TITAN PHARMACEUTICALS INC
Form S-1/A
August 30, 2018
TABLE OF CONTENTS
As filed with the Securities and Exchange Commission on August 30, 2018
Registration No. 333-226841

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 1
TO
FORM S-1
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933

Titan Pharmaceuticals, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	2836	94-3171940
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

400 Oyster Point Blvd., Suite 505
South San Francisco, California 94080
(650) 244-4990
(Address, including zip code, and telephone number,
including area code, of Registrant's principal executive offices)

Sunil Bhonsle, Chief Executive Officer
Titan Pharmaceuticals, Inc.
400 Oyster Point Blvd., Suite 505
South San Francisco, California 94080
(650) 244-4990
(Name, address, including zip code, and telephone number, including area code, of agent for service)
Copies to:

Fran Stoller, Esq. Loeb & Loeb LLP 345 Park Avenue New York, New York 10154 Telephone: (212) 407-4000 Fax: (212) 407-4990	Ivan K. Blumenthal, Esq. Anthony J. Marsico, Esq. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. 666 Third Avenue New York, NY 10017 Telephone: (212) 935-3000 Fax: (212) 983 3115

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.
If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.
If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective

registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act of 1934.

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
		Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

TABLE OF CONTENTS

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Class A Units consisting of:		
(i) Common Stock, par value $0.001 per share(2)	$ 2,587,500	$ 322.14
(ii) Warrants to purchase Common Stock(3)		
Class B Units consisting of:		
(i) Series A Convertible Preferred Stock, par value $0.001 per share	$ 14,662,500	$ 1,825.48
(ii) Warrants to purchase Common Stock(3)		
(iii) Common Stock issuable upon conversion of the Series A Convertible Preferred Stock(2)		
Common Stock issuable upon the exercise of the Warrants to purchase Common Stock(2)	$ 10,781,250	$ 1,342.27
Underwriter's Warrants to Purchase Common Stock(2)	$ 660,000	$ 82.17
Common Stock Underlying Underwriter's Warrants(3)(4)		
Total	$ 28,691,250	$ 3,572.06(5)

(1)
Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(o) of the Securities Act of 1933, as amended. Includes shares and warrants to be sold upon exercise of the underwriters' option to purchase additional shares and warrants. See "Underwriting."

(2)
Pursuant to Rule 416, the securities being registered hereunder include such indeterminate number of additional securities as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions.

(3)
No fee pursuant to Rule 457(g) under the Securities Act of 1933, as amended.

(4)
Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(g) under the Securities Act. The underwriter's warrants are exercisable at a per share exercise price equal to 110% of the public offering price per share of common stock. The proposed maximum aggregate offering price of the underwriter's warrants is $660,000,

which is equal to 110% of $600,000 (4% of $15,000,000).

(5)
$2,229.80 was previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to Section 8(a), may determine.

TABLE OF CONTENTS

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities, nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUSSUBJECT TO COMPLETIONDATED AUGUST 30, 2018

3,000,000 Class A Units Consisting of Common Stock and Warrants and
12,750 Class B Units Consisting of Series A Convertible Preferred Stock and Warrants

We are offering 3,000,000 Class A Units consisting of one share of our common stock and one warrant to purchase 0.5 of a share of our common stock, at an exercise price equal to per whole share of common stock, which warrants will be exercisable upon issuance and will expire five years from date of issuance. The shares of common stock and warrants that are part of a Class A Unit are immediately separable and will be issued separately in this offering.

We are also offering to those purchasers, if any, whose purchase of Class A Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering, the opportunity, in lieu of purchasing Class A Units, to purchase Class B Units. Each Class B Unit will consist of one share of our newly designated Series A Convertible Preferred Stock, or the Series A Preferred, with a stated value of $1,000 and be convertible into shares of our common stock at the public offering price of the Class A Units, together with the equivalent number of warrants as would have been issued to such purchaser if they had purchased Class A Units based on the public offering price. The shares of Series A Preferred do not generally have any voting rights unless and until converted into shares of common stock. The shares of Series A Preferred and warrants that are part of a Class B Unit are immediately separable and will be issued separately in this offering.

The number of shares of our common stock outstanding after this offering will fluctuate depending on how many Class B Units are sold in this offering and whether and to what extent holders of Series A Preferred shares convert their shares to common stock.

Our common stock is listed on The Nasdaq Capital Market under the symbol “TTNP”. On August 29, 2018, the last reported sale price of our common stock on The Nasdaq Capital Market was $0.75 per share. The public offering price per Class A Unit will be determined between us and the underwriter based on the closing price of our common stock on the pricing date and market conditions at the time of pricing, and may be at a discount to the current market price. The public offering price of the Class B Units will be $1,000 per unit.

Assuming an offering price of $0.75 per Class A unit, the Series A Preferred included in the Class B Units will be convertible into an aggregate total of 17,000,000 shares of Common Stock and the warrants included in the Class B Units will be exercisable for an aggregate total of 8,500,000 shares of Common Stock.

There is no established trading market for the warrants or the Series A Preferred, and we do not expect an active trading market to develop. We do not intend to list the warrants or the Series A Preferred on any securities exchange or other trading market. Without an active trading market, the liquidity of the warrants and the Series A Preferred will be limited.

Our business and an investment in our securities involves a high degree of risk. See “Risk Factors” beginning on page 9 of this prospectus for a discussion of information that you should consider before investing in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Total

	Per Class A Unit	Per Class B Unit	
Public offering	$	$	$
Underwriting discounts and commissions(1)	$	$	$
Proceeds to us, before expenses	$	$	$

(1) The underwriters will receive compensation in addition to the underwriting discount and commissions. See "Underwriting" beginning on page 48 of this prospectus for a description of compensation payable to the underwriters.

We have granted a 45-day option to the underwriters to purchase additional shares of common stock and/or additional warrants to purchase shares of common stock, in amounts up to 15% of the common stock, warrants and/or common stock issuable upon conversion of the Series A Preferred included in the Units sold in the offering.

The underwriters expect to deliver the securities against payment therefor on or about , 2018.

Sole Book-Running Manager

A.G.P.

Co-Manager

CIM Securities, LLC

, 2018

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

You should rely only on the information contained or incorporated by reference in this prospectus. Neither we nor the underwriters have authorized anyone to provide you with information different from, or in addition to, that contained or incorporated by reference in this prospectus or any free writing prospectus prepared by or on behalf of us or to which we may have referred you in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor any of the underwriters is making an offer to sell or seeking offers to buy these securities in any jurisdiction where, or to any person to whom, the offer or sale is not permitted. The information contained or incorporated by reference in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or of any sale of shares of our common stock, and the information in any free writing prospectus that we may provide you in connection with this offering is accurate only as of the date of that free writing prospectus. Our business, financial condition, results of operations and future growth prospects may have changed since those dates

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. The industry publications and industry data contained in this prospectus have been obtained from sources believed to be reliable.

For investors outside the United States: Neither we nor any of the underwriters have taken any action that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities covered hereby and the distribution of this prospectus outside of the United States.

TABLE OF CONTENTS

PROSPECTUS SUMMARY

This summary provides an overview of selected information contained elsewhere or incorporated by reference in this prospectus and does not contain all of the information you should consider before investing in our securities. You should carefully read this prospectus and the registration statement of which this prospectus is a part in their entirety before investing in our securities, including the information discussed under "Risk Factors" and our financial statements and notes thereto that are incorporated by reference in this prospectus. Unless otherwise indicated herein, the terms "Titan," "we," "our," "us," or "the Company" refer to Titan Pharmaceuticals, Inc.

Company Overview

We are a pharmaceutical company developing proprietary therapeutics utilizing our proprietary long-term drug delivery platform for the treatment of select chronic diseases for which steady state delivery of a drug provides an efficacy and/or safety benefit. We are currently transitioning to a commercial stage enterprise having recently re-acquired Probuphine®, a product approved in the U.S. for management of opiate dependence.

Probuphine, our first product candidate based on our proprietary ProNeura™ platform, is a subdermal implant that provides continuous delivery of buprenorphine for six months. Probuphine was approved by the United States Food and Drug Administration, or FDA, in May 2016 for the maintenance treatment of opioid dependence in patients who are stable on low to moderate doses of daily sublingual buprenorphine treatment. We licensed development and commercialization rights of Probuphine for the U.S. and Canadian markets to Braeburn Pharmaceuticals, Inc., or Braeburn, in December 2012. Braeburn subsequently sublicensed the Canadian rights to Knight Therapeutics Inc., or Knight, in February 2016. In April 2018, Knight announced that it had received regulatory approval from Health Canada to commercialize the product for the maintenance treatment of stable patients with opioid use disorder.

In early 2018, Braeburn substantially reduced its field sales force and medical liaison personnel following its receipt of a complete response letter from the FDA for its weekly and monthly depot injection products. Anticipating a negative impact on Probuphine sales in the U.S., we began discussing with Braeburn terms for the return of the Probuphine U.S. commercialization rights to Titan. On May 25, 2018, we entered into an agreement with Braeburn under which we received a $1 million payment from Braeburn and Braeburn's undertaking to provided transition services through 2018 to assist with commercialization activities and help maintain continuity in product supply for patients and their physicians.

Since reacquiring the rights, we have begun implementation of a strategy to relaunch Probuphine to targeted market segments that we believe are best suited to benefit from this product. We intend to use a substantial portion of the proceeds of this offering to build our infrastructure, including a small sales and marketing team, which will enable us to successfully transition to a commercial enterprise and position Probuphine as a specialty product.

On March 21, 2018, we entered into an agreement, or the Purchase Agreement, with L. Molteni & C. Dei Frattelli Alitti Società Di Esercizio S.P.A., or Molteni, pursuant to which Molteni acquired the European intellectual property related to Probuphine and exclusive right to commercialize the Titan supplied product in Europe, as well as certain countries of the Commonwealth of Independent States, the Middle East and North Africa, or the Molteni Territory, in exchange for upfront, milestone and earn-out payments for up to 15 years on net sales of Probuphine in the Molteni Territory. We are working with Molteni in connection with the Marketing Authorization Application, or MAA, currently under review by the European Medicines Agency, or EMA, with the goal of receiving approval to commercialize Probuphine in the European Union, or EU, in the first half of 2019.

We believe that our ProNeura long term drug delivery platform has the potential to be used in the treatment of other chronic conditions where maintaining stable, around the clock blood levels of a medication may benefit the patient and improve medical outcomes. Our goal is to expand our product pipeline using the ProNeura implant platform, and, depending on available funds, we have been opportunistically evaluating other drugs and disease settings for use with the ProNeura platform in

TABLE OF CONTENTS

potential treatment applications such as Parkinson's disease, where conventional treatment is limited by variability in blood drug levels and poor patient compliance. The pursuit of any of these programs in the short-term will depend on our ability to obtain the necessary funding through either government grants or third party collaborations.

Our Market Opportunity

Opioid Use Disorder, or OUD, is a severe, chronic, relapsing brain disease characterized by compulsive drug seeking and use, despite the harmful consequences. Sufferers experience cravings of opioids, accompanied by lack of impulse control. OUD is a progressive disease that is characterized by cycles of relapse and remission and often results in disability or death if left untreated. It is estimated that during 2016, 2.3 million people were diagnosed with OUD and close to 12 million people used opioids. According to government publications, the U.S. societal costs of opioid abuse total $78.5 billion annually and over 115 people die each day as a direct result of their addiction. The U.S. government considers OUD an epidemic and has made available substantial funds through federal and state agencies to control the spread of the epidemic and support evidence-based treatments.

Current treatment approaches to OUD include abstinence-based 12-step programs, a rarely successful therapeutic approach, drug counseling and medication assisted therapies, or MAT. Cravings may persist for years even in the face of abstinence from illicit opiates, leading to a high incidence of relapse in patients not maintained on longer term MAT. The current MAT gold standard is daily treatment with sublingual buprenorphine, a medication that controls the withdrawal symptoms and cravings without inducing opioid euphoria in patients. A 30-day depot formulation was recently approved by the FDA and similar depot buprenorphine products are under FDA review in both weekly and monthly formulations. Unlike methadone, sublingual buprenorphine can be prescribed as an outpatient treatment, making it a convenient option for patients, and U.S. sales of formulations of buprenorphine are approximately $2.0 billion annually. There are challenges, however, associated with daily dosed formulations, including:

- voluntary compliance;
- potential reinforcement of drug-taking behavior;
- variable levels of medication in the blood; and
- diversion, abuse and accidental pediatric overdose.

Probuphine is a safe, effective long-term, subdermal treatment for selected patients that addresses these challenges by:

- releasing buprenorphine continuously for six months;
- providing a stable level of medication in the blood, avoiding peaks and troughs of oral dosing; and
- minimizing or eliminating the potential for diversion or accidental overdose.

Our Commercial Strategy for Probuphine Relaunch

We are currently transitioning all the Probuphine commercialization activities from Braeburn to Titan which include the supply chain and logistics functions, as well as the Medical Affairs and Risk Evaluation Mitigation Strategy, or REMS, training and reporting activities. We expect to complete most of the transition during the third quarter of 2018, and expect to commence the relaunch of Probuphine under the Titan brand in 2018. We are pursuing a targeted market strategy that focuses on establishing a beachhead in select market segments where Probuphine can provide meaningful benefit for the patient allowing for sustained market penetration and sales growth. We plan to establish a small

commercial team of no more than 10 specialists with experience in product marketing and supply chain logistics, medical liaison and training functions, third party payer medical access and field sales. This team will focus initially on four key market segments, specifically:

- High Probuphine-prescribing physicians with long-term recovery oriented treatment programs. There are a substantial number of certified physicians who are currently treating OUD with Probuphine, all of whom are identified in our data base. Our plan is to initially focus

TABLE OF CONTENTS

on the top tier of prescribers to facilitate the growth of their businesses through increased utilization of Probuphine. Utilizing some of the top tier providers, we will establish centers of excellence that will provide sites for referrals from other health care providers. In addition, our medical access specialists will provide resources to help lessen the complexity of the supply chain and reimbursement process. In the longer term, some top tier Probuphine providers will also engage in investigator sponsored research which can generate new and clinically meaningful data, some of which will help us assess the potential for label expansion.

- Residential treatment facilities. Historically, these facilities have mostly relied on 12-step programs with the goal of complete and sustained abstinence while avoiding any MAT. However, the success of such programs has not withstood scrutiny, as it has been increasingly recognized that a very high percentage of patients with opiate addiction ultimately relapse. Consequently, the use of MAT as part of the management of OUD has been increasing, and is expected to rise substantially in the near term. Our plan is to establish alliances with a few large programs.

- Academic institutions with addiction treatment and training programs. We plan to form alliances with institutions that already have the necessary trained personnel and equipment for doing small procedures, and facilitate the introduction and/or increased use of Probuphine for appropriate patients. This will also serve to introduce Probuphine to the next generation of addiction specialists. In the longer term, we expect that key opinion leaders, or KOLs, at some of these sites will initiate investigator sponsored studies which can generate clinically meaningful data while helping us assess the potential for label expansion.

- Criminal justice system. In recent years there has been increasing recognition that the rate of recidivism among inmates with opiate addiction is very high. In addition, the incidence of overdose and death is high for recently released inmates who have “detoxed” while incarcerated (often through abrupt withdrawal or “cold turkey”). Early data suggests the use of MAT in this population can decrease recidivism and the incidence of overdose deaths. Our plan is to initially establish pilot projects with a few select criminal justice programs, with the goal of generating meaningful data that potentially supports the use of Probuphine in this setting.

We expect that demonstration of early success in these market segments will serve to increase partnering opportunities, which will then sustain and accelerate future growth of Probuphine.

Risks Related to Our Business

- We may not be successful in transitioning from a research and development company to a commercial enterprise.

- If Probuphine does not achieve broad market acceptance by physicians, patients or others in the medical community or coverage by third-party payors, our business will be suffer.

- We must comply with extensive government regulations.

- The Probuphine REMS program has adversely impacted sales and marketing efforts to date and may continue to do so, which could materially adversely impact our business prospects.

- The FDA-approved product labeling for Probuphine allows prescribing for a limited patient population.

-

Probuphine is a controlled substance subject to DEA regulations and failure to comply with these regulations, or the cost of compliance with these regulations, may adversely affect our business.

- We may be subject to enforcement action if we engage in improper marketing or promotion of Probuphine.

- We rely on third parties to provide services in connection with the manufacture and distribution of Probuphine, and these third parties may not perform satisfactorily.

- We are solely reliant on the efforts of third parties to commercialize Probuphine outside of the United States.

TABLE OF CONTENTS

- Our current ProNeura programs are at a very early stage and we may not be able to successfully develop these products or any other product based on our ProNeura drug delivery technology.

- Clinical trials required for new product candidates are expensive and time-consuming, and their outcome is uncertain.

- We face risks associated with third parties conducting preclinical studies and clinical trials of our products.

- We face risks associated with product liability lawsuits that could be brought against us.

- We may be unable to protect our patents and proprietary rights.

- We face intense competition.

- Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of our products.

- We may not be able to implement our business plan if we are unable to attract and retain key personnel and consultants.

Corporate Information

We were incorporated under the laws of the State of Delaware on February 7, 1992. Our principal executive offices are located 400 Oyster Point Boulevard, Suite 505, South San Francisco, CA 94080. Our telephone number is (650) 244-4990. Our website address is www.titanpharm.com. We make our periodic and current reports that are filed with the SEC available, free of charge, on our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, and that can be accessed through, our website is not incorporated into and is not a part of this prospectus.

This prospectus may contain references to our trademark and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other company.

TABLE OF CONTENTS

THE OFFERING

Class A Units offered

3,000,000 Class A Units with each Class A Unit consisting of one share of our common stock and a warrant to purchase 0.5 of a share of our common stock at an exercise price equal to per whole share of common stock. The Class A Units will not be certificated and the share of common stock and warrant that are part of such unit will be immediately separable and will be issued separately in this offering.

Class B Units offered

12,750 Class B Units are also being offered to those purchasers, if any, whose purchase of Class A Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering. Each Class B Unit will consist of one share of our Series A Preferred, with a stated value of $1,000 and convertible into shares of our common stock, at the public offering price of the Class A Units, together with the equivalent number of warrants as would have been issued to such purchaser if they had purchased Class A units based on the public offering price. The shares of Series A Preferred generally do not have any voting rights but are convertible into shares of common stock. The Class B Units will not be certificated and the shares of Series A Preferred and warrants that are part of such unit are immediately separable and will be issued separately in this offering.

Warrants

Each warrant included in the Units will have an exercise price equal to per whole share of common stock, will be exercisable upon issuance, and will expire five years from the date of issuance.

Underwriters' option to purchase additional securities

We have granted a 45-day option to the underwriters to purchase additional shares of common stock and/or additional warrants to purchase shares of common stock, in amounts up to 15% of the common stock, warrants and/or common stock issuable upon conversion of the Series A Preferred included in the Units sold in the offering.

Common stock to be outstanding immediately after this offering

24,203,744 shares. If the underwriters' option to purchase additional securities is exercised in full, the total number of shares of our common stock outstanding immediately following the option exercise will be 24,653,744 shares. Excludes shares of common stock that may be issued upon exercise of the warrants and conversion of the Series A Preferred to be issued in this offering. Excludes shares of common stock that may be issued upon exercise of the warrants and conversion of the Series A Preferred to be issued in this offering and exercise of the representative's warrants.

TABLE OF CONTENTS

Series A Convertible Preferred Stock

The Series A Preferred will be convertible into shares of our common stock (subject to adjustment as provided in the related certificate of designation of preferences, rights and limitations) at any time at the option of the holder, at the public offering price of the Class A Units. See "Description of Securities — Preferred Stock — Series A Convertible Preferred Stock" for a discussion of the terms of the Series A Preferred.

Use of proceeds

We estimate that the net proceeds in this offering will be approximately $13.6 million, or approximately $15.7 million if the underwriters exercise their option to purchase additional securities in full, at an assumed public offering price of $0.75 per Class A Unit and $1,000 per Class B Unit, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We anticipate that we will use the net proceeds from this offering for our operations and for other general corporate purposes, including, but not limited to, building our infrastructure, including a small sales and marketing team, to commercialize Probuphine, conduct of the Phase IV trials required by the FDA, our internal research and development programs and general working capital. See "Use of Proceeds" on page 29.

Risk factors

See "Risk Factors" beginning on page 9 and the other information included in this prospectus for a discussion of factors you should carefully consider before investing in our securities.

Nasdaq Capital Market symbol

Our common stock currently trades on The Nasdaq Capital Market under the symbol "TTNP"

There is no established public trading market for the warrants or Series A Preferred, and we do not expect an active trading market to develop. We do not intend to list the warrants or the Series A Preferred on any securities exchange or other trading market. Without an active trading market, the liquidity of the warrants and the Series A Preferred will be limited.

The number of shares of our common stock that will be outstanding immediately after this offering is based on 21,203,744 shares of common stock outstanding as of August 29, 2018, and excludes as of such date:

- 3,498,650 shares of common stock issuable upon exercise of outstanding options at a weighted average exercise price of $3.39 per share, of which 2,839,235 shares are vested as of such date;

- 1,119,750 shares of common stock reserved for future issuance under the Titan Pharmaceuticals, Inc. 2015 Omnibus Equity Incentive Plan, as amended, or the 2015 Plan;

- 1,708,181 shares of common stock issuable upon exercise of warrants outstanding at a weighted average exercise price of $2.37;

- 2,000,000 shares of common stock issuable upon conversion of $2.4 million principal amount of outstanding indebtedness;

TABLE OF CONTENTS

- shares of our common stock issuable upon exercise of the warrants to be issued in this offering; and

- shares of our common stock issuable upon conversion of the Series A Preferred to be issued in this offering.

The number of shares of our common stock outstanding after this offering will fluctuate depending on how many Class B Units are sold in this offering and whether and to what extent holders of Series A Preferred shares convert their shares to common stock.

To the extent we sell any Class B Units in this offering, the same aggregate number of common stock equivalents resulting from this offering would be convertible under the Series A Preferred issued as part of the Class B Units.

Except as otherwise indicated herein, all information in this prospectus, including the number of shares that will be outstanding after this offering, assumes no exercise by the underwriters of their option to purchase additional securities and excludes shares of our common stock issuable upon exercise of the representative's warrants (4% of the shares of common stock sold in this offering, including shares issuable upon conversion of the Series B Preferred but excluding any securities sold upon exercise of the underwriter's option to purchase additional securities or shares issuable upon exercise of the warrants).

TABLE OF CONTENTS

SUMMARY CONSOLIDATED FINANCIAL DATA

(in thousands, except per share data)

The following table summarizes our selected financial data for the periods and as of the dates indicated. Our selected statements of operations data for the years ended December 31, 2017 and 2016, respectively, and our selected balance sheet data as of December 31, 2017 and 2016, have been derived from our audited financial statements, which are incorporated by reference in this prospectus. Our selected statements of operations data for each of the six month periods ended June 30, 2018 and 2017, and our selected balance sheet data as of June 30, 2018, have been derived from our unaudited financial statements, which are incorporated by reference in this prospectus. The interim unaudited financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair presentation of the information for the periods presented. Our financial statements are prepared and presented in accordance with generally accepted accounting principles in the United States. Our historical results are not necessarily indicative of the results to be expected for any future periods. Our selected financial data should be read together with the section entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and with our financial statements and their related notes, which are incorporated by reference in this prospectus.

	Six Months Ended June 30,		Years Ended December 31,	
	2018	2017	2017	2016
	(Unaudited)			
Statement of Operations Data:				
Total revenue	$ 3,732	$ 117	$ 215	$ 15,065
Operating expenses:				
Cost of goods sold	70	—	—	—
Research and development	3,713	4,627	9,648	6,126
General and administrative	2,995	2,548	5,069	4,596
Other income (expense), net	(428)	602	195	792
Net income (loss) applicable to common stockholders	$ (3,474)	$ (6,456)	$ (14,307)	$ 5,135
Basic net income (loss) per common share	$ (0.16)	$ (0.30)	$ (0.67)	$ 0.25
Diluted net income (loss) per common share	$ (0.16)	$ (0.33)	$ (0.70)	$ 0.20
Shares used in computing:				
Basic net income (loss) per common share	21,204	21,199	21,203	20,744
Diluted net income (loss) per common share	21,204	21,201	21,228	21,459

	As of June 30, 2018 (Unaudited)
Balance Sheet Data:	
Cash and cash equivalents	$ 1,614
Total assets	$ 4,617
Total liabilities	$ 5,930
Total stockholders’ equity (deficit)	$ (1,313)

TABLE OF CONTENTS

RISK FACTORS

Any investment in our securities involves a high degree of risk. Investors should carefully consider the risks described below and all of the information contained or incorporated by reference in this prospectus before deciding whether to purchase our common stock. Our business, financial condition or results of operations could be materially adversely affected by these risks if any of them actually occur. This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks we face as described below and elsewhere in this prospectus.

Risks Related to Our Business

We may not be successful in transitioning from a research and development company to a commercial enterprise.

Since our inception, we have been engaged in product research and development and have never directly commercialized any product. Since we regained the U.S. commercial rights to Probuphine in May 2018, we have been largely dependent on Braeburn's provision of support services, as well as those of advisors and consultants, as we transition to a commercial enterprise. We do not currently employ a sales force or have any internal sales and marketing capabilities. Without hiring or contracting for an experienced and active sales force, we will not be in a position to relaunch Probuphine and sales, if any, will continue to be limited. We will face intense competition for sales and marketing personnel with the necessary experience in addiction, reimbursement, specialty pharmacies and our targeted markets and there can be no assurance that we will be successful in our efforts to transition to a commercial stage company.

If Probuphine does not achieve broad market acceptance by physicians, patients or others in the medical community or coverage by third-party payors, our business will suffer.

Although Braeburn commenced a full commercial launch of Probuphine in the first quarter of 2017, minimal progress was made and for the year ended December 31, 2017 we derived royalty revenues of only $215,000 from sales of Probuphine. The commercial success of Probuphine and our product relaunch will depend upon its acceptance by physicians, patients, healthcare payors and the medical community. Coverage and reimbursement of Probuphine by third-party payors is also necessary for commercial success. Since its initial commercial launch by Braeburn, Probuphine's adoption by physicians has been hindered both by the Risk Evaluation and Mitigation Strategy, or REMS, requirements mandated by the product label, which are more expansive than those required for other buprenorphine products, as well as the current payment and reimbursement model, which differs from some of the existing treatment options for opioid addiction. For example, the current standard of care for outpatient treatment of opioid addiction is oral daily buprenorphine, which typically requires frequent patient visits and a per visit fee, which the patient may pay directly to the healthcare provider in cash. Reimbursement for an implantable drug product that requires administration by a healthcare provider requires drug codes as well as a separate procedure code for the insertion and removal procedures and less frequent office visits. Physicians may prefer more frequent patient visits and the accompanying reimbursement and payment model, which oftentimes includes cash payments. The commercial success of Probuphine depends on several factors, including:

- our ability to train and certify healthcare providers to insert and remove implants of Probuphine in accordance with the REMS;
- the perceived and actual advantages of our Probuphine over current and emerging treatment options;
- the willingness of healthcare providers to prescribe, and the target patient population to try novel products;
- the competitiveness of our pricing;
-

the willingness of healthcare providers to accept alternative reimbursement models, such as the “buy-and-bill” system, where prescribers are required to buy Probuphine inventory themselves and

TABLE OF CONTENTS

then bill patients or payors following the procedure, or the specialty pharmacy distribution model, where a specialty pharmacy carries inventory and ships it to healthcare providers as requested and prescribed, and directly handles the subsequent billing and payment process with payors;

- our ability to provide adequate support to physicians and other healthcare providers to lessen the burden of current reimbursement models;

- our ability to establish and maintain adequate levels of coverage for Probuphine from commercial health plans and government health programs, which we refer to collectively as third-party payors, particularly in light of the availability of other branded and generic competitive products;

- the willingness for patients to pay out-of-pocket in the absence of third-party coverage and the success of patient assistance programs;

- our ability to promote products through marketing and sales activities and any other arrangements; and

- our ability to successfully educate prescribers and patients on the applicable product's efficacy and safety.

In light of the difficulties encountered to date, we cannot predict either the timing or the degree to which Probuphine will be accepted by the medical community. If we are unable to generate ample royalty revenue from Probuphine, we will be unable to fund our research and development programs without additional financing, which may not be available on acceptable terms, and our business will be materially harmed.

We must comply with extensive government regulations.

The research, development, manufacture labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of pharmaceutical products are subject to an extensive regulatory approval process by the FDA in the U.S. and comparable health authorities in foreign markets. The process of obtaining required regulatory approvals for drugs is lengthy, expensive and uncertain. Approval policies or regulations may change and the FDA and foreign authorities have substantial discretion in the pharmaceutical approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Regulatory approval may entail limitations on the indicated usage of a drug, which may reduce the drug's market potential. Even if regulatory clearance is obtained, post-market evaluation of the products, if required, could result in restrictions on a product's marketing or withdrawal of the product from the market, as well as possible civil and criminal sanctions. Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval process and are commercialized.

The New Drug Application, or NDA, for Probuphine mandated the post-approval completion of several Phase IV clinical trials. Prior to the reversion of the commercialization rights to us, Braeburn had been in negotiations with the FDA with respect to the various trial protocols and had not commenced the required clinical trials. Upon transfer of the NDA back to us, we began communicating with the FDA regarding the Phase IV requirements. There can be no assurance that the FDA will provide us with the time we need to initiate and complete the necessary clinical trials, or that we will have the necessary funds to do so, in which event we may be subject to possible sanctions, including monetary penalties or suspension of Probuphine commercial activities. Furthermore, unexpected negative findings from a Phase IV trial could negatively impact the product label and/or acceptance by patients, healthcare providers and insurers.

The Probuphine REMS program has negatively impacted initial uptake in sales and may continue to do so, which could materially adversely impact our business prospects.

There is currently a REMS program in place for Probuphine as required by the FDA. The REMS program was implemented by Braeburn in May 2016 and is designed to mitigate the risk of complications of migration, protrusion, expulsion and nerve damage associated with the insertion and removal of Probuphine and the risks of accidental overdose, misuse and abuse. The REMS program requires training and certification of healthcare providers who prescribe and implant Probuphine and provide patient

TABLE OF CONTENTS

counseling. Probuphine distribution is restricted to healthcare providers who have completed training and received certification under the REMS program. We believe the REMS program has been an obstacle to acceptance of Probuphine to date by the medical community. Healthcare providers may be unwilling to undergo training and certification in order to be able to prescribe or implant Probuphine due to time constraints or concerns with the product. If we are unable to adequately address this issue, our ability (or the ability of potential future commercial partners) to generate revenue from sales of Probuphine could be materially compromised, which would have a material adverse effect on our business, results of operations, financial condition and prospects. In addition, if a patient suffers an injury during the insertion and removal of Probuphine, we may become liable to patients, clinicians or others or result in our non-compliance with the REMS program. Non-compliance with the REMS program may bring serious consequences to us, including warning letters from the FDA, fines, criminal charges and other prohibitions and exclusions as well as reputational damage.

The FDA-approved product labeling for Probuphine allows prescribing for a limited patient population.

Probuphine was approved with an indicated use limited to the long-term maintenance treatment of opioid dependence in clinically stable patients on 8 mg or less a day of oral buprenorphine. The approved labeling also contains other limitations on use and warnings and contraindications for risks. If potential purchasers or those influencing purchasing decisions, such as physicians and pharmacists or third party payers, react negatively to Probuphine because of their perception of the limitations or safety risks in the approved product labeling, it may result in lower product acceptance and lower product revenues.

In addition, our promotion of Probuphine must reflect only the specific approved indication as well as other limitations on use, and disclose the safety risks associated with the use of Probuphine as set out in the approved product labeling. We must submit all promotional materials to the FDA at the time of their first use. If the FDA raises concerns regarding our promotional materials or messages, we may be required to modify or discontinue using them and provide corrective information to healthcare practitioners, and we may face other adverse enforcement action.

Probuphine is a controlled substance subject to Drug Enforcement Agency, or DEA, regulations and failure to comply with these regulations, or the cost of compliance with these regulations, may adversely affect our business.

Probuphine contains buprenorphine, a regulated Schedule III “controlled substance” under the Controlled Substances Act, which establishes, among other things, certain registration, production quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Our failure to comply with DEA requirements could result in the loss of our ability to supply Probuphine, significant restrictions on Probuphine, civil penalties or criminal prosecution.

The DEA, and some states, also conduct periodic inspections of registered establishments that handle controlled substances. Facilities that conduct research, manufacture, store, distribute, import or export controlled substances must be registered to perform these activities and have the security, control and inventory mechanisms required by the DEA to prevent drug loss and diversion. Failure to maintain compliance, particularly non-compliance resulting in loss or diversion, can result in regulatory action that could have a material adverse effect on our business, results of operations, financial condition and prospects. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

Individual states also have controlled substances laws. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs, as well. While some states automatically schedule a drug when the DEA does so, in other states there has to be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could have a material adverse effect on the commercial attractiveness of such product. We or our partners must also obtain

TABLE OF CONTENTS

separate state registrations in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

We may be subject to enforcement action if we engage in improper marketing or promotion of Probuphine.

Our promotional materials and training methods must comply with the Federal Food, Drug and Cosmetic Act, or the FDCA, and FDA regulations and other applicable laws and regulations, including the prohibition of the promotion of unapproved, or "off-label", use. Companies may not promote drugs for off-label use, which include uses that are not described in the product's labeling and that differ from those approved by the FDA. Physicians may prescribe drug products for off-label uses and such off-label uses are common across some medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDCA and FDA regulations restrict communications on the subject of off-label uses of drug products by pharmaceutical companies. The Office of Inspector General of the Department of Health and Human Services, or OIG, the FDA, and the Department of Justice, or DOJ, all actively enforce laws and regulations prohibiting promotion of off-label use and the promotion of products for which marketing approval has not been obtained.

Other federal, state and foreign regulatory agencies, including the U.S. Federal Trade Commission, have issued guidelines and regulations that govern how we promote our products, including how we use endorsements and testimonials.

If we are found to be out of compliance with the requirements and restrictions described above, and we are investigated for or found to have improperly promoted off-label use, we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions, and the off-label use of our products may increase the risk of product liability claims. In addition, management's attention could be diverted from our business operations and our reputation could be damaged.

In addition to FDA and related regulatory requirements, we are subject to health care "fraud and abuse" laws, such as the federal False Claims Act, the anti-kickback provisions of the federal Social Security Act, and other state and federal laws and regulations. Federal and state anti-kickback laws prohibit, among other things, payments or other remuneration to induce or reward someone to purchase, prescribe, endorse, or recommend a product that is reimbursed under federal or state healthcare programs. If we provide payments or other remuneration to a healthcare professional to induce the prescribing of our products, we could face liability under state and federal anti-kickback laws.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product or submitting inflated best price information to the Medicaid Rebate program. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment. Even if it is determined that we have not violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which would harm our business, prospects, operating results, and financial condition. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be challenged under one or more of such laws.

Additionally, requirements under the federal Open Payments program, created under Section 6002 of the Affordable Care Act and its implementing regulations, require that manufacturers of drugs for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to HHS information related to "payments or other transfers of value" provided to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and

TABLE OF CONTENTS

teaching hospitals. The Open Payments program also requires that manufacturers and applicable group purchasing organizations report annually to HHS ownership and investment interests held in them by physicians (as defined above) and their immediate family members. Manufacturers' reports are filed annually with the Centers for Medicare & Medicaid Services ("CMS") by each March 31, covering the previous calendar year. CMS posts disclosed information on a publicly available website. There are also an increasing number of state laws that restrict or prohibit pharmaceutical manufacturers' interactions with health care providers licensed in the respective states, and that require pharmaceutical manufacturers to, among other things, establish comprehensive compliance programs, adopt marketing codes of conduct, file periodic reports with state authorities regarding sales, marketing, pricing, and other activities, and register/license their sales representatives. A number of state laws require manufacturers to file reports regarding payments and items of value provided to health care providers (similar to the federal Open Payments program). Many of these laws contain ambiguities as to what is required to comply with the laws. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private qui tam actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. With respect to any of our products sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable privacy laws and post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

We obtain some of our raw materials, components and finished goods from a single source or a limited group of suppliers. The partial or complete loss of one of these suppliers could cause significant production delays, an inability to meet customer demand and a substantial loss in revenue.

We use a number of single-source suppliers for certain of our raw materials, components and finished goods, including:

- the supplier of the active ingredient for Probuphine;
- the supplier of the finished Probuphine implants; and
- the manufacturer of the Probuphine applicator.

We are in the process of qualifying a new ethylene-vinyl acetate, or EVA, manufacturer. In addition, the vendor that used to sterilize the Probuphine implants indicated that it will no longer sterilize Schedule III controlled substances, including Probuphine. While we are in the process of qualifying another sterilization vendor and will also be transitioning to a new sterilization process, we cannot guarantee that such qualification or transition will be successful. Our use of these and other single-source suppliers of raw materials, components and finished goods exposes us to several risks, including disruptions in supply, price increases, late deliveries and an inability to meet customer demand. This could lead to customer dissatisfaction, damage to our reputation or customers switching to competitive products. Any interruption in supply could be particularly damaging to our ability to develop and commercialize Probuphine.

Finding alternative sources for these raw materials, components and finished goods would be difficult and in many cases entail a significant amount of time, disruption and cost. Any disruption in supply from any single-source supplier or manufacturing location could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

TABLE OF CONTENTS

We rely on third parties to provide services in connection with the manufacture and distribution of Probuphine, and these third parties may not perform satisfactorily.

We do not own or operate, and currently do not plan to own or operate, facilities for production and packaging of Probuphine or our other product candidates. We are dependent on third parties for the timely supply of specified raw materials, equipment, contract manufacturing, formulation or packaging services, product distribution services, customer service activities and product returns processing. For example, we contract with DPT Laboratories, Ltd., or DPT, for the manufacture of Probuphine, which in turn depends on delivery of the active ingredient buprenorphine hydrochloride and milled EVA, which we currently source from Teva Pharmaceuticals, Inc. and Southwest Research Institute, respectively. We are similarly dependent on third parties for the manufacture and sterilization of Probuphine applicators and the assembly and distribution of packaged kits.

Our reliance on third parties for the activities described above will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture our product in accordance with regulatory requirements, or proprietary specifications, or adhere to product processing best practices, or if there are disagreements between us and these third parties, our business could be materially adversely impacted.

We are solely reliant on the efforts of third parties to commercialize Probuphine outside of the United States.

Our ability to generate revenues from the sale of Probuphine in the European Union and the rest of the Molteni Territory, assuming regulatory approval is ultimately obtained, will be wholly dependent on Molteni's ability to successfully launch and commercialize the product in the Molteni Territory. We are similarly dependent on the efforts of Knight with respect to product launch and commercialization in Canada. We do not have control over the amount and timing of resources that Molteni will dedicate to these efforts. We will be similarly dependent on the development, regulatory and marketing efforts of third parties with respect to revenues, if any, from sales of Probuphine in additional territories.

Our dependence on third party collaborators and license agreements subjects us to a number of risks, including:

- our collaborators may not comply with applicable regulatory guidelines with respect to developing or commercializing our products, which could adversely impact sales or future development of our products;

- we and our collaborators could disagree as to future development plans and our collaborators may delay, fail to commence or stop future clinical trials or other development; and

- there may be disputes between us and our collaborators, including disagreements regarding the license agreements, that may result in the delay of or failure to achieve developmental, regulatory and commercial objectives that would result in milestone or royalty payments and/or the delay or termination of any future development or commercialization of our products.

In addition, collaborators may, to the extent permitted by our agreements, develop products that divert resources from our products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Moreover, disagreements could arise with our collaborators or strategic partners over rights to our intellectual property and our rights to share in any of the future revenues from products or technologies resulting from use of our technologies, or our activities in separate fields may conflict with other business plans of our collaborators.

Our ProNeura development programs are at very early stages and will require substantial additional resources that may not be available to us.

To date, we have conducted limited research and development activities based on our ProNeura delivery system beyond Probuphine. We will require substantial additional funds to support our research and development activities, and the anticipated costs of preclinical studies and clinical trials, regulatory approvals and eventual commercialization of ProNeura for Parkinson's disease or any therapeutic based on our ProNeura platform technology. If we are unable to obtain substantial government grants, enter into

14

TABLE OF CONTENTS

third party collaborations or generate sufficient revenues from the sale of Probuphine to fund our ProNeura programs, we will need to seek additional sources of financing, which may not be available on favorable terms, if at all. If we do not succeed in obtaining the requisite funding for our ProNeura programs, we will be unable to initiate clinical trials or obtain approval of any product candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development, forego sales and marketing efforts and forego attractive business opportunities.

To the extent we raise additional capital through the sale of equity securities, the issuance of those securities could result in dilution to our stockholders. In addition, if we obtain debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, thus limiting funds available for our business activities. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our commercialization efforts or curtail our operations. In addition, we may be required to obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves or license rights to technologies, product candidates or products on terms that are less favorable to us than might otherwise be available.

Our current ProNeura programs are at a very early stage and we may not be able to successfully develop these products or any other product based on our ProNeura drug delivery technology.

Our ability to successfully develop any future product candidates based on our ProNeura drug delivery technology is subject to the risks of failure and delay inherent in the development of new pharmaceutical products, including: delays in product development, clinical testing, or manufacturing; unplanned expenditures in product development, clinical testing, or manufacturing; failure to receive regulatory approvals; emergence of superior or equivalent products; inability to manufacture on our own, or through any others, product candidates on a commercial scale; and failure to achieve market acceptance.

Because of these risks, our research and development efforts may not result in any commercially viable products. If a significant portion of these development efforts are not successfully completed, required regulatory approvals are not obtained or any approved products are not commercially successfully, our business, financial condition, and results of operations may be materially harmed.

Our development and commercialization strategy for ProNeura depends, in part, upon the FDA’s prior findings regarding the safety and efficacy of the active drug incorporated into the implant based on data not developed by us, but upon which the FDA may rely in reviewing our NDA submissions.

The current strategy for our ProNeura development programs is based, in part, on the expectation that the products we develop will be eligible for approval through the regulatory pathway under Section 505(b)(2) of the FDCA. Section 505(b)(2) of the FDCA allows an NDA to rely in part on data in the public domain or the FDA’s prior conclusions regarding the safety and effectiveness of an approved drug product, which could expedite our development programs by potentially decreasing the amount of clinical data that would need to be generated in order to obtain FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for product approval. If this were to occur, the time and financial resources required to obtain FDA approval for any additional ProNeura products, and complications and risks associated with regulatory approval, would likely substantially increase. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway may result in new competitive products reaching the market more quickly than those we have under development, which would adversely impact our competitive position and prospects. Even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee that this regulatory pathway will ultimately lead to accelerated product development or earlier approval. Moreover, notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), over the last few years, some pharmaceutical companies and others have objected to the FDA’s interpretation of Section 505(b)(2). If the FDA changes its interpretation of Section 505(b)(2), or if the FDA’s interpretation is successfully challenged in court, this result could delay or even prevent the FDA from approving any Section 505(b)(2) NDAs that we submit. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of any new ProNeura products.

TABLE OF CONTENTS

Clinical trials required for new product candidates are expensive and time-consuming, and their outcome is uncertain. In order to obtain FDA approval to market a new drug product based on our ProNeura drug delivery technology, we must demonstrate proof of safety and effectiveness in humans. To meet these requirements, we must conduct "adequate and well controlled" clinical trials. Conducting clinical trials is a lengthy, time-consuming, and expensive process. The length of time may vary substantially according to the type, complexity, novelty, and intended use of the product candidate, and often can be several years or more per trial. Delays associated with products for which we are directly conducting clinical trials may cause us to incur additional operating expenses. The commencement and rate of completion of clinical trials may be delayed by many factors, including, for example:

- inability to manufacture sufficient quantities of qualified materials under cGMP, for use in clinical trials;
- slower than expected rates of patient recruitment;
- failure to recruit a sufficient number of patients; modification of clinical trial protocols;
- changes in regulatory requirements for clinical trials; the lack of effectiveness during clinical trials;
- the emergence of unforeseen safety issues;
- delays, suspension, or termination of the clinical trials due to the institutional review board responsible for overseeing the study at a particular study site; and
- government or regulatory delays or "clinical holds" requiring suspension or termination of the trials.

The results from early clinical trials are not necessarily predictive of results obtained in later clinical trials. Accordingly, even if we obtain positive results from early clinical trials, we may not achieve the same success in future clinical trials. Clinical trials may not demonstrate statistically significant safety and effectiveness to obtain the requisite regulatory approvals for product candidates.

The failure of clinical trials to demonstrate safety and effectiveness for the desired indications could harm the development of that product candidate and other product candidates. This failure could cause us to abandon a product candidate and could delay development of other product candidates. Any delay in, or termination of, our clinical trials would delay the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. Any change in, or termination of, our clinical trials could materially harm our business, financial condition, and results of operations.

We face risks associated with third parties conducting preclinical studies and clinical trials of our products.

We depend on third-party laboratories and medical institutions to conduct preclinical studies and clinical trials for our products and other third-party organizations to perform data collection and analysis, all of which must maintain both good laboratory and good clinical practices. We also depend upon third party manufacturers for the production of any products we may successfully develop to comply with cGMP of the FDA, which are similarly outside our direct control. If third party laboratories and medical institutions conducting studies of our products fail to maintain both good laboratory and clinical practices, the studies could be delayed or have to be repeated.

We face risks associated with product liability lawsuits that could be brought against us.

The testing, manufacturing, marketing and sale of human therapeutic products entail an inherent risk of product liability claims. We currently have a limited amount of product liability insurance, which may not be sufficient to

cover claims that may be made against us in the event that the use or misuse of our product candidates causes, or merely appears to have caused, personal injury or death. In the event we are forced to expend significant funds on defending product liability actions, and in the event those funds come from operating capital, we will be required to reduce our business activities, which could lead to significant losses. Adequate insurance coverage may not be available in the future on acceptable terms, if at all. If

TABLE OF CONTENTS

available, we may not be able to maintain any such insurance at sufficient levels of coverage and any such insurance may not provide adequate protection against potential liabilities. Whether or not a product liability insurance policy is obtained or maintained in the future, any claims against us, regardless of their merit, could severely harm our financial condition, strain our management and other resources or destroy the prospects for commercialization of the product which is the subject of any such claim.

We may be unable to protect our patents and proprietary rights.

Our future success will depend to a significant extent on our ability to:

- obtain and keep patent protection for our products and technologies on an international basis;
- enforce our patents to prevent others from using our inventions;
- maintain and prevent others from using our trade secrets; and
- operate and commercialize products without infringing on the patents or proprietary rights of others.

We cannot assure you that our patent rights will afford any competitive advantages, and these rights may be challenged or circumvented by third parties. Further, patents may not be issued on any of our pending patent applications in the U.S. or abroad. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before a potential product can be commercialized, any related patent may expire or remain in existence for only a short period following commercialization, reducing or eliminating any advantage of the patent. If we sue others for infringing our patents, a court may determine that such patents are invalid or unenforceable. Even if the validity of our patent rights is upheld by a court, a court may not prevent the alleged infringement of our patent rights on the grounds that such activity is not covered by our patent claims.

In addition, third parties may sue us for infringing their patents. In the event of a successful claim of infringement against us, we may be required to:

- pay substantial damages;
- stop using our technologies and methods;
- stop certain research and development efforts;
- develop non-infringing products or methods; and
- obtain one or more licenses from third parties.

If required, we cannot assure you that we will be able to obtain such licenses on acceptable terms, or at all. If we are sued for infringement, we could encounter substantial delays in development, manufacture and commercialization of our product candidates. Any litigation, whether to enforce our patent rights or to defend against allegations that we infringe third party rights, will be costly, time consuming, and may distract management from other important tasks.

We also rely in our business on trade secrets, know-how and other proprietary information. We seek to protect this information, in part, through the use of confidentiality agreements with employees, consultants, advisors and others.

Nonetheless, we cannot assure you that those agreements will provide adequate protection for our trade secrets, know-how or other proprietary information and prevent their unauthorized use or disclosure. To the extent that consultants, key employees or other third parties apply technological information independently developed by them or by others to our proposed products, disputes may arise as to the proprietary rights to such information, which may not be resolved in our favor.

We face intense competition.

Competition in the pharmaceutical and biotechnology industries is intense. We face, and will continue to face, competition from numerous companies that currently market, or are developing, products for the treatment of the diseases and disorders we have targeted. Many of these entities have significantly greater research and development capabilities, experience in obtaining regulatory approvals and manufacturing, marketing, financial and managerial resources than we have. We also compete with universities and other

TABLE OF CONTENTS

research institutions in the development of products, technologies and processes, as well as the recruitment of highly qualified personnel. Our competitors may succeed in developing technologies or products that are more effective than the ones we have under development or that render our proposed products or technologies noncompetitive or obsolete. In addition, our competitors may achieve product commercialization or patent protection earlier than we will.

The commercial opportunity for Probuphine could be significantly harmed if competitors are able to develop alternative formulations and/or drug delivery technologies outside the scope of our capabilities. Our principal competition in the opioid addiction treatment market comes from manufacturers of oral buprenorphine products, including Indivior PLC, which markets the Suboxone and Subutex brands, as well from manufacturers of weekly or monthly injectable treatments, one of which was recently launched by Indivior PLC. Our competitors may also develop, acquire or license products that are more effective, more useful, better tolerated, subject to fewer or less severe side effects, more widely prescribed or accepted or less costly than ours and may also be more successful than we are in manufacturing and marketing their products. In addition, state pharmacy laws may permit pharmacists to substitute generic products for branded products if the products are therapeutic equivalents, or may permit pharmacists and pharmacy benefit managers to seek prescriber authorization to substitute generics in place of our products, which could significantly diminish demand for Probuphine. If we are unable to compete effectively with the marketed therapeutics of our competitors or if such competitors are successful in developing products that compete with Probuphine, our business, results of operations, financial condition and prospects may be materially adversely affected.

If we or our collaborators are unable to achieve and maintain adequate levels of coverage and reimbursement for Probuphine on reasonable pricing terms, or we or our collaborators fail to do so for any of our other product candidates for which we may receive regulatory approval, their commercial success may be severely limited.

Successful sales of Probuphine or any other product we may successfully develop will depend on the availability of adequate coverage and reimbursement from third-party payors, as well as the ease of use and transparency of such processes and systems once in place. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors are critical to new product acceptance. Third-party payors, whether governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products such as ours when more established or lower cost therapeutic alternatives are already available or subsequently become available. Decisions regarding the extent of coverage and amount of reimbursement to be provided for products and product candidates that we develop will be made on a plan-by-plan basis. As a result, the coverage determination process is often a time-consuming and costly process that may require us or our partners to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained.

Reimbursement for implantable drug products that require administration by a healthcare provider generally requires a drug code, and separate reimbursement codes are required for the insertion and removal procedures. The timely availability of a drug code or procedure code that covers our product or describes the procedures performed using our products, or a change to an existing code that describes such procedures is critical for successful commercialization and the lack of such codes may adversely affect reimbursement for our products and these procedures, including lower reimbursement rates, denials and delays in reimbursement if pre-authorization is required. Even if coverage is approved, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. While Probuphine was approved by the FDA in late May 2016, the procedure codes (G codes) for insertion only, removal only, and insertion plus removal were approved only in late 2017 and went into effect in January 2018.

TABLE OF CONTENTS

In addition, the market for our products may depend on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Also, regional healthcare authorities and individual hospitals are increasingly using competitive bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for Probuphine or any of our product candidates for which we may receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of our products.

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If our products are not widely included on the formularies of these plans, our ability to market our products may be adversely affected.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. In March 2010, the Patient Protection and Affordable Health Care Act of 2010, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively "ACA", was signed into law, which includes measures to significantly change the way health care is financed by both governmental and private insurers.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Additionally, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

TABLE OF CONTENTS

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the United States, including from countries where the products are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decision to decrease our prices to better compete, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

We may not be able to implement our business plan if we are unable to attract and retain key personnel and consultants.

As a company with a limited number of personnel, we are highly dependent on the services of our executive management and scientific staff, in particular Sunil Bhonsle, our President and Chief Executive Officer, Marc Rubin, our Executive Chairman and Katherine DeVarney our Executive Vice President and Chief Scientific Officer. The loss of one or more of such individuals could substantially impair ongoing research and development programs and could hinder our ability to obtain corporate partners.

Our ability to commercialize Probuphine effectively depends in large part upon our ability to attract and retain highly qualified sales, marketing and support personnel. We compete in our hiring efforts with other pharmaceutical and biotechnology companies and it may be difficult and could take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required and because of our limited resources.

In addition, we retain scientific and clinical advisors and consultants to assist us in formulating our clinical and commercial strategies. Competition to hire and retain consultants from a limited pool is intense. Further, because these advisors are not our employees, they may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, and typically they will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We face potential liability related to the privacy of health information we obtain from clinical trials sponsored by us or our collaborators, from research institutions and our collaborators, and directly from individuals.

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws, and federal and state consumer protection laws, govern the collection, use, and disclosure of personal information. In addition, most health care providers, including research institutions from which we or our collaborators obtain patient health information, are subject to privacy and security regulations promulgated under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act. Although we are not directly subject to HIPAA, we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

TABLE OF CONTENTS

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred net losses in almost every year since our inception and we may never achieve or sustain profitability.

We have incurred net losses in almost every year since our inception. Our financial statements have been prepared assuming that we will continue as a going concern. For the six months ended June 30, 2018 and 2017, we had net losses of approximately $3.47 million and $6.46 million, respectively, and had net cash used in operating activities of approximately $2.86 million and $5.63 million, respectively. For the year ended December 31, 2017, we had a net losses of approximately $14.31 million and had net cash used in operating activities of approximately $13.04 million. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

To date, we have devoted most of our financial resources to our corporate overhead and research and development, including our drug discovery research, preclinical development activities and clinical trials. We expect to continue to incur net losses and negative operating cash flow for the foreseeable future, and we expect these losses to increase as we add infrastructure and personnel to support our transition to a commercial enterprise. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate significant revenues. There can be no assurance that we will ever achieve profitability.

We will require additional proceeds to fund our operations and to continue as a going concern.

We currently estimate that our available cash at June 30, 2018, together with the approximately $1.1 million received from Molteni in August 2018 and the proceeds of this offering, will be sufficient to fund our Probuphine commercial efforts and Phase IV clinical program through 2019. We will require additional funds to advance our ProNeura development programs during such period and to complete the regulatory approval process necessary to commercialize any products we might develop. While we are currently evaluating the alternatives available to us, including government grants and third-party collaborations for one or more of our ProNeura programs, our efforts to address our liquidity requirements may not be successful. We may also need additional funds to complete the required post-approval clinical trials and there can be no assurance that revenues for operations or any other source of capital will be available to us on acceptable terms. While we expect to have adequate resources in order to operate our business through the next 12 months, our auditors may have doubt about our ability to continue as a going concern in future periods, and our financial statements relating to those periods may not be prepared on a going-concern basis based on any such doubts. In addition, if one or more of the risks discussed in these risk factors occur or our expenses exceed our expectations, we may be required to raise further additional funds sooner than anticipated. The inclusion of a going concern modification in our independent registered public accounting firm's report for the year ended December 31, 2017, or in any future report, may materially and adversely affect our stock price or our ability to raise new capital.

Our need for future financing may result in the issuance of additional securities which will cause investors to experience dilution.

Our cash requirements may vary from those now planned depending upon numerous factors, including the result of future research and development activities. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development and initiate and conduct clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. We may seek additional funding through a combination of equity offerings or debt financings. Our securities may be offered to other investors at a price lower than the price per share offered to current stockholders, or upon terms which may be deemed more favorable than those offered to current stockholders. In addition, the issuance of securities in any future financing may dilute an investor's equity ownership and have the effect of depressing the market price for our securities. Moreover, we may issue derivative securities, including options and/or warrants, from time to time, to procure qualified personnel or for other business reasons.

TABLE OF CONTENTS

The issuance of any such derivative securities, which is at the discretion of our board of directors, may further dilute the equity ownership of our stockholders. No assurance can be given as to our ability to procure additional financing on terms deemed favorable to us. To the extent additional capital is required and cannot be raised successfully, we may then have to limit our then current operations and/or may have to curtail certain, if not all, of our business objectives and plans.

Our net operating losses and research and development tax credits may not be available to reduce future federal and state income tax payments.

At December 31, 2017, we had federal net operating loss and tax credit carryforwards of $261.0 million and $8.9 million, respectively, and state net operating loss and tax credit carryforwards of $107.1 million and $8.8 million, respectively, available to offset future taxable income, if any. Current federal and state tax laws include substantial restrictions on the utilization of net operating loss and tax credits in the event of an ownership change and we cannot assure you that our net operating loss and tax carryforwards will continue to be available.

Our loan agreement contains restrictions on our operations and could result in certain adverse results.

Our Amended and Restated Venture Capital and Loan Agreement, or Loan Agreement, with Molteni and Horizon Technology Finance Corporation, or Horizon, contains a variety of affirmative covenants, including, without limitation, payment obligations, information delivery requirements and certain notice requirements. Additionally, we are bound by certain negative covenants setting forth actions that are not permitted to be taken during the term of the Loan Agreement without consent of Molteni, as the majority lender, including, without limitation, incurring certain additional indebtedness, making certain asset dispositions, entering into certain mergers, acquisitions or other business combination transactions or incurring any non-permitted lien or other encumbrance on our assets. Subject to certain forbearance provisions in effect through December 31, 2019, upon the occurrence of an event of default under the Loan Agreement (subject to any applicable cure periods), all amounts owed thereunder would begin to bear interest at a rate that is 5.0% higher than the rate that would otherwise be applicable and the outstanding loan may be declared immediately due and payable. Furthermore, the loan is secured by a perfected security interest in all of our assets, including our Probuphine and ProNeura intellectual property, which could be foreclosed upon in the event of a default that is not waived or cured.

Risks Related to this Offering and our Common Stock

Our share price may be volatile, which could subject us to securities class action litigation and prevent you from being able to sell your shares at or above your purchase price.

The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of our clinical trials;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
-

competition from existing products or new products that may emerge;

- announcements by us, our potential future collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures, or capital commitments;

- issuance of new or updated research or reports by securities analysts;

- fluctuations in the valuation of companies perceived by investors to be comparable to us;

TABLE OF CONTENTS

- inconsistent trading volume levels of our shares;
- additions or departures of key management or scientific personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- market conditions for biopharmaceutical stocks in general; and
- general economic and market conditions.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our common stock. In addition, such fluctuations could subject us to securities class action litigation, which could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

There is no active, public market for the warrants or Series A Preferred being offered in this offering.

There is no established public trading market for the warrants or the Series A Preferred being offered in this offering. We do not intend to apply to list the warrants or the Series A Preferred on a securities exchange. Without an active trading market, the liquidity of the warrants and the Series A Preferred will be limited.

Holders of Series A Preferred will have limited voting rights.

Except with respect to certain material changes in the terms of the Series A Preferred and certain other matters and except as may be required by Delaware law, holders of Series A Preferred will have no voting rights. You will have no right to vote for any members of our board of directors.

Holders of the warrants will not have rights of common stockholders until such warrants are exercised.

The warrants being offered do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price for a limited period of time. Specifically, commencing on the date of issuance, holders of the warrants may exercise their right to acquire the common stock and pay the exercise price prior to five years from the date of

issuance, after which date any unexercised warrants will expire and have no further value.

Future sales of our common stock, or the perception that future sales may occur, may cause the market price of our common stock to decline, even if our business is doing well.

Sales by our stockholders of a substantial number of shares of our common stock in the public market could occur in the future. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

TABLE OF CONTENTS

Exercise of options or warrants or conversion of convertible securities may have a dilutive effect on your percentage ownership and may result in a dilution of your voting power and an increase in the number of shares of common stock eligible for future resale in the public market, which may negatively impact the trading price of our shares of common stock.

The exercise or conversion of some or all of our outstanding options, warrants, or convertible securities could result in significant dilution in the percentage ownership interest of investors in this offering and in the percentage ownership interest of our existing common stockholders and in a significant dilution of voting rights and earnings per share.

As of August 10, 2018, we had outstanding warrants to purchase up to 1,708,181 shares of our common stock at a weighted exercise price of $2.37 per share and outstanding and options outstanding under our stock incentive plans to purchase up to 3,498,650 shares of our common stock at a weighted average exercise price of $3.39 per share. At such date there was also an aggregate of $2.4 million principal amount of outstanding indebtedness that is convertible into 2,000,000 shares of our common stock. To the extent options and/or warrants and/or conversion rights are exercised (including with respect to the warrants and any Series A Preferred issued in this offering), additional shares of common stock will be issued, and such issuance will dilute stockholders.

Investors in this offering will experience immediate and substantial dilution in net tangible book value.

The public offering price per share of common stock in this offering will be substantially higher than the net tangible book value per share of our outstanding shares of common stock. Accordingly, investors in this offering will pay a price per share that substantially exceeds the net tangible book value per share of our common stock. Based on an at an assumed public offering price of $0.75 per Class A Unit and $1,000 per Class B Unit, investors in this offering will incur immediate dilution of $0.45 per share. See “Dilution” for a more complete description of how the value of your investment will be diluted upon the completion of this offering.

We may seek to raise additional funds, finance acquisitions or develop strategic relationships by issuing securities that would dilute your ownership. Depending on the terms available to us, if these activities result in significant dilution, it may negatively impact the trading price of our shares of common stock.

We have financed our operations, and we expect to continue to finance our operations, acquisitions, if any, and the development of strategic relationships by issuing equity and/or convertible securities, which could significantly reduce the percentage ownership of our existing stockholders. Further, any additional financing that we secure, including any debt financing, may require the granting of rights, preferences or privileges senior to, or pari passu with, those of our common stock. Any issuances by us of equity securities may be at or below the prevailing market price of our common stock and in any event may have a dilutive impact on your ownership interest, which could cause the market price of our common stock to decline. We may also raise additional funds through the incurrence of debt or the issuance or sale of other securities or instruments senior to our shares of common stock. The holders of any securities or instruments we may issue may have rights superior to the rights of our common stockholders. If we experience dilution from the issuance of additional securities and we grant superior rights to new securities over common stockholders, it may negatively impact the trading price of our shares of common stock and you may lose all or part of your investment.

Our management will have broad discretion over the use of proceeds from this offering and may not use the proceeds effectively.

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used for our operations and for other general corporate purposes, including, but not limited to, building our infrastructure, including a small sales and marketing team, to commercialize Probuphine, conduct of the Phase IV trials required by the FDA, our internal research and development programs and general working capital. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not improve our operating results or enhance the value of our common stock.

TABLE OF CONTENTS

Our failure to meet the continued listing requirements of Nasdaq could result in a de-listing of our common stock. On April 9, 2018, we received a notice from Nasdaq that because our stockholders' equity is less than $2,500,000, we are no longer in compliance with the minimum stockholders' equity requirement for continued listing pursuant to Nasdaq Listing Rule 5550(b)(1). Following our submission of a plan of compliance, we were granted an extension of 180 calendar days, or until October 8, 2018, to regain compliance. At June 30, 2018, we had a stockholders' deficit of approximately 1.3 million. The proceeds of this offering, together with the proceeds from Molteni in August 2018, pursuant to the Purchase Agreement will enable us to achieve the minimum stockholders' equity requirement.

If we fail to satisfy the continued listing requirements of Nasdaq, such stockholders' equity requirement or the minimum closing bid price requirement, Nasdaq may take steps to de-list our common stock. Such a de-listing would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a de-listing, we would take actions to restore our compliance with Nasdaq's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions provide that:

- the authorized number of directors can be changed only by resolution of our board of directors;
- our bylaws may be amended or repealed by our board of directors or our stockholders;
- stockholders may not call special meetings of the stockholders or fill vacancies on the board of directors;
- our board of directors is authorized to issue, without stockholder approval, preferred stock, the rights of which will be determined at the discretion of the board of directors and that, if issued, could operate as a "poison pill" to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that our board of directors does not approve;
- our stockholders do not have cumulative voting rights, and therefore our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors; and
- our stockholders must comply with advance notice provisions to bring business before or nominate directors for election at a stockholder meeting.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our

outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

TABLE OF CONTENTS

We have never paid any cash dividends and have no plans to pay any cash dividends in the future.

Holders of shares of our common stock are entitled to receive such dividends as may be declared by our board of directors. To date, we have paid no cash dividends on our shares of our preferred or common stock and we do not expect to pay cash dividends in the foreseeable future. In addition, the declaration and payment of cash dividends is restricted under the terms of our existing Loan Agreement. We intend to retain future earnings, if any, to provide funds for operations of our business. Therefore, any return investors in our preferred or common stock may have will be in the form of appreciation, if any, in the market value of their shares of common stock.

TABLE OF CONTENTS

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. All statements other than statements of historical facts contained or incorporated by reference in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “sh “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- our ability to implement our business plan;
- our ability to raise additional capital to meet our liquidity needs;
- our ability to generate sufficient proceeds from this offering;
- our ability to generate product revenues;
- our ability to achieve profitability;
- our ability to satisfy U.S. (including the FDA), and international regulatory requirements;
- our ability to obtain market acceptance of our technology and products;
- our ability to compete in the market;
- our ability to advance our clinical trials;
- our ability to fund, design and implement clinical trials;
- our ability to demonstrate that our product candidates are safe for human use and effective for indicated uses;
- our ability to gain acceptance of physicians and patients for use of our products;
-

our dependency on third-party researchers and manufacturers and licensors;

- our ability to effectively implement cost-cutting measures;
- our ability to establish and maintain strategic partnerships, including for the distribution of products;
- our ability to attract and retain sufficient, qualified personnel;
- our ability to obtain or maintain patents or other appropriate protection for the intellectual property;
- our dependency on the intellectual property licensed to us or possessed by third parties;
- our ability to adequately support future growth;
- our ability to maintain our Nasdaq listing; and
- potential product liability or intellectual property infringement claims.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and

TABLE OF CONTENTS

trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this prospectus, and in the documents incorporated by reference, particularly in the ‘Risk Factors’ section, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

The forward-looking statements included in this prospectus, and documents incorporated by reference in this prospectus, represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus contains estimates made, and other statistical data published, by independent parties and by us relating to market size and growth and other data about our industry. We obtained the industry and market data in this prospectus from our own research as well as from industry and general publications, surveys and studies conducted by third parties. This data involves a number of assumptions and limitations and contains projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. We caution you not to give undue weight to such projections, assumptions and estimates.

TABLE OF CONTENTS

USE OF PROCEEDS

We estimate that the net proceeds from sale of Units offered by us will be approximately $13.6 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and assuming a public offering price of $0.75 per Class A Unit and $1,000 per Class B Unit. If the underwriters' option to purchase additional securities is exercised in full, we estimate that our net proceeds will be approximately $15.7 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and assuming a public offering price of $0.75 per Class A Unit and $1,000 per Class B Unit.

We anticipate that we will use the net proceeds from this offering for our operations and for other general corporate purposes, including, but not limited to, building our infrastructure, including a small sales and marketing team, to commercialize Probuphine, conduct of the Phase IV trials required by the FDA and general working capital.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

TABLE OF CONTENTS

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization, as of June 30, 2018:

- on an actual basis; and
- on an as adjusted basis after giving effect to the sale of 3,000,000 Class A Units, at the assumed public offering price of $0.75 per Class A Unit and 12,750 Class B Units, at the public offering price of $1,000 per Class B Unit, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us.

You should consider this table in conjunction with “Use of Proceeds,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included elsewhere in this prospectus and our financial statements and unaudited as adjusted financial information and related notes thereto, which are incorporated by reference in this prospectus.

	As of June 30, 2018 (unaudited)	
	Actual	As Adjusted
Cash and cash equivalents	$ 1,613,564	$ 15,223,564
Total liabilities	$ 5,930,277	$ 5,930,277
Total stockholders’ equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized, 0 shares issued and outstanding, actual; 12,750 shares issued and outstanding, as adjusted	—	13
Common Stock, $0.001 par value, 125,000,000 shares authorized, 21,203,744 shares issued and outstanding, actual; 24,203,744 shares issued and outstanding, as adjusted	21,204	24,204
Additional paid in capital	325,411,154	339,018,141
Accumulated deficit	(326,745,543)	(326,745,543)
Total stockholders’ equity	(1,313,185)	12,296,815

The number of shares of our common stock that will be outstanding immediately after this offering is based on 21,203,744 shares of common stock outstanding as of June 30, 2018, and excludes as of such date:

- 3,647,863 shares of common stock issuable upon exercise of outstanding options, at a weighted average exercise price of $3.42 per share, of which 2,795,862 shares are vested as of such date;
- 46,000 shares of common stock reserved for future issuance under the 2015 Plan;
- 1,708,181 shares of common stock issuable upon exercise of warrants at a weighted average exercise price of $2.37;
- 2,000,000 shares of common stock issuable upon conversion of $2.4 million principal amount of outstanding indebtedness;
- shares of our common stock issuable upon exercise of the warrants to be issued in this offering; and

- shares of our common stock issuable upon conversion of the Series A Preferred to be issued in this offering.

The number of shares of our common stock outstanding after this offering will fluctuate depending on how many Class B Units are sold in this offering and whether and to what extent holders of Series A Preferred shares convert their shares to common stock.

To the extent we sell any Class B Units in this offering, the same aggregate number of common stock equivalents resulting from this offering would be convertible under the Series A Preferred issued as part of the Class B Units.

TABLE OF CONTENTS

The foregoing information assumes no exercise by the underwriters of their option to purchase additional securities and excludes shares of our common stock issuable upon exercise of the representative's warrants (4% of the shares of common stock sold in this offering, including shares issuable upon conversion of the Series B Preferred but excluding any securities sold upon exercise of the underwriter's option to purchase additional securities or shares issuable upon exercise of the warrants).

TABLE OF CONTENTS

DILUTION

If you purchase shares of our securities in this offering, you will experience dilution to the extent of the difference between the public offering price per share in this offering and our as adjusted net tangible book value per share immediately after this offering. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. As of June 30, 2018, our net tangible book value was approximately $(1,313,185), or approximately $(0.06) per share.

After giving effect to the assumed sale by us of 20,000,000 shares of our common stock in this offering at a public offering price of $0.75 per share (which was the last reported sale price of our common stock on the Nasdaq Capital Market on August 29, 2018), and the accompanying common warrants at a purchase price of $0.01 per common warrant and assuming no sale of any Series A Preferred shares in this offering and excluding the proceeds, if any, from the exercise of the common warrants and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our pro forma net tangible book value as of June 30, 2018 would have been approximately $12.3 million, or approximately $0.30 per share. This represents an immediate increase in pro forma net tangible book value of $0.36 per share to existing stockholders and an immediate dilution of $0.45 per share to new investors purchasing securities in this offering. The following table illustrates this per share dilution:

Assumed public offering price per share of common stock		$ 0.75
Historical net tangible book value per share as of June 30, 2018	$ (0.06)	
Increase in pro forma net tangible book value per share after this offering	$ 0.36	
Pro forma net tangible book value per share after giving effect to this offering		0.30
Dilution per share to new investors		$ (0.45)

The information above and below assumes that no Series A Preferred shares are issued in this offering. The information above assumes that the underwriters do not exercise their over-allotment option. If the underwriters exercise their over-allotment option in full, the pro forma net tangible book value will increase to $0.33 per share, representing an immediate increase to existing stockholders of $0.39 per share and an immediate dilution of $0.42 per share to new investors.

A $0.25 increase (decrease) in the assumed public offering price of $0.75 per share would result in an incremental increase (decrease) in our pro forma net tangible book value of approximately $4.7 million or approximately $0.11 per share, and would result in an incremental increase (decrease) in the dilution to new investors of approximately $0.14 per share, assuming that the number of shares of our common stock sold by us remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. A $0.50 increase (decrease) in the assumed public offering price of $0.75 per share would result in an incremental increase (decrease) in our pro forma net tangible book value of approximately $9.3 million or increase approximately $0.23 per share, and would result in an incremental increase (decrease) in the dilution to new investors of approximately $0.27 per share, assuming that the number of shares of our common stock sold by us remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We may also increase or decrease the number of shares of common stock we are offering from the assumed number of shares of common stock set forth above. An increase (decrease) of 250,000 in the assumed number of shares of common stock sold by us in this offering would result in an incremental increase (decrease) in our pro forma net tangible book value of approximately $0.2 million or approximately $0.002 per share, and would result in an incremental increase (decrease) in the dilution to new investors of approximately $0.002 per share, assuming that the assumed public offering price of the common stock remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. An increase (decrease) of 500,000 in the assumed number of shares of common stock sold by us in this offering would result in an incremental increase (decrease) in our pro forma net tangible book value of approximately $0.3 million or approximately $0.005 per share and would result in an incremental increase (decrease) in the dilution to new investors of approximately $0.005 per share, assuming that the assumed public offering price of the common stock remains the same and after deducting the estimated

32

TABLE OF CONTENTS

underwriting discount and estimated offering expenses payable by us. The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of securities in this offering and other terms of this offering determined at pricing. The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of securities in this offering and other terms of this offering determined at pricing.

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of outstanding options or warrants and the common warrants offered hereby. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

TABLE OF CONTENTS

MARKET FOR COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our common stock has been listed on The Nasdaq Capital Market since October 2015. The following table sets forth, for the periods indicated, our high and low sales prices on The Nasdaq Capital Market.

	High	Low
2018		
First Quarter	$ 1.45	$ 0.94
Second Quarter	$ 1.15	$ 0.60
Third Quarter (through August 29, 2018)	$ 1.10	$ 0.74
2017		
First Quarter	$ 4.80	$ 3.15
Second Quarter	$ 3.40	$ 1.80
Third Quarter	$ 2.15	$ 1.20
Fourth Quarter	$ 2.85	$ 1.13
2016		
First Quarter	$ 4.91	$ 2.98
Second Quarter	$ 7.41	$ 4.76
Third Quarter	$ 6.17	$ 4.80
Fourth Quarter	$ 6.10	$ 3.80

Holders

As of August 29, 2018, we had 110 registered holders of record of our common stock. A substantially greater number of holders of our common stock are “street name” or beneficial holders, whose shares of record are held by banks, brokers, other financial institutions, and registered clearing agencies.

Dividend Policy

We do not anticipate paying dividends on our common stock. We currently intend to retain all of our future earnings, as applicable, to finance the growth and development of our business. Our Loan Agreement prohibits the payment of dividends while the debt remains outstanding. Any future determination as to the payment of cash dividends on our common stock, if otherwise permissible at the time, will be at our board of directors’ discretion and will depend on our financial condition, operating results, capital requirements and other factors that our board of directors considers to be relevant.

TABLE OF CONTENTS

BUSINESS

The following information relates primarily to our Probuphine business, activities and prospects. For additional information regarding our business, we refer you to the documents that are incorporated by reference herein. See "Incorporation Of Certain Documents By Reference."

Overview

We are a pharmaceutical company developing proprietary therapeutics utilizing our proprietary long-term drug delivery platform, ProNeura, for the treatment of select chronic diseases for which steady state delivery of a drug provides an efficacy and/or safety benefit. We are currently transitioning to a commercial stage enterprise having recently re-acquired Probuphine, a product approved in the U.S. for management of opiate dependence. ProNeura is a continuous drug delivery system consisting of a small, solid rod made from a mixture of ethylene-vinyl acetate, or EVA, and a drug substance. The resulting product is a solid matrix that is placed subdermally, normally in the inside part of the upper arm in a simple physician office based procedure, and is removed in a similar manner at the end of the treatment period. The drug substance is released continuously through the process of dissolution resulting in a steady rate of release generally similar to intravenous administration avoiding the fluctuating peak and trough levels of oral dosing that pose problems in many disease settings.

Probuphine

Overview

Probuphine, our first marketed product based on our ProNeura drug delivery technology, is a six-month buprenorphine implant for the maintenance treatment of opioid addiction in patients who have achieved and sustained prolonged clinical stability on a dose of up to 8 mg per day of oral buprenorphine, which represents approximately twenty-five percent of oral buprenorphine prescriptions. Treatment with Probuphine requires a healthcare provider to be trained and certified under the Probuphine REMS program to insert a set of four implants, each smaller than a one-inch matchstick, sub-dermally in the patient's upper arm under local anesthetic during a short in-office procedure lasting about 15 minutes. After insertion, Probuphine delivers buprenorphine continuously for six months. Thereafter, the implants are removed and can be replaced with a new set of implants in the opposite arm.

The development and commercialization rights to Probuphine for the U.S. and Canada were licensed to Braeburn in December 2012 and following FDA approval in May 2016, Braeburn commenced a full commercial launch during the first quarter of 2017. Progress was slow and we received royalty revenues of only $215,000 for the year ended December 31, 2017. In early 2018, Braeburn substantially reduced its field sales force and medical liaison personnel following its receipt of a complete response letter from the FDA for its weekly and monthly depot injection products. Anticipating a negative impact on Probuphine sales in the U.S., we began discussing with Braeburn terms for the return of the Probuphine U.S. commercialization rights to Titan and on May 25, 2018, we entered into an agreement under which we received a $1 million payment from Braeburn and Braeburn's undertaking to provided transition services through 2018.

Based on feedback from key opinion leaders, we believe that access to care for patients with Probuphine has been negatively impacted by issues related to the complexity, timing and amount of reimbursement to patients and their doctors from insurance providers, as well as the requirements of the REMS program. Although the opioid addiction epidemic continues to be a major concern for our country, the hurdles to penetrating the market and growing sales of Probuphine have been considerable. We believe that a more focused commercialization strategy is necessary for success. These include re-segmenting target customer markets and focusing on high Probuphine-prescribing physicians with long-term recovery oriented treatment programs, residential treatment facilities that utilize MAT, academic institutions with addiction residency and fellowships programs, and the criminal justice system. We also plan to expand the specialty pharmacy network in order to better utilize the third party payor system. Additionally, we believe Probuphine can benefit from the trend of opioid addiction treatment's move towards extended release formulations, such as one month depot injections, the first of which was approved by the FDA at the end of 2017. These products will enable clinicians and patients to become accustomed to longer duration procedure-oriented treatment, which may encourage the potential use of Probuphine during the maintenance treatment stage.

TABLE OF CONTENTS

In March 2017, we received confirmation from the EMA that Probuphine is eligible for a centralized review and approval process. While the preparation of the MAA was in progress, we met with the review teams of the two EMA member countries appointed as rapporteur (Ireland) and co-rapporteur (United Kingdom) to familiarize them with the development of Probuphine and the safety and efficacy data set, as well as receive their advice on the MAA preparation and presentation. The MAA was submitted to the EMA on November 6, 2017. We were also granted Small Manufacturing Entity, or SME, status in Europe, which provides for some monetary benefits during the application process and commercialization. On March 21, 2018, we entered into the Purchase Agreement pursuant to which Molteni acquired the European intellectual property related to Probuphine, including the MAA, and will have the exclusive right to commercialize the Titan supplied Probuphine product in Europe, as well as certain countries of the Commonwealth of Independent States, the Middle East and North Africa. We have continued to assist Molteni in the MAA review process and during the second quarter we had meetings with the rapporteur and co-rapporteur regulatory review teams to present our strategy to address specific questions asked by these regulatory agencies as part of the review process. Together with Molteni, we are now preparing the full response to all questions that were asked, and we expect to submit these to the EMA no later than mid-September 2018. Based on the overall review process timeline the final recommendation and potential approval would occur during the first half of 2019.

Agreements

Braeburn

In December 2012, we entered into a license agreement, or the Braeburn Agreement with Braeburn pursuant to which we granted Braeburn an exclusive right and license to commercialize Probuphine in the United States of America and its territories, including Puerto Rico, and Canada. Under the Braeburn Agreement, as subsequently amended, Braeburn made a non-refundable up-front license fee payment of $15.75 million in 2012 and a milestone payment of $15 million upon FDA approval of the NDA in May 2016. The agreement also entitled us to royalties on net sales of Probuphine ranging in percentage from the mid-teens to the low twenties. In February 2016, Braeburn entered into a Distribution and Sublicense Agreement, or the Knight Agreement, with Knight Therapeutics Inc., or Knight, in which it appointed Knight as the exclusive distributor of Probuphine in Canada and granted Knight an exclusive license to commercialize Probuphine in Canada.

On May 25, 2018, we entered into a Termination and Transition Services Agreement, or the Transition Agreement, with Braeburn pursuant to which we regained all rights to the commercialization and clinical development of Probuphine granted under the Braeburn Agreement and Braeburn agreed to provide assistance