

June 15, 2016



# **Titan Pharmaceuticals Announces Rigorous Sensitivity Analyses Confirm Effectiveness of Probuphine(R) for Opioid Dependence**

## **Poster on Analyses Presented at College of Problems of Drug Dependence 78th Annual Meeting**

PALM SPRINGS, CA -- (Marketwired) -- 06/15/16 -- [Titan Pharmaceuticals, Inc.](#) (NASDAQ: TTNP) today announced the planned presentation of data from four post hoc sensitivity analyses of the final Phase 3 trial of Probuphine®, a six-month subdermal buprenorphine implant for the long-term maintenance treatment of opioid dependence, at a poster session on June 15 during The College on Problems of Drug Dependence 78th Annual Meeting in Palm Springs. The sensitivity analyses, commonly conducted following the primary analysis to test the robustness of the data, consistently support previous findings that participants who were clinically stable on sublingual buprenorphine at a dose of 8mg a day or less maintained stability when transferred to treatment with Probuphine.

On May 26, 2016, the [U.S. Food and Drug Administration approved Probuphine](#) for the long-term maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged stability on low-to-moderate doses of buprenorphine.

The poster, titled "Sensitivity Analyses of a Comparative Trial of 6-month Buprenorphine Implants (Probuphine) and Sublingual Buprenorphine in Stable Opioid Dependent Patients," will be presented on June 15 from 12:15 p.m. to 2:15 p.m. by Frank J. Vocci, Ph.D., Friends Research Institute. The data presented are from the double-blind, double-dummy study, which was designed to compare the efficacy of Probuphine to sublingual buprenorphine in stable patients maintained on 8mg or less daily doses of sublingual buprenorphine.

The primary efficacy endpoint was the proportion of responders, defined as participants with at least four of six months without evidence of illicit opioid use by urine test and by self-report. As previously reported, the study met its primary endpoint as well as all secondary endpoints, and the treatment was well tolerated by the study subjects. Post-hoc sensitivity analyses of responder rates were performed to further test the pre-specified endpoints and primary analysis detailed in the Statistical Analysis Plan provided to the FDA. Additional details are included in the poster presentation, which was co-authored by Richard N. Rosenthal, MD, Professor of Psychiatry and Medical Director of Addiction Psychiatry at the Icahn School of Medicine at Mount Sinai; Michelle R. Lofwall, M.D., University of Kentucky College of Medicine, Center on Drug and Alcohol Research in Lexington, Kentucky; Sonnie Kim, Ph.D., Braeburn Pharmaceuticals; Katherine L. Beebe, Ph.D., Titan Pharmaceuticals;

Michael Chen, Ph.D., TCM Groups, Inc.; and Frank J. Vocci, Ph.D., Friends Research Institute.

"These post hoc sensitivity analyses showed that even under the most conservative method, the Probuphine long-acting subdermal implant demonstrated efficacy in direct comparison with sublingual buprenorphine," said co-lead investigator and an author of the presentation Richard N. Rosenthal, M.D., Professor of Psychiatry and Medical Director of Addiction Psychiatry at the Icahn School of Medicine at Mount Sinai. "Importantly, the analyses also supported previous findings that participants treated with the Probuphine implant were more likely to remain free of illicit opioids compared with those on sublingual buprenorphine. These results hold great promise for Probuphine as a new option for clinicians and patients seeking greater access to medications for the maintenance treatment of opioid addiction."

"This study further demonstrated the robustness of the data in the pre-specified analysis provided to the FDA, and we are pleased to be presenting the results at this scientific meeting," said Kate Beebe, Ph.D., executive vice president and chief development officer of Titan Pharmaceuticals. "To date, Braeburn has certified more than 800 health care providers nationwide under the Probuphine REMS program, a reflection of the great need for new treatments for opioid addiction."

Probuphine was developed using Titan's proprietary platform technology, ProNeura™, a non-biodegradable drug delivery implant designed to provide continuous, long-term steady state levels of medication in the blood. Titan licensed rights to Probuphine in the U.S. and Canada to Braeburn Pharmaceuticals in 2012.

### ***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™, 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, and 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](http://probuphinerems.com/wp-content/uploads/2016/02/final-approved-pi.pdf) or by following this link <http://probuphinerems.com/wp-content/uploads/2016/02/final-approved-pi.pdf>.

***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™, 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 [www.titanpharm.com](http://www.titanpharm.com).

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*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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