development programs and any other statements that are not historical facts. Such statements involve risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from management's current expectations include those risks and uncertainties relating to the regulatory approval process, the development, testing, production and marketing of our drug candidates, patent and intellectual property matters and strategic agreements and relationships. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.

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