October 22, 2019

Titan Pharmaceuticals To Present Two Posters On Probuphine® At The 10th American Conference On Pharmacometrics

SOUTH SAN FRANCISCO, Calif., Oct. 22, 2019 /PRNewswire/ -- Titan Pharmaceuticals, Inc. (NASDAQ: TTNP) today announced that it has two poster presentations on Probuphine (buprenorphine) implant, Titan's novel 6-month maintenance treatment for Opioid Use Disorder ("OUD") in eligible patients, at the 10th American Conference on Pharmacometrics taking place on October 20-23, 2019 in Orlando, FL.

The poster presentations will provide details of the results from computer modeling studies that assessed the population pharmacokinetic ("PK") parameters, exposure-response profiles, and drug-drug interaction ("DDI") potential of the patient plasma levels of buprenorphine during treatment with Probuphine subdermal implants. These analyses are based on data from Titan's PRO-805, PRO-806, PRO-807, PRO-810 and PRO-811 Phase 3 clinical studies with Probuphine in subjects with OUD.

"We are pleased to present the findings on Probuphine's PK, exposure-response and DDI profiles at this conference," said Titan's Executive Vice President and Chief Scientific Officer, Kate DeVarney, Ph.D. "The population PK study found that the only significant demographic impacts on buprenorphine absorption and clearance from Probuphine treatment were body mass index and body weight, respectively. The exposure-response analysis established that there was a plateau for maximum efficacy at a relatively low range of plasma buprenorphine concentrations and that the clinical response as measured by urine testing was not significantly enhanced at higher concentrations in this Emax model. Finally, the DDI simulation study suggests that buprenorphine exposure from Probuphine is not significantly affected by a strong inhibitor of CYP3A4, and is decreased by only 25-30% with a strong inducer of CYP3A4."

Dr. DeVarney continued, "Taken together, these results suggest that the PK profiles for

Probuphine are highly predictable, and that the maximum clinical benefit of buprenorphine for the treatment of OUD can be achieved in eligible patients at relatively low blood concentration levels. Further, the potential for DDI on buprenorphine exposure from Probuphine is similar to that reported for other marketed buprenorphine formulations."

Poster Presentation Details:

Poster Presentation #1: Population Pharmacokinetic Modeling and Exposure-Response Analysis of Probuphine Implants in Opioid Use Disorder Subjects
Authors: Olivier Barriere, Nathalie H. Gosselin, and Nada Farhat, Certara Strategic Consulting; Markus Jerling, Markus Jerling Consulting AB; and Sunil Sreedharan, Titan Pharmaceuticals, Inc.
Date: Tuesday, October 22, 2019

Poster Presentation #2: Evaluation of Drug-Drug Interaction Potential of Probuphine Implants using a Physiologically-Based Pharmacokinetic Model
Authors: Jogarao Gobburu, University of Maryland School of Pharmacy; and Sunil Sreedharan, Titan Pharmaceuticals Inc.
Date: Wednesday, October 23, 2019

About Probuphine

Probuphine is the only subdermal implant designed to deliver buprenorphine continuously for six months following insertion.

Probuphine was developed using ProNeura®, the continuous drug delivery system developed by Titan that consists of a small, solid implant made from a mixture of ethylene-vinyl acetate and a drug substance. The resulting construct is a solid matrix that is placed subdermally, normally in the upper inner arm in an outpatient office procedure and removed in a similar manner at the end of the treatment period. The U.S. Food and Drug Administration ("FDA") approved Probuphine in May 2016, and it is the first and only buprenorphine implant available for the maintenance treatment of opioid addiction in eligible patients.

IMPORTANT SAFETY INFORMATION INCLUDING INDICATION AND **BOXED WARNING**

INDICATION

PROBUPHINE is an implant that contains the medicine buprenorphine. PROBUPHINE is used to treat certain adults who are addicted to (dependent on) opioid drugs (either prescription or illegal). PROBUPHINE is indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses (doses no more than 8 mg per day) of a buprenorphine-containing product.

PROBUPHINE is part of a complete treatment program that also includes counseling and behavioral therapy.

It is not known if PROBUPHINE is safe or effective in children less than 16 years of age.

IMPORTANT SAFETY INFORMATION

WARNING: COMPLICATIONS FROM INSERTION AND REMOVAL OF PROBUPHINE
See Full Prescribing Information for complete Boxed Warning

Serious complications may happen from insertion and removal of PROBUPHINE, including:

- Nerve or blood vessel injury in your arm
- Movement of implant (migration). PROBUPHINE or pieces of it can move into blood vessels, possibly to your lung, and could lead to death
- Implant sticks out of the skin (protrusion)
- Implant comes out by itself (expulsion)

Call your healthcare provider right away if:

- PROBUPHINE sticks out of the skin or comes out by itself
- You have bleeding or symptoms of infection at the site after insertion or removal, including excessive or worsening itching, pain, irritation, redness, or swelling
- You have numbness or weakness in your arm after the insertion or removal procedure
- You have weakness or numbness in your arm, or shortness of breath

If the implant comes out by itself, keep it away from others, especially children, as it may cause severe difficulty in breathing and possibly death.

Because of the risk of complications of, migration, protrusion, expulsion and nerve injury with insertion and removal of PROBUPHINE, it is only available through a restricted program called the PROBUPHINE REMS Program. Healthcare providers who prescribe and/or insert PROBUPHINE must be certified with the program by enrolling and completing live training.

- PROBUPHINE is not available in retail pharmacies
- PROBUPHINE must be inserted or removed only in the facility of the certified prescriber

Implants may be difficult to locate if inserted too deeply, if you manipulate them, or if you gain significant weight after insertion. Your healthcare provider may do special procedures or tests, or refer you to a surgical specialist to remove the implants if they are difficult to locate.

The medicine in PROBUPHINE can cause serious and life-threatening problems, especially if you take or use certain other medicines or drugs. Call your healthcare provider right away or get emergency help if you:

Feel faint or dizzy, have mental changes such as confusion, slower breathing than you normally have, severe sleepiness, blurred vision, problems with coordination, slurred speech, cannot think well or clearly, high body temperature, slowed reflexes, feel agitated, stiff muscles or have trouble walking.

These can be signs of an overdose or other serious problems.

Coma or death can happen if you take anxiety medicines or benzodiazepines, sleeping pills, tranquilizers, or sedatives, antidepressants, or antihistamines, or drink alcohol during treatment with PROBUPHINE. Tell your healthcare provider if you are taking any of these

medicines or if you drink alcohol.

Who should not use PROBUPHINE?

Do not use PROBUPHINE if you are allergic to buprenorphine or any of its ingredients, this includes buprenorphine hydrochloride and the inactive ingredient ethylene vinyl acetate or EVA.

PROBUPHINE may not be right for you. Before starting PROBUPHINE tell your doctor about all of your medical conditions, including:

Trouble breathing or lung problems, an enlarged prostate gland (men), a head injury or brain problem, problems urinating, a curve in your spine that affects your breathing, liver problems, gallbladder or adrenal gland problems, Addison's disease, low thyroid hormone levels (hypothyroidism), a history of alcoholism, a history of keloid formation, connective tissue disease (such as scleroderma), or history of MRSA infections, mental problems such as hallucinations, an allergy to numbing medicines or medicines used to clean your skin, are pregnant or plan to become pregnant or are breastfeeding or plan to breastfeed.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

What should I avoid while being treated with PROBUPHINE?

- **Do not drive, operate heavy machinery, or perform any other dangerous activities until you know how this medication affects you**
- **You should not drink alcohol** during treatment. You should not take anxiety medicines or benzodiazepines, sleeping pills, tranquilizers, or sedatives that are not prescribed to you during treatment with PROBUPHINE, as this can lead to slowed breathing, drowsiness, delayed reaction time, loss of consciousness or even death

What are the possible side effects of PROBUPHINE?

PROBUPHINE can cause serious side effects, including:

- **Infection at the insertion or removal site.** Infection may happen at the implant site during insertion or removal. Do not try to remove PROBUPHINE yourself
- **Opioid withdrawal.** If PROBUPHINE comes out of your arm or if you stop treatment, tell your doctor right away as you can have symptoms of shaking, sweating more than normal, feeling hot or cold more than normal, runny nose, watery eyes, goose bumps, diarrhea, vomiting and muscle aches
- **Physical dependency**
- **Liver problems**. Call your doctor right away if you notice signs of liver problems that may include your skin or the white part of your eyes turning yellow (jaundice)
- **Allergic reaction.** If you get a rash, hives, itching, swelling of your face, or wheezing, low blood pressure, dizziness or decrease in consciousness
- **Decrease in blood pressure**. You may feel dizzy when you get up from sitting or lying down

Tell your healthcare provider if you develop any of the symptoms listed.

Common side effects of PROBUPHINE include: Headache, nausea, toothache, constipation, depression, vomiting, back pain, mouth and throat pain.

Common risks with the minor surgical procedure: Itching, pain, irritation, redness, swelling, bleeding, or bruising at the insertion or removal site. Scarring around the insertion site.

Please read Full Prescribing Information, including **BOXED WARNING regarding IMPLANT MIGRATION, PROTRUSION, EXPULSION and NERVE DAMAGE ASSOCIATED WITH INSERTION AND REMOVAL.**

Titan encourages you to report negative side effects of prescription drugs to the FDA. You can visit www.fda.gov/safety/medwatch/ or call 1-800-FDA-1088.

About Titan Pharmaceuticals

Titan Pharmaceuticals, Inc. (NASDAQ:TTNP), based in South San Francisco, CA, is a commercial stage company developing proprietary therapeutics with its ProNeura® long-term, continuous drug delivery technology. The company's lead product is Probuphine® (buprenorphine) implant, a novel and long-acting formulation of buprenorphine for the long-term maintenance treatment of opioid dependence. Approved by the U.S. Food and Drug Administration in May 2016, 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 also has the potential to be used in developing products for treating other chronic conditions such as Parkinson's disease and hypothyroidism, where maintaining consistent, around-the-clock blood levels of medication may benefit the patient and improve medical outcomes. For more information about Titan, please visit www.titanpharm.com.

Forward-Looking Statements

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 commercialization of Probuphine, 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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View original content to download multimedia:http://www.prnewswire.com/news-releases/titan-pharmaceuticals-to-present-two-posters-on-probuphine-at-the-10th-american-conference-on-pharmacometrics-300942654.html

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