



# *Innovations* *in* MEDICINE™

TITAN PHARMACEUTICALS, INC. 

## Safe Harbor

**The presentation 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. Reference is made in particular to the description of our plans and objectives for future operations, assumptions underlying such plans and objectives and other forward-looking terminology such as “may,” “expects,” “believes,” “anticipates,” “intends,” “projects,” or similar terms, variations of such terms or the negative of such terms. Forward-looking statements are based on management’s current expectations. Actual results could differ materially from those currently anticipated and such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to availability of financing, difficulties or delays in development, testing, regulatory approval, production and marketing of the Company’s drug candidates, adverse side effects or inadequate therapeutic efficacy of the Company’s drug candidates that could slow or prevent product development or commercialization and the uncertainty of patent protection for the Company’s intellectual property or trade secrets.**

# Titan Pharmaceuticals Overview

**Titan Pharmaceuticals is a specialty pharmaceutical company focused on developing innovative treatments for chronic conditions based on its proprietary long-term drug delivery platform, ProNeura™**

- **Probuphine®: A long acting formulation of buprenorphine for the maintenance treatment of opioid dependence**
  - Final Phase 3 clinical study requested by the FDA in progress; expected completion by mid year 2015 and resubmission of the NDA in late 2015
  - Partnership established for the U.S. and Canadian rights on attractive terms
  - Potential application in treatment of chronic pain
- **ProNeura for Parkinson's disease (Ropinirole)**
  - Non clinical proof-of-principle study completed in primate model of PD
  - Expect to file Investigational New Drug application with FDA in 2015
- **ProNeura Technology Platform**
  - Proprietary long-term drug delivery technology providing around-the-clock medication over periods of six months to a year
  - Applications in chronic conditions where clinical benefit could be achieved by continuous, stable medication levels in the blood

## Probuphine: Highlights

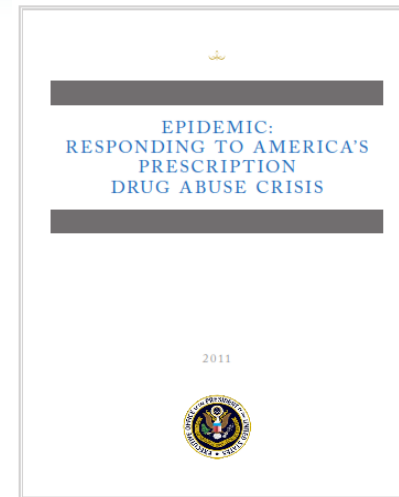
### **Probuphine is expected to be the first long acting buprenorphine product on the market for the treatment of opioid dependence**

- Probuphine provides six month sustained release of buprenorphine, a drug already on the market as a daily dosed sublingual tablet/film
- Expanding market with U.S. sales of daily dosed buprenorphine products exceeding \$1.5 billion; Probuphine peak sales potential: \$300-\$500 mil
- Strong U.S. and Canadian partnership with Braeburn Pharmaceuticals
  - Upfront: \$15.75 mil; Approval: \$15 mil; Sales Milestones: \$165 mil;
  - Tiered royalties: mid teens – low twenties
- U.S. patent life to 2024
- Potential application in treating chronic pain
- Regulatory status:
  - NDA accepted for Priority Review in January 2013 and FDA Advisory Committee voted in favor of approval of Probuphine in March 2013
  - FDA issued a Complete Response Letter (CRL) on April 30, 2013 requesting additional clinical testing
  - Final clinical study in progress and resubmission of NDA expected in late 2015

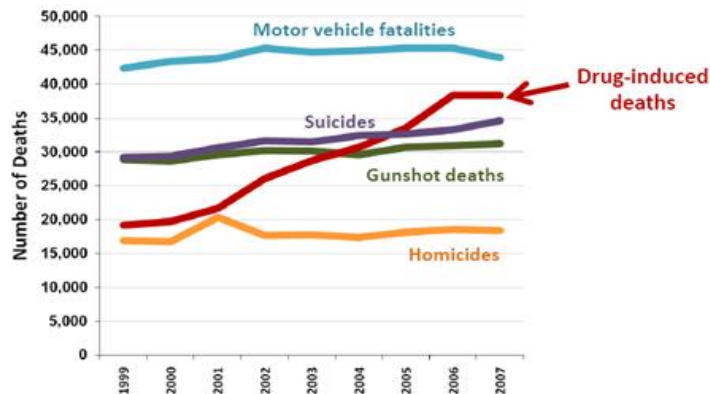
# Opioid Dependence - Viewed as an Epidemic

## Recognized as an epidemic by the federal government

- Opioid dependence is recognized by the government as a medical epidemic that warrants immediate and significant resource allocation
- NIDA (part of NIH) provided a \$7.6 million grant (2010-2011) in support of Probuaphine development

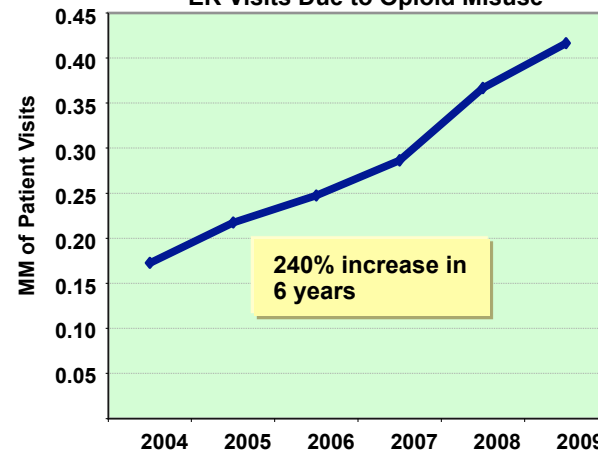


Drug-Induced Deaths Second Only to Motor Vehicle Fatalities, 1999–2007



Source: National Center for Health Statistics, Centers for Disease Control and Prevention. National Vital Statistics Reports Deaths: Final Data for the years 1999 to 2007 (2001 to 2010).

ER Visits Due to Opioid Misuse



Sources: EPIDEMIC: RESPONDING TO AMERICA'S PRESCRIPTION DRUG ABUSE CRISIS, Executive Office of the President of the United States (2011); 2009 National Survey on Drug Use and Health (NSDUH); "A Wave of Addiction and Crime, with the Medicine Cabinet to Blame", New York Times (Sept 23, 2010)

# Opioid Dependence - Disease Overview

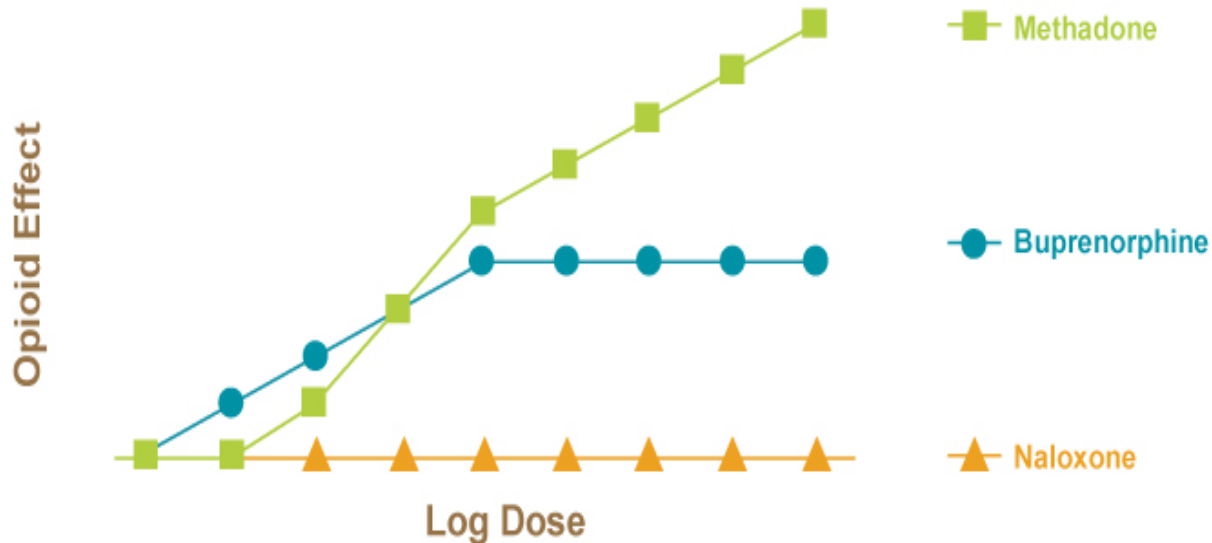
- **Addiction is a primary, chronic disease of brain reward, motivation, memory and related neurobiological circuitry\***
  - Inability to consistently abstain
  - Impairment in behavioral control
  - Craving
  - Diminished recognition of significant problems with one's behaviors
- **Addiction involves cycles of relapse and remission**
- **Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death**

*\*American Society of Addiction Medicine, Inc., 2011*

# Opioid Dependence - Treatment Overview

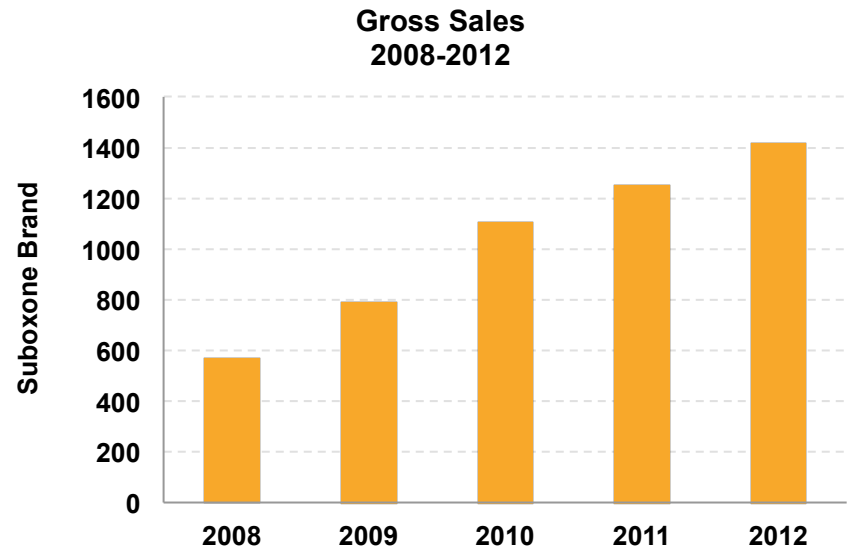
- In the U.S. buprenorphine has replaced methadone as the gold standard in treating opioid dependence
- Buprenorphine is a mixed partial agonist at the mu receptor and an antagonist at the kappa receptor
  - Ceiling effect
  - Improved safety profile
  - Lack of euphoria

Ceiling Effect of Buprenorphine



# Opioid Dependence - Expanding Market

- **Daily buprenorphine is the current gold standard**
  - U.S. sales of daily oral formulations of buprenorphine (Suboxone®) exceeded \$1.4B in 2012
  - U.S. buprenorphine prescriptions have far outstripped those of methadone since 2006
- **Challenges with oral buprenorphine**
  - Compliance
  - Fluctuating levels of drug
  - Diversion, abuse



Source: IMS Health



# Probuphine: Active Buprenorphine Along with Inert EVA Polymer



Each implant contains 80 mg of buprenorphine HCl which has been blended and extruded with ethylene vinyl acetate (EVA) co-polymer

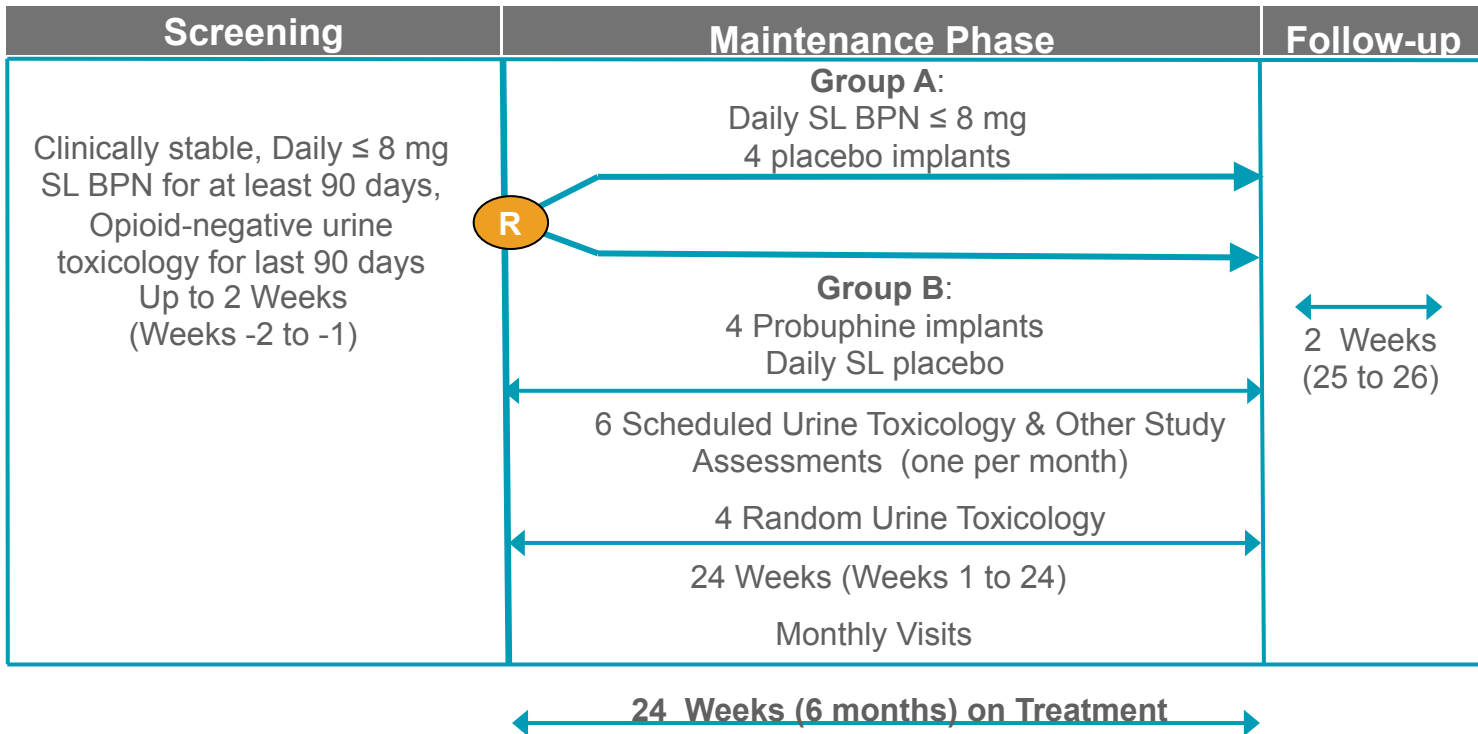
**Probuphine is a subdermal implant capable of delivering continuous and persistent around the clock blood levels of buprenorphine for 6 months following a single treatment, enhancing patient compliance and retention**

## Probuphine Clinical Summary

- **Six clinical studies completed to date with final Phase 3 study under way**
  - Small dose finding study
  - Two well-controlled safety and efficacy studies showing clinical and statistical superiority over placebo and non-inferiority to Suboxone published in *Journal of American Medical Association* and in the journal *Addiction*
  - Two open label long-term treatment safety studies
  - Relative bioavailability study
- **Mild-to-moderate adverse events typical of the safety profile of buprenorphine; low number of serious adverse events similar to placebo**
- **Well-tolerated implant procedure**
- **No evidence of implant diversion or misuse**

# Pro-814 Study Design:

The final clinical study is a randomized, double blind and double dummy design that will provide information for a non-inferiority comparison of a six-month treatment with a dose of four Probuphine implants to treatment with 8 mg or less of an approved daily dosed sublingual formulation of buprenorphine.



**R** Randomization takes place on Day 1 (day of implant)  
SL BPN = sublingual buprenorphine or sublingual buprenorphine/naloxone

# Target Patient Profile

## **Initial market research indicates that physicians would recommend Probuphine across wide patient population**

- Patients stabilized on buprenorphine therapy
  - Serious and committed patients with good treatment history
- Patients that have a high relapse history
  - Patients with treatment compliance problems
- New patients
  - Patients seeking discrete treatment or living in remote areas
- Young patients (18-25 yrs)
  - Needing long term maintenance, active lifestyle
- Incarcerated patients – short term
  - Means of controlling incarceration-induced withdrawal

# Probuphine Value Proposition

Probuphine is the first and only potential treatment for opioid dependence that can provide continuous and persistent around the clock blood levels of buprenorphine for six months, enhancing patient compliance and retention and preventing diversion

<b>Efficacy</b>	<b>Effective in reducing illicit opioid use</b> <b>Enhanced compliance may lead to superior outcomes</b>
<b>Safety</b>	<b>Lower drug exposure may provide superior safety and tolerability</b>
<b>Ease of Use</b>	<b>Unique delivery system dosed once every six months</b> <b>Continuous buprenorphine delivery</b> <ul style="list-style-type: none"><li>• Non-fluctuating blood levels, around the clock medication</li><li>• Potential 100% compliance</li></ul>
<b>Diversion</b>	<b>Limited access to implants</b> <ul style="list-style-type: none"><li>• Subdermal placement</li><li>• Specific distribution (non-retail)</li></ul>

# Potential for the Treatment of Chronic Pain

- **Buprenorphine has several advantages over other opioids used for chronic pain**
  - Safer than other opioids
    - Ceiling effect for respiratory depression, relatively long half-life, minimal euphoric effect
- **Buprenorphine transdermal patch (3-7 days) is approved in U.S., Europe and Australia for the treatment of moderate to severe chronic pain**
  - Therapeutic window of 0.1 – 0.5 ng/ml plasma level can be delivered with 1 to 2 Probuphine implants
- **Probuphine value proposition for treating chronic pain**
  - Around the clock non-fluctuating therapeutic levels, no on/off therapy cycling, enhances compliance and increases patient convenience
  - Braeburn Pharmaceuticals holds the U.S. and Canadian rights to the chronic pain indication

Sources: NEJM 2003;349:1943-53 Sittl, Expert Rev. Neurotherapeutics 2005;5(3): 315-323

# Titan: Adding Value Beyond Probuphine

## Proprietary ProNeura Technology Platform

- Novel long-term drug delivery technology providing around-the-clock medication over periods of six months to a year clinically validated through the Probuphine program
- Applicable to other chronic treatments where clinical benefit is possible through:
  - Low dose around the clock drug administration
  - Stable blood level of medication
  - Subdermal drug delivery eliminating first-pass metabolic effects
- Product development program in Parkinson's disease in progress
  - Established non-clinical proof of concept with continuous dopamine agonist treatment in a PD model with funding from NIH grants
- Evaluation of additional compounds in other disease settings underway
- Titan has an expert team in place with an established product development track record

# Parkinson's Disease Overview

## Parkinson's Disease

- Parkinson's disease (PD) is characterized by the loss of dopaminergic neurons which leads to increasing activity in the brain region which influences movement and motor function

## Treatment

- Early-stage PD patients are treated with drugs designed to replace dopamine in the brain. However, these therapeutics typically lose their benefits after several years of chronic treatment, and trigger serious side effects
- About one third of the treated patients develop motor response fluctuations and/or drug-induced dyskinesias within only 2 years of treatment, increasing to over 50% within 3-5 years of treatment

## Research

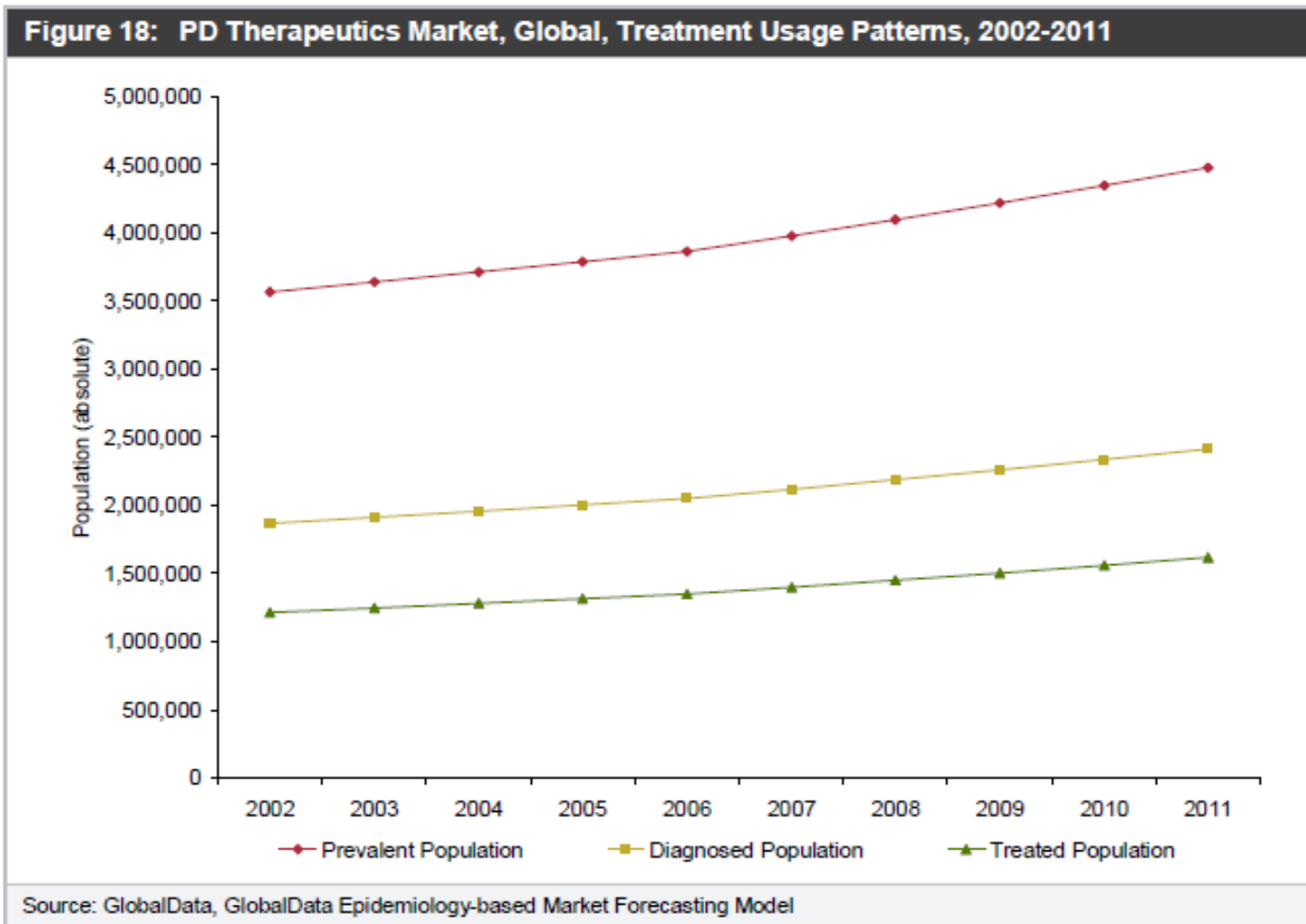
- Clinical and nonclinical research indicates that these motor side effects arise from the pulsatile dopaminergic stimulation resulting from current oral treatment modalities
- Continuous dopaminergic stimulation (CDS) by subcutaneous infusion has been shown to palliate these motor complications and to also delay or prevent the onset of dyskinesias.

## Product Opportunity

- Titan's ProNeura™ drug delivery technology provides a clinically-validated platform to safely and conveniently provide CDS for several months from a single treatment. Further, the subdermal placement of these implants eliminates many of the device-related complications associated with existing treatment modalities.



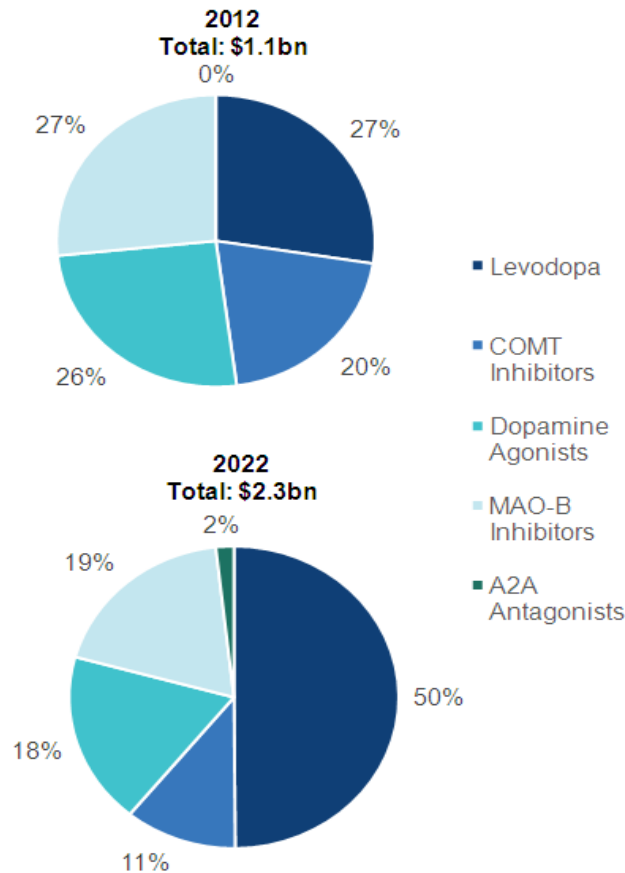
# Parkinson's Disease: Treated Population Increasing Worldwide



Based on information from Titan and other sources believed to be reliable and prepared exclusively for Titan. Woodside Capital Partners is not responsible for any use that Titan may make of this material.

# Parkinson's Disease: Therapeutics Market

## Sales for PD in the US by Drug Class 2012–2022



About 1.5 million people in the U.S. have Parkinson's disease according to the Parkinson's Disease Foundation. The number is expected to double by 2030 because of the aging population.

## Sales of Dopamine Agonists, US

Year	Total PD Sales	% DA	\$ DA
2012	\$1.1bn	26%	286m
2022	\$2.3bn	18%	414m

Source: GlobalData

Based on information from Titan and other sources believed to be reliable and prepared exclusively for Titan. Woodside Capital Partners is not responsible for any use that Titan may make of this material.

# ProNeura – Parkinson's Disease Program

- **Non-clinical Proof of Concept**

- Evaluation of ProNeura technology in MPTP Parkinsonian monkey model
- Ropinirole (Requip®), a dopamine agonist marketed by GSK in the US for PD, was safely and continuously delivered from ProNeura-ropinirole implants inserted subdermally
- No local skin irritation at implant site
- Sustained non-fluctuating plasma ropinirole level for several months following implantation
- Controlled PD symptoms without triggering dyskinesias in severely lesioned primates

- **Next Steps**

- Optimize implant formulation of ropinirole; develop non-clinical study plan to support Investigational New Drug (IND) application
- Design POC clinical study with assistance of the Scientific Advisory Board
- Pre-IND meeting with the FDA
- Complete non-clinical studies to enable IND filing in late 2015
- Prepare for conducting clinical study

# Titan Pharmaceuticals Summary

***Titan Pharmaceuticals is a specialty pharmaceutical company focused on developing innovative treatments for chronic conditions based on its proprietary long-term drug delivery platform, ProNeura™***

- **Probuphine, a long-acting controlled-release buprenorphine product for opioid dependence**
  - Growing \$1.5 billion market in opioid dependence; potential in chronic pain
  - \$300-\$500M in potential annual peak sales in opioid dependence alone
  - Addresses significant unmet needs: *reduction in opioid use, increased compliance, avoidance of diversion and abuse*
  - Attractive U.S. partnership: upfront \$15.75M (12/12); approval, \$15M; sales milestones, \$165M; tiered royalties in mid-teens to low-twenties
  - NDA submission in late 2015
- **ProNeura for Parkinson's (ROPINIROLE)**
  - Dopamine Agonist; continuous long term delivery in convenient outpatient setting
  - Potential to reduce motor fluctuations, dyskinesias and increase 'on' time
  - Expected IND filing in 2015; proof-of-principle clinical study in 2016
- **Proprietary ProNeura long-term drug delivery platform**
  - Around-the-clock medications over six months to a year
  - Broad base of potential applications in chronic treatments

