

TITAN PHARMACEUTICALS

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ProNeura® platform technology provides continuous delivery, maintaining a stable blood level of select drugs for the treatment of chronic conditions

ProNeura has demonstrated viability with prior product approvals in the U.S., Canada and EU

Titan is a development-stage company, focusing on two key ProNeura-based product candidates:

- Kappa opioid receptor agonist (TP-2021) implant for moderate-to-severe chronic pruritus
- Nalmefene implant for the treatment of opioid use disorder (OUD) in adults following detoxification from opioids



EXPERIENCED MANAGEMENT EXECUTIVE TEAM & BOARD OF DIRECTORS



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Executive Chairman, Director



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Director



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Director



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Director



NOVEL DRUG DELIVERY PLATFORM- PRONEURA

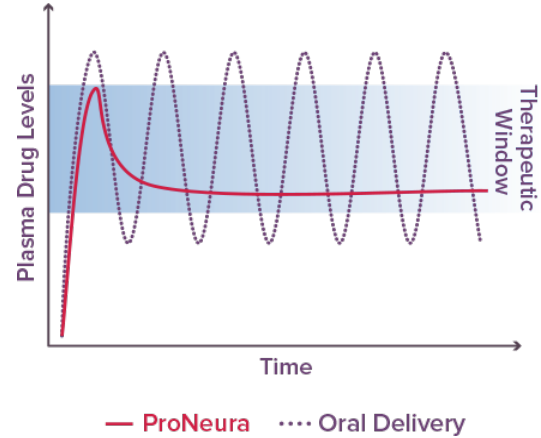
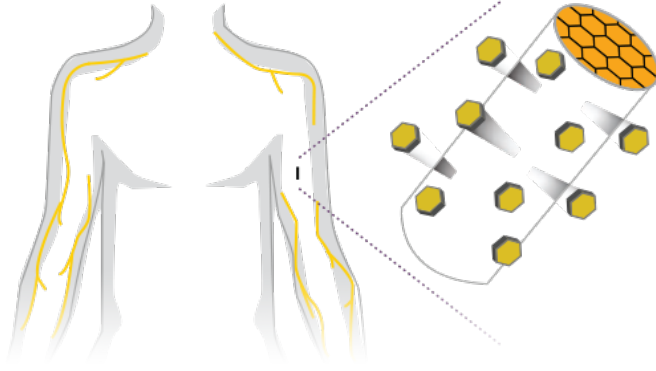
LONG-TERM, CONTINUOUS DRUG DELIVERY



- Active pharmaceutical ingredient (API) uniformly distributed throughout the ethylene vinyl acetate co-polymer (EVA) matrix
- No reservoir; therefore, no risk of drug dumping
- Controlled rate of drug delivery and essentially 100% bioavailability
- Intellectual Property
 - Issued patents for heterogeneous co-extruded implantable devices for drug delivery of a wide variety of compounds

PRONEURA

MECHANISM OVERVIEW



- Inserted subdermally
- Drug is released continuously through the process of dissolution
- Results in a stable level of medication in the blood, avoiding peaks and troughs of oral dosing
- Around-the-clock long-term treatment (6 months or longer) in outpatient setting

▲ **Higher drug loading %, lower EVA%**

- = Larger sized pores
- = Higher rate of drug release

▲ **Larger sized implants**

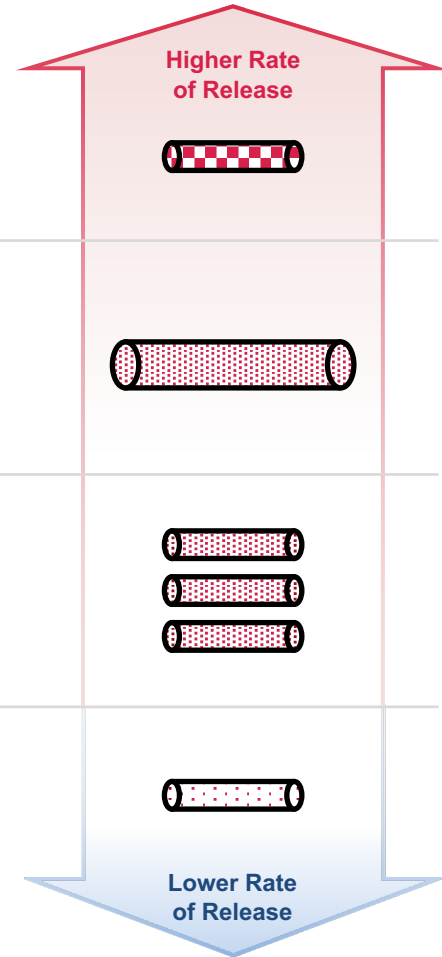
- = Greater surface area
- = Increased number of pores
- = Higher rate of drug release

▲ **Multiple implants**

- = Greater overall surface area
- = Increased number of pores
- = Higher rate of drug release

▼ **Lower drug loading %, greater EVA%**

- = Smaller-sized pores
- = Fewer pores
- = Lower rate of drug release





About Chronic Pruritus

- Potentially debilitating condition defined as moderate-to-severe itch lasting longer than 6 weeks
- Estimated U.S. patient population = **23 - 44 million**¹
- Significant unmet need
 - Current treatments are only marginally effective
 - Often associated with undesirable side-effects

1. Mollanazar N., et al. Epidemiology of Chronic Pruritus: Where Have We Been and Where Are We Going? **Current Dermatology Reports** 4:20–29 (2015)

KAPPA OPIOID RECEPTOR AGONISTS (KOAs) FOR PRURITUS

THE SCIENCE

- Antipruritic effect thought to be related to their binding to kappa-opioid receptors (KORs) on keratinocytes, immune cells, and peripheral itch neurons
- Nalfurafine is a CNS-penetrant antipruritic marketed in Japan for the treatment of uremic pruritus in individuals with chronic kidney disease undergoing hemodialysis
 - Not approved in U.S. or EU
- Peripherally-restricted KOAs, such as CR845 (Korsuva™) demonstrated efficacy in treating pruritus with a limited side-effect profile¹

1. Cara Therapeutics (2020) Study to Evaluate IV CR845 in Hemodialysis Patients With Moderate-to-Severe Pruritus (<https://clinicaltrials.gov/ct2/show/NCT02858726>)

- Cara Therapeutics recently filed an NDA for Korsuva, a KOA peptide, for the treatment of moderate-to-severe uremic pruritus in patients undergoing hemodialysis
- For this potential indication, Korsuva is given several times per week, immediately following hemodialysis
- Non clinical experiments indicate that TP-2021 has comparable potency to Korsuva

ProNeura implant containing TP-2021 could potentially eliminate the need for daily or weekly administration by delivering low-dose, non-fluctuating medication levels for six months or longer following a single in-office procedure

NEXT STEPS



Q2-Q3 2021

- Multiple dose proof of concept study of TP-2021 in an animal model of induced pruritus

H2 2021

- Initiate IND-enabling safety and pharmacology studies following pre-IND guidance from the FDA

- NIDA-funded development program: \$8.7 mil for formulation development and IND related non-clinical studies
 - Completed formulation development
 - Pre-IND meeting with FDA provided clear guidance on non-clinical requirements
 - Expected completion in mid-2021
- Nalmefene approved by the FDA in 1995 as an injectable formulation (Revex®) for the management and reversal of opioid overdose, including respiratory depression
- Oral nalmefene was approved by the EMA in 2013 for treating alcohol dependence
- Nalmefene is ideal for delivery with Titan's ProNeura platform
 - 1-2 implants/subject could potentially provide ~80% blockage of mu opioid receptors
 - 6 months or longer delivery for prevention of relapse to opioid dependence after detoxification

Innovative & Proprietary ProNeura Drug Delivery Platform

Success Bringing Product From Preclinical Through to Regulatory Approval

Improved Overall Cost Structure and Reduced Quarterly Cash Burn

Large & Growing Market Opportunities

Experienced Management Team

Thank You