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Titan Pharmaceuticals Reports Positive Results From Phase 3 Study of Probuphine for Opioid Addiction

New Drug Application Expected to Be Resubmitted in Second Half of 2015 Titan to Host Conference Call Today at 9 a.m. EDT

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 06/08/15 -- Titan Pharmaceuticals, Inc. (OTCQB: TTNP) today reported positive topline results from the Phase 3 double blind, double dummy clinical study of Probuphine®, the company's subdermal implant containing buprenorphine HCl for the long-term maintenance treatment of opioid addiction. This study met the pre-specified primary endpoint of non-inferiority, as well as all secondary efficacy endpoints. It was conducted by Titan's commercialization and development partner Braeburn Pharmaceuticals and developed in consultation with the U.S. Food and Drug Administration (FDA) prior to initiating the study.

The subjects in this Phase 3 study were clinically stable patients receiving maintenance treatment with an approved sublingual dose of buprenorphine/naloxone at a daily dose of 8mg or less for at least three months prior to entering the trial. The study enrolled 177 subjects who were randomized to receive either the Probuphine implants or sublingual tablets for a treatment period of six months. Subjects in one group received four Probuphine implants plus daily placebo sublingual tablets, and subjects in the second group received four placebo implants plus daily sublingual buprenorphine/naloxone tablets (£8mg/day).

The objective of the study was to show non-inferiority between the two treatment groups and the primary efficacy analysis was a non-inferiority comparison of the proportions of treatment responders in each group. A responder was defined as having at least four out of six months free of illicit opioids based on urine testing and subject self-report. Analyses conducted according to the pre-planned Statistical Analysis Plan indicate response rates of 96.4% for the Probuphine arm and 87.6% for the sublingual buprenorphine/naloxone arm. The two-sided 95% confidence interval (0.009, 0.167) of the treatment difference (Probuphine - sublingual buprenorphine/naloxone) was well within the pre-defined successful margin for non-inferiority. The overall safety and tolerability profiles for each treatment group were also comparable. The implantation procedures were also generally well tolerated and comparable to observations from earlier studies with Probuphine.

"This study provided the best opportunity to assess the safety and effectiveness of maintenance treatment with Probuphine based on a comparison with the current standard of care. We are extremely pleased with these strong results, which we believe underscore the important clinical benefits that Probuphine may be able to provide," said Kate Glassman Beebe, PhD, Titan's executive vice president and chief development officer. "We appreciate

the hard work by the Braeburn team in completing this study rapidly, and we would like to thank the subjects, clinical investigators and their staff who participated in this trial. We would also like to extend a special thanks to NIDA (National Institute on Drug Abuse) for its early support of the overall development program. We look forward to resubmitting the NDA later this year and to potentially securing approval for the product in the first half of 2016."

"These positive results and the potential availability of Probuphine as a treatment option next year are very important to the clinical community, as there is a critical need for addiction treatments that have the potential to increase patient compliance and decrease the risk of diversion," said Dr. Walter Ling, a clinical investigator in the study and founding director of Integrated Substance Abuse Programs at the David Geffen School of Medicine at University of California, Los Angeles. "As a subdermal implant, Probuphine could minimize the risk of abuse, and, with continuous drug delivery providing around-the-clock medication for six months, Probuphine could become a particularly valuable new tool in the maintenance treatment of opioid addiction."

Highlights of the trial include:

- There were 177 subjects randomized in the study and 173 subjects were included in the Intent to Treat (ITT) population; 89 in the sublingual buprenorphine/naloxone arm and 84 in the Probuphine arm.
- There were 78 (87.6%) responders in the sublingual buprenorphine/naloxone arm and 81 (96.4%) responders in the Probuphine arm.
- The number of subjects with all six months testing negative for urines with no evidence of illicit opioid use was significantly higher in the Probuphine arm (88%) than the sublingual buprenorphine/naloxone arm (72%), ($p=0.008$).
- In order to further evaluate the observed numerical difference between the proportion of responders on the two treatment arms, a sequential superiority analysis was conducted that indicates a statistically significant difference in favor of Probuphine over the sublingual buprenorphine/naloxone treatment arms ($p< 0.05$).
- Symptoms of opioid withdrawal and cravings across the six month study were comparable in both treatment arms.
- The overall safety profile was comparable between treatment groups, and the implant insertion and removal procedures were generally well tolerated; 23% of Probuphine treated subjects and 13.5% of subjects in the sublingual buprenorphine/naloxone group had an implant site adverse event, the majority of which were assessed by the clinical investigators as "mild" in severity.

"We are very pleased with these results, and look forward to resubmitting the Probuphine NDA in the next few months," said Behshad Sheldon, president and CEO of Braeburn Pharmaceuticals. "Long-acting buprenorphine products such as Probuphine have an important role to play in combatting a national epidemic of opioid addiction. We are committed to developing convenient, long-term treatment options for opioid addiction and welcome the opportunity to make Probuphine, if approved by the FDA, available to physicians and patients as our first product."

This clinical study was designed in consultation with the FDA to address a key question in the Complete Response Letter issued in April 2013 regarding the clinical benefit of Probuphine. Titan and Braeburn intend to resubmit the New Drug Application (NDA) for Probuphine to the FDA in the second half of this year. The NDA is still considered to be

under priority review by the FDA based on Probuphine's potential for decreased abuse, diversion, overdose, and pediatric exposure risk.

If approved by the FDA, Probuphine would be the first marketed product to provide maintenance treatment of opioid addiction continuously for six months following a single procedure. 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. It is administered in a short subdermal insertion procedure in a physician's office, and removed similarly at the end of the treatment period.

"Opioid addiction, from heroin to prescription painkillers, remains at crisis levels in the United States. It is ruining lives, tearing apart families and in some cases devastating entire communities," said Dr. Genie L. Bailey, a clinical investigator in the study and clinical associate professor of psychiatry and human behavior at the Warren Alpert Medical School of Brown University. "While we have advanced our understanding of the science of addiction, there is no question that significant unmet medical need remains as patients and their families continue to struggle with this disease. Probuphine holds great promise, not just because of its potential for treating opioid addiction, but also because, as a six-month implant, it allows patients to resume their lives without the constant reminder of their addiction."

Conference Call

Titan will host a live conference call at 9 a.m. EDT/6 a.m. PDT today to discuss the Phase 3 results. The call can also be accessed by dialing *888-471-3843*, participant code 9999615, five minutes prior to the start time. The live webcast of the call may be accessed by visiting the Titan website at www.titanpharm.com. A replay of the call will be available on the Titan website approximately two hours after completion of the call and will be archived for two weeks.

About Opioid Addiction

According to recent estimates, there are 2.2 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. 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 an investigational 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 has 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*).

About Titan Pharmaceuticals
Titan Pharmaceuticals Inc. (OTCQB: 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 candidate 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 six months or longer. Titan has granted North American commercial rights for Probuphine to Braeburn Pharmaceuticals. If approved, Probuphine would be 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 dopamine agonist may benefit the patient and improve medical outcomes. For more information about Titan, please visit 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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