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# Titan Pharmaceuticals Receives \$15 Million Milestone Payment Following FDA Approval of Probuphine(R)

## More Than 800 Health Care Providers Already Certified Under the Probuphine REMS Program

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 06/13/16 -- [Titan Pharmaceuticals, Inc.](#) (NASDAQ: TTNP) today announced it has received a \$15 million milestone payment from development and commercialization partner Braeburn Pharmaceuticals following the [approval by the U.S. Food and Drug Administration](#) of Probuphine®, the first 6-month maintenance treatment of opioid dependence. Under terms of the licensing agreement, Braeburn will pay Titan tiered royalties on net sales in the U.S. and Canada at rates ranging from the mid-teens to low-twenties, and additionally, Titan is eligible for up to \$165 million in milestone payments based on achievement of certain annual sales targets.

"The FDA's approval of Probuphine is an important validation of our ProNeura™ continuous, long-term drug delivery platform," said Titan President and CEO Sunil Bhonsle. "The \$15 million milestone payment helps support the near-term development activities for the ProNeura product candidates for Parkinson's disease and hypothyroidism. We applaud Braeburn's focused efforts in the commercial launch of Probuphine and look forward to the additional resources Probuphine could potentially generate for Titan as we evaluate development opportunities for other chronic diseases and add to our product pipeline."

Immediately following the FDA approval of Probuphine, Braeburn commenced commercial launch activities, starting with the training for healthcare providers outlined in the approved Risk Evaluation and Mitigation Strategies (REMS). To date, Braeburn has certified 807 health care providers who are now qualified to prescribe and/or perform the treatment procedure. This comprehensive training program is being conducted across 55 cities nationwide. Braeburn expects to train at least 2,000 health care providers by the end of July 2016, and more than 4,000 healthcare providers by the end of the year.

"We are encouraged by the overwhelmingly positive response to Probuphine from the medical community in such a short period, and are very pleased with Braeburn's commitment to ensure swift and broad access to this important long-term, maintenance treatment for opioid addiction," said Kate Beebe, PhD., Titan's executive vice president and chief development officer. "Along with the positive response from providers, Braeburn has also received interest from several insurance companies in discussing the addition of Probuphine to their formularies. The medical communications program is also in progress, with recent presentations of pharmacoeconomic modeling data at the Academy of Managed Care Pharmacy (AMCP) and Council of State and Territorial Epidemiologists (CSTE)

showing that Probuphine patients were predicted to have a 45% lower chance of relapse, an 80% lower chance of going to rehab and a 98% lower chance of pediatric exposure vs. patients taking oral buprenorphine."

Probuphine was developed using Titan's long-term, continuous drug delivery platform, ProNeura. It is the first implant for the maintenance treatment of opioid dependence in patients who have sustained clinical stability on low-to-moderate doses of buprenorphine, specifically 8 mg or less per day. Probuphine will be available under a REMS-controlled distribution procedure and patients can only receive the treatment from certified health care providers who have been specially trained to insert the implants just under the skin of the inside of the upper arm through a simple, in-office procedure. A Probuphine health care provider locator is available at [www.probuphineREMS.com](http://www.probuphineREMS.com).

Probuphine is the only treatment for opioid dependence that delivers buprenorphine continuously for six months. Buprenorphine is the most commonly prescribed medication for the treatment of opioid dependence, but until the availability of Probuphine it was only available in daily dosed sublingual (oral) formulations. Probuphine offers the potential to address issues associated with oral buprenorphine such as poor compliance, misuse, diversion and accidental pediatric exposure.

Titan granted exclusive commercialization rights to Probuphine in the U.S. and Canada to Braeburn in 2012 and, per the Licensing Agreement, Titan will transfer the U.S. New Drug Application (NDA) to Braeburn this week. Titan has retained rights to reference the information in the NDA for potential approval of Probuphine outside of the U.S. 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™, 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).

*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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