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Titan Announces Positive Results from the First Studies of TP-2021 Implant in an Established Animal Model of Chronic Pruritus

SOUTH SAN FRANCISCO, Calif., June 23, 2021 /PRNewswire/ -- Titan Pharmaceuticals, Inc. (NASDAQ: TTNP) today announced that the in vivo study of its human kappa-opioid receptor agonist ("TP-2021," formerly JT-09) ProNeura®-based implant in an established 5'-guanidinonaltrindole (5'-GNTI) itch-induced mouse model, has demonstrated the potential to provide extended efficacy and durability in the treatment of moderate-to-severe chronic pruritus (itch).

As previously reported, subcutaneously injected (0.3mg/kg) TP-2021 was compared to difelikefalin (Korsuva™, which is in late-stage development by Cara Therapeutics, Inc. across multiple indications, including intravenous treatment of hemodialysis patients with chronic pruritus), and was observed to be equally potent in reducing scratching and grooming behaviors in this established animal itch model, in studies conducted in collaboration with Charles Chavkin, Ph.D., the Allan and Phyllis Treuer Endowed Chair of Pain Research and Professor, Department of Pharmacology, at the University of Washington Health Sciences Center, Seattle, WA.

Based on the positive data with subcutaneous injection of TP-2021 and the selective binding exhibited by TP-2021 at the kappa opioid receptor, Titan tested ProNeura-based TP-2021 implants in an initial study, also conducted in collaboration with Dr. Chavkin. Following implantation of one TP-2021 prototype implant, the treated and untreated control mice were repeatedly challenged with 5'-GNTI. The results from these studies demonstrated that the experimental TP-2021 implants provided sustained itch suppression for a period of 14 days post-implantation. In addition, mice were sampled for pharmacokinetic analysis following subcutaneous acute injection with TP-2021 (0.3 mg/Kg) in saline or following implantation with one TP-2021 implant. The results indicate that the mouse implant provided sustained plasma concentrations of TP-2021 that were well above the levels observed to provide

therapeutic anti-pruritus activity after acute administration. This is a clear early demonstration of the potential of TP-2021 implants for long-term treatment of pruritus, and of Titan's proprietary ProNeura implant platform to provide in-vivo long-term delivery of peptides at biologically-active concentrations.

"Chronic pruritus is a debilitating condition with no satisfactory medical treatment available today, and the recent advances with kappa opioid receptor agonist treatments are very promising,' said Dr. Chavkin. "The results of these nonclinical studies with TP-2021 implants are very encouraging, and indicate that sustained delivery of kappa opioid receptor agonists should be able to provide long-term anti-pruritus benefits in humans. The concept of long-term treatment using implants can potentially provide an important breakthrough, with continuous delivery of therapeutic blood levels of medication, potentially avoiding the need for frequent IV administration."

"TP-2021 is a small peptide, and the sustained delivery and associated biological activity of peptides has historically been difficult to attain beyond several hours after administration, typically due to enzymatic degradation in the blood," said Kate Beebe DeVarney, Ph.D., President and Chief Operating Officer of Titan. "Having established that ProNeura-based prototype implants can provide continuous delivery of TP-2021 in this murine efficacy model, we will now fine-tune and optimize the TP-2021 implant to show significantly longer duration of release in larger animal models. This will further support the capability of attaining substantially longer target plasma levels in humans, with the goal of delivering efficacious therapy for six months or longer following a single subdermal implantation. We have extensive prior experience with this process, and believe we have the necessary proprietary know-how to manufacture cGMP quality implants required to complete the requisite nonclinical safety and pharmacology studies that will allow filing of an Investigational New Drug (IND) application for human clinical development of this novel treatment."

Marc Rubin, M.D. Titan's Executive Chairman, added, "At Titan we have successfully returned our focus to product development, our true and proven core competency. Importantly, in addition to our progress on TP-2021 and on the nalmefene implant development program for Opioid Use Disorder, which is supported by a grant from the National Institute on Drug Abuse, we have confidence that the ProNeura platform has the potential for application in a number of additional settings, and we look forward to future partnering opportunities in order to further expand Titan's product development pipeline."

About Chronic Pruritus

Chronic pruritus is an unpleasant and often debilitating condition, resulting in the need to scratch that lasts more than 6 weeks. It is a prevalent and bothersome symptom associated with both cutaneous and systemic conditions. Due to its complex pathogenesis and numerous contributing factors, effective treatment of chronic pruritus therapy remains challenging.

About Titan Pharmaceuticals

Titan Pharmaceuticals, Inc. (NASDAQ: TTNP) is a development-stage biotechnology company developing proprietary therapeutics using its clinically proven ProNeura® long-term, continuous drug delivery technology. The ProNeura technology has the potential to be used in developing products for treating a number of chronic conditions 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 our ability to raise capital, the completion of final steps in the winding down of U.S. commercial activities related to 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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