TITAN PHARMACEUTICALS INC
Form 10-K
April 01, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2018

or

.. **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to .

Commission file number 001-13341

TITAN PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3171940**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
400 Oyster Point Blvd., Suite 505, South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip code)**

Registrant's telephone number, including area code: (650) 244-4990

Securities registered pursuant to Section 12(b) of the Act: Common Stock, $0.001 par value

Securities registered pursuant to Section 12(g) of the Act: Common Stock, $0.001 par value

Indicate by check mark if the registrant is a well-known seasoned issuer as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to the filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). x Yes ¨ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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. (Check one):

Large accelerated filer	¨	Accelerated filer	¨
Non-accelerated filer	x	Smaller Reporting Company	x
		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 13(a) of the Exchange Act. ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant based on the closing price on June 29, 2018 was approximately $22.6 million.

As of March 25, 2019, 13,413,628 shares of common stock, $0.001 par value, of the registrant were issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

NONE

PART I

NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements in this Annual Report on Form 10-K or in the documents incorporated by reference herein may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act"). Reference is made in particular to the description of our plans and objectives for future operations, assumptions underlying such plans and objectives and other forward-looking terminology such as "may," "expects," "believes," "anticipates," "intends," "projects," or similar terms, variations of such terms or the negative of such terms. Forward-looking statements are based on management's current expectations. Actual results could differ materially from those currently anticipated due to a number of factors, including but not limited to, uncertainties relating to the commercialization of Probuphine®, financing and strategic agreements and relationships; difficulties or delays in the regulatory approval process; uncertainties relating to manufacturing, sales, marketing and distribution of our drug candidates that may be successfully developed and approved for commercialization; adverse side effects or inadequate therapeutic efficacy of our drug candidates that could slow or prevent product development or commercialization; dependence on third party suppliers; the uncertainty of protection for our patents and other intellectual property or trade secrets; and competition.

We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based.

References herein to "we," "us," "Titan," and "our company" refer to Titan Pharmaceuticals, Inc. unless the context otherwise requires.

Probuphine ® and ProNeura™ are trademarks of our company. This Annual Report on Form 10-K also includes trade names and trademarks of companies other than Titan.

Item 1. Business

Overview

We are a pharmaceutical company developing 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 have been transitioning to a commercial stage enterprise since May 25, 2018 when we reacquired Probuphine (buprenorphine) implant, or Probuphine, from our former licensee. Probuphine is the first product based on our ProNeura technology approved in the U.S. and Canada for the maintenance treatment of opioid use disorder, or OUD, in eligible patients. Since the reacquisition, we have been implementing a strategic plan focused on building a new foundation in support of an effective U.S. product relaunch targeting select OUD market segments best suited for Probuphine. Importantly, this included the establishment of a small experienced commercial team and the engagement of new strategic partners to facilitate the product order and distribution process in order to expand patient access to treatment with Probuphine.

ProNeura consists 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 in the inside part of the upper arm in a short physician office-based outpatient 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 diffusion-controlled dissolution, resulting in a steady rate of release (generally similar to intravenous administration), thereby avoiding the fluctuating peak and trough levels of oral dosing that often pose problems in many disease settings. 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. While our primary focus is on the commercialization of Probuphine, we are also engaged in research and development efforts on a product pipeline based on this platform technology.

Probuphine

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, a patient population that represents approximately 25% of oral buprenorphine prescriptions. Treatment with Probuphine requires a healthcare provider to be trained and certified under the Probuphine Risk Evaluation and Mitigation Strategy, or REMS, program to insert a set of four implants (each approximately the size of a one-inch matchstick), sub-dermally in the patient’s upper arm under local anesthetic during a short (about 15 minutes) in-office procedure. 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 originally licensed to Braeburn Pharmaceuticals, Inc., or Braeburn, in December 2012 and, following U.S. Food and Drug Administration, or FDA, approval in May 2016, Braeburn commenced a commercial launch during the first quarter of 2017. Progress was slow and we received royalty revenues of approximately $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 discussions for the return of the commercialization rights to Titan and on May 25, 2018, we entered into an agreement under which we received a $1 million payment from Braeburn, all of the Probuphine inventory and Braeburn's undertaking to provide certain transition services through the end of 2018.

During the latter half of 2018, we engaged the services of key consultants with expertise in launching and commercializing specialty pharmaceutical products, such as Probuphine, to fully understand Braeburn's product launch activities and its subsequent failure in the market. Based on feedback from key opinion leaders and these consultants, we believe that access to care for patients with Probuphine was 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 restrictive requirements of the REMS program. Notwithstanding the enormity of the opioid addiction epidemic in 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. This includes re-segmenting target customer markets and focusing on the following;

- high Probuphine-prescribing physicians with long-term recovery oriented treatment programs;
- residential treatment facilities, Veterans Administration hospitals and clinics that utilize medically assisted treatment, or MAT;
- academic institutions with addiction residency and fellowship programs; and
- the criminal justice system.

In addition, it is essential to improve access to reimbursement by third party payors which requires engaging the services of large specialty pharmacy organizations with pre-established relationships with the third-party payor plans. We also believe that Probuphine will benefit from the trend of opioid addiction treatment's move towards extended release formulations of buprenorphine, such as one month depot injections, the first of which was approved by the FDA at the end of 2017. The availability of one month depot injection formulations should enable clinicians and patients to become accustomed to longer duration procedure-oriented treatments, which in turn may lead to increased use of Probuphine during the maintenance treatment stage.

To implement the Probuphine relaunch, we undertook an equity financing in late September 2018 and engaged Dane Hallberg as our Chief Commercial Officer the following month. By the end of 2018, we had retained a small experienced sales and marketing team and began to address the product supply chain issues, notably the third-party payor pre-approval process and the logistics and distribution system, both of which have negatively impacted the product's acceptance and uptake. This has included identifying the need for a better centralized logistics service (referred to as a 'hub') that can service the combined process of product ordering and pre-approval by payors, as well as the expansion of the specialty pharmacy network to accelerate the pre-approval process and improve product distribution. In March 2019, we engaged the services of AllianceRx Walgreens Specialty Pharmacy, which we expect will help alleviate bottle necks in the third-party payor approval and product shipment process and are seeking to expand this network with a few additional large specialty pharmacies. We have also chosen AppianRx as our new hub which will be operational in early second quarter 2019. We believe that the engagement of AppianRx will lead to significant improvements in the automation and streamlining of the product supply chain process.

We are also committed to commencing two Phase 4 clinical studies with Probuphine during 2019 that were required by the FDA approval letter. One study will provide safety and pharmacokinetic information on both the implantation of Probuphine to a previously used anatomical site, as well as an alternate site, such as the abdomen. The second study is a registration study to evaluate the incidence of implant protrusion, migration and breakage during the treatment with Probuphine. We have been in discussions with the FDA regarding study design and protocol, and expect to commence the first study during the second quarter of 2019.

Probuphine received approval from the Canadian Health Authority in April 2018, and our licensee, Knight Therapeutics, Inc., or Knight, commenced its product launch in late October 2018. Knight is marketing Probuphine as a specialty product that, in addition to the typical benefits, can address some of the key needs in the Canadian market, particularly in providing buprenorphine maintenance treatment to OUD patients in rural communities where access to a clinic for frequent visits to fill prescriptions is not possible.

In March 2018, we entered into a purchase agreement with Molteni Farmaceuticci of Italy, or Molteni, pursuant to which Molteni acquired the European intellectual property related to Probuphine, including the Marketing Authorization Application, or MAA, that had been submitted to the European Medicines Agency, or EMA, in November 2017 and 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 been assisting Molteni in the MAA review process and during the second quarter of 2018 we had meetings with the rapporteur and co-rapporteur regulatory review teams to present our strategy and to address specific questions posed by these regulatory agencies. Together with Molteni, we have provided responses to all of the EMA's questions and expect that the final recommendation of the EMA on the Probuphine MAA and potential approval to occur during the second quarter of 2019.

ProNeura Continuous Drug Delivery Platform

Our ProNeura continuous drug delivery system consists 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 short 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 diffusion-controlled dissolution. This results in a continuous, steady rate of release generally similar to intravenous administration. We believe that such long-term, almost linear release characteristics are desirable as they avoid the fluctuating peak and trough levels of oral dosing that often poses problems in a range of disease settings.

The ProNeura platform was developed to address the need for a simple, practical method to achieve continuous long-term drug delivery, and, depending on the characteristics of the compound to be delivered, can potentially provide treatment on an outpatient basis over extended periods of up to 12 months. We believe that the benefits of this technology have been demonstrated by the clinical results seen to date with Probuphine, and, in addition, that the development and regulatory process have been affirmed by the FDA approval of this product. We have demonstrated the feasibility of the ProNeura platform with small molecules, hormones, and bio-active peptides. The delivery system works with both hydrophobic and hydrophilic molecules. We have also shown the flexibility of the platform by experimenting with the release characteristics of the EVA implants, layering the implants with varying concentrations of drug, and generating implants of different sizes and porosity to achieve a desired delivery profile. Formulation development is conducted at a dedicated pilot plant established by Titan at the South West Research Institute, or SWRI, in San Antonio, Texas that includes cGMP manufacturing and testing capabilities. We also receive support services from the vast array of SWRI groups with expertise in manufacturing and material sciences. The facilities are

compliant with both FDA and Drug Enforcement Agency, or DEA, requirements enabling us to work with controlled substances, and the manufacturing scale is ideal for product development during non-clinical and clinical testing stages.

Our Product Pipeline

Our goal is to expand our product pipeline using the ProNeura implant platform. We have been opportunistically evaluating other drugs for use with this technology, focusing on drugs where conventional treatment may be adversely impacted by fluctuating blood drug levels and/or poor patient compliance, and where existing therapeutic compounds have sufficient potency to be effective at low doses. With our resources focused on commercialization of Probuphine, further development of the ProNeura platform is currently being limited to non-clinical product development activity that is funded by external grants or other partners.

ProNeura-Ropinirole for Parkinson's Disease

Parkinson's disease, or PD, is a disease of the central nervous system characterized by the loss of dopaminergic neurons, which leads to increasing activity in the brain region that influences movement and motor function. According to the Parkinson's Disease Foundation, more than one million people in the U.S. suffer from PD, and this number is projected to double by 2030. Early stage PD patients are treated with daily doses of drugs designed to replace dopamine in the brain. However, these therapeutics typically lose their benefits after several years of chronic treatment and trigger serious side effects. About one-third of the treated patients develop motor response fluctuations and/or drug-induced dyskinesias within three to five years of treatment, and these symptoms are present in almost all patients after 10 to 12 years. Clinical and nonclinical research indicates that these motor side effects arise from the pulsatile dopaminergic stimulation resulting from current oral treatment. Continuous dopaminergic stimulation, or CDS, by subcutaneous infusion has been shown to palliate these motor complications, as well as to delay or prevent the onset of dyskinesias. We believe our ProNeura drug delivery technology provides a clinically-validated platform to safely and conveniently provide CDS for several months from a single treatment. Further, the subdermal placement of these implants eliminates many of the device-related complications associated with existing treatment modalities.

Based on these principles we designed an implant to deliver the drug ropinirole and conducted appropriate non-clinical studies, including a non-clinical study in an MPTP Parkinsonian primate model and demonstrated that a sustained non-fluctuating plasma level of ropinirole could be delivered safely for several months following implantation and could control PD symptoms without triggering dyskinesias in severely lesioned primates. Following further optimization of the implant and completion of the Investigational New Drug application, or IND, enabling non-clinical studies, we submitted the IND application to the FDA in early 2017 and it was cleared in August 2017 for commencement of the proposed Phase 1/2 clinical study. The trial is an open-label, sequential, dose escalation study that will enroll approximately 20 subjects with idiopathic Parkinson's disease. The primary objectives are to characterize the pharmacokinetic profile of the ropinirole implants, to evaluate their safety and tolerability, and to explore potential signals of efficacy using established disease-specific assessment scales. The first patient in the first cohort of the Phase 1/2 clinical study was treated in early October 2017 and in July 2018 the Data Safety Monitoring Board, or DSMB, completed a review of the data from the first cohort of patients and recommended that the trial continue with enrollment of the second cohort of patients. However, we chose to postpone further activity in this clinical study in order to focus our limited resources on commercialization of Probuphine. We do not anticipate further progress with this study until sufficient funds are available to support this program, either from a partner or future revenues from Probuphine.

Other ProNeura Product Feasibility Programs

Further development of the ProNeura platform has been limited to non-clinical product development activity that is funded by external grants and/or other partners.

We have conducted a feasibility assessment of a subcutaneous implant using our proprietary ProNeura sustained release technology to administer an opioid antagonist. We believe that a product able to deliver non-fluctuating, therapeutic levels of a mu-opioid receptor antagonist continuously for up to six months may be ideally suited for the prevention of opioid relapse and overdose in patients who have gone through a detoxification program. In September 2018, we were awarded a grant by the National Institute for Drug Addiction, or NIDA, in support of this program. The grant provides for approximately $2.67 million in funding during the first year and approximately $6.08 million during the second year subject to the terms and conditions specified in the grant, including our fund matching obligation in the amount of approximately $1.33 million during the first year. Funding during the second year is also subject to satisfactory progress of the project and the availability of funds to NIDA, although, as recently communicated by NIDA, it does not include any company fund matching obligations.

We are collaborating with the Walter Reed Army Institute of Research, or WRAIR, and SWRI in the early non-clinical evaluation of the ProNeura platform in malaria prophylaxis. The early data from this collaboration is encouraging and has been presented by the WRAIR staff at several conferences, and WRAIR has now received additional funding from the Department of Defense to continue the program with additional non-clinical testing of the atovaquone and proguanil implant formulations in large animal studies. WRAIR is also pursuing additional grant funding for testing other compounds that have shown promise as a prophylactic treatment for malaria and we will

collaborate with WRAIR and SWRI as needed for the preparation of these implant formulations that, if successful, could be available to us for potential commercialization.

During 2018, in collaboration with J.T. Pharmaceuticals, we conducted initial non-clinical testing for the development of a novel kappa opioid receptor agonist implant for the treatment of chronic pain. Based on this early work, we have collaborated on a National Institute of Health, or NIH, grant application and further development in 2019 will be possible only if the grant is approved. If successfully developed, this product would offer a potential non-addictive opioid analgesic for the treatment of chronic pain.

We have also conducted initial formulation studies and early *in vitro* testing for the potential development of an implant with a currently approved peptide for the treatment of adult type 2 diabetes mellitus. Additionally, in 2017 we completed early non-clinical development focused on formulation optimization of an implantable triiodothyronine (T3) product for the treatment of hypothyroidism. Any further development in these programs will depend on availability of additional funds through grants and/or interest from partners.

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 pursuant to which it granted Knight exclusivity to commercialize and distribute 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, in addition to $1 million and all available inventory of Probuphine, Braeburn agreed to provide assistance to Titan through December 28, 2018 to help ensure that patients and their doctors continued to have support and access to this treatment. As part of the Transition Agreement, we assumed a significant number of Braeburn's commercial contracts relating to the commercialization of Probuphine in the U.S., including the Knight Agreement.

Knight

Under the Knight Agreement, as amended in August 2018, we granted Knight an exclusive license to commercialize Probuphine in Canada as well as a right of first negotiation in the event we intend to license our right to commercialize any of our other products in Canada. We are entitled to receive royalty payments from Knight on net sales of Probuphine in Canada ranging in percentage from the low-teens to the mid-thirties. In addition, we will be the exclusive supplier of Probuphine to Knight subject to a supply agreement between us and Knight. During the term of the Knight Agreement, we may not commercialize any product in Canada containing buprenorphine that is intended for a treatment duration of six months or more.

Unless earlier terminated, the initial term of the Knight Agreement will expire on the 15th anniversary of the date of the first commercial sale of Probuphine for opioid addiction in Canada, which occurred during the fourth quarter of 2018. If Probuphine is approved for another indication in Canada after the fifth anniversary of the first commercial sale of Probuphine for opioid addiction in Canada, we must negotiate in good faith whether to extend the initial term.

After the initial term, the Knight Agreement will automatically renew for two-year periods until either party provides the other party with written notice of its intent not to renew at least 180 days prior to the expiration of the initial term or then-current term. We or Knight may terminate the Knight Agreement in the event that (i) either party determines in good faith that it is not advisable for Knight to continue to commercialize Probuphine in Canada as a result of a bona fide safety issue, (ii) the other party has filed for bankruptcy, reorganization, liquidation or receivership proceedings, or (iii) the other party materially breached the agreement and has not cured such breach within a specified time period. In addition, subject to certain exceptions and requirements, we may terminate the Knight Agreement (i) if Knight discontinues the commercial sale of Probuphine for a period of at least three months and fails to resume sales within the specified cure period, or (ii) in the event that Knight commences any legal proceedings seeking to challenge the validity or ownership of any of our patents related to Probuphine.

In the event of termination, among other things, Knight shall (i) cease commercialization of Probuphine in Canada, (ii) transfer title to all current and pending regulatory submissions and regulatory approvals for Probuphine to us and (iii) pay any royalty payments generated by Knight’s sales of Probuphine in Canada due to us.

Molteni

On March 21, 2018, we entered into and on August 3, 2018 amended an Asset Purchase, Supply and Support Agreement, or the Purchase Agreement, with Molteni pursuant to which Molteni acquired the European intellectual property related to Probuphine, including the MAA under review by the EMA, 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, or the Molteni Territory. We received an initial payment of €2.0 million ($2,448,000) for the purchased assets and an additional payment of €950,000 ($1,107,000) upon execution of the amendment. We will receive the following additional potential payments totaling up to €2.5 million (approximately $2,850,000) upon the achievement of certain regulatory and product label milestones, including: an aggregate of €1.0 million of milestone payments upon approval of the product reimbursement price in certain key countries, provided that the payments, which are subject to a 50% reduction if the EMA marketing authorization is not received on or prior to September 30, 2019, shall not be payable in the event such authorization is not received on or prior to March 31, 2020. Additionally, Titan is entitled to receive earn-out payments for up to 15 years on net sales of Probuphine in the Molteni Territory ranging in percentage from the low-teens to the mid-twenties.

The Purchase Agreement provides that Titan will supply Molteni with semi-finished product (i.e., the implant and the applicator) on an exclusive basis at a fixed price through December 31, 2019, with subsequent price increases not to exceed annual cost increases to Titan under its current manufacturing agreement and for the purchase of the active pharmaceutical ingredient.

Molteni will be prohibited from marketing a Competitor Product (as defined in the Purchase Agreement) in the Territory for the five year period following approval of the MAA. Thereafter, Molteni will be required to pay Titan a low single digit royalty on net sales by Molteni of any Competitor Product.

On March 21, 2018, we entered into an agreement, or the Loan Agreement, which amended and restated our prior loan agreement with Horizon Technology Finance Corp., or Horizon. Under the Loan Agreement, Horizon assigned $2,400,000 of the $4,000,000 outstanding principal balance of the loan to Molteni and Molteni was appointed collateral agent and assumed majority and administrative control of the debt. Molteni has the right to convert its portion of the debt into shares of our common stock at a conversion price of $7.20 per share and is required to effect this conversion of debt to equity if we complete an equity financing resulting in gross proceeds of at least $10,000,000 at a price per share of common stock in excess of $7.20 and repay the $1,600,000 principal balance of Horizon's loan amount.

In consideration of Molteni's entry into the Purchase Agreement and the Loan Agreement, on March 21, 2018, we entered into an agreement with Molteni. or the Rights Agreement, pursuant to which, as amended, we agreed to (i) issue Molteni seven-year warrants to purchase 90,000 shares of our common stock at an exercise price of $7.20 per share, (ii) provide Molteni customary demand and piggy-back registration rights with respect to the shares of common stock issuable upon conversion of its loan and exercise of its warrants, (iii) appoint one member of Titan's board of directors if Mr. Seghi Recli is not then serving on the board and (iv) provide board observer rights to Molteni if it has not designated a board nominee, as well as certain information rights. The board designation, observer and information rights will terminate at such time as Molteni ceases to beneficially own at least one percent of our outstanding capital stock (inclusive of the shares issuable upon conversion of its note and exercise of its warrants).

In connection with the August 2018 amendment to the Purchase Agreement, Molteni made a convertible loan to us of €550,000 (approximately $642,000) upon submission of the response to the 120-day letter from EMA on September 14, 2018 in accordance with the amendment. The convertible loan will convert automatically into shares of our common stock upon the issuance by the EMA of marketing approval for Probuphine at a conversion price per share equal to the lower of (i) $3.42 (the closing price on the loan funding date) and (ii) the closing price on the conversion date. In the event the EMA has not granted marketing approval by December 31, 2019, the loan will become due and payable, together with accrued interest at the rate of 9.5% plus the amount by which the one-month LIBOR exceeds 1.1%.

Intellectual Property

Our goal is to obtain, maintain and enforce patent protection for our product candidates, formulations, processes, methods and any other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. However, patent protection may not afford us with complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management and research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which may not be patentable, and for inventions for which patents may be difficult to enforce, we currently rely and will in the future rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

In June 2010, the United States Patent and Trademark Office (“USPTO”) issued a patent covering methods of using Probuphine for the treatment of opiate addiction. Titan is the owner of this patent which claims a method for treating opiate addiction with a subcutaneously implanted device comprising buprenorphine and EVA, a biocompatible copolymer that releases buprenorphine continuously for extended periods of time. This patent will expire in April 2024. A U.S. continuation application is currently pending which includes claims related to Probuphine for the treatment of pain. Related patents covering use of Probuphine with the continuous delivery technology for the treatment of opiate addiction have also been issued in Australia, Canada, Europe, India, Japan, Mexico, New Zealand, and Hong Kong. On March 21, 2018, we executed the Purchase Agreement with Molteni whereby the European intellectual property covering Probuphine, including the European patent, was acquired by Molteni. Patents covering certain dopamine agonist implants, including ropinirole implant, have already been issued or allowed in the United States, Europe, Japan, China, Australia, Canada, South Korea, Mexico, New Zealand, South Africa, Israel and Hong Kong.

We have filed additional patent applications for a heterogeneous implant designed with some unique properties that may provide benefits to the structural integrity of the implants and potentially enhance drug delivery. Corresponding patents have been granted in the US, Australia, Europe, Japan, South Korea, Mexico, Singapore, and South Africa, while applications remain pending in Canada, Hong Kong, and India.

Future court decisions or changes in patent law might materially affect the patents or patent applications, including, but not limited to, their expiration dates.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly evolving technology and intense competition. Many companies, including major pharmaceutical companies and smaller specialized biotechnology companies, are engaged in the development and commercialization of therapeutic agents designed for the treatment of the same diseases and disorders that we target. Many of our competitors have substantially greater financial and other resources, larger research and development staff and more experience in the regulatory approval process. Moreover, potential competitors have or may have patents or other rights that conflict with patents covering our technologies.

With respect to Probuphine, there are currently no other six-month implant formulations of buprenorphine on the market or in development. The primary competition it faces comes from Indivior, PLC (formerly the pharmaceutical business of Reckitt Benckiser Group, PLC), which markets globally a sublingual buprenorphine product (tablet and film formulations under the trade name Subutex and Suboxone) for the treatment of opioid dependence that currently holds the dominant market share of global sales. Indivior recently received FDA approval for a one month depot injection (tradename Sublocade) that became commercially available in the first quarter of 2018. Probuphine also faces competition from two additional proprietary daily dose formulations that have been approved by the FDA; the first is a sublingual tablet with the trade name of Zubsolv marketed by Orexo and the second is a buccal patch with the trade name of Bunavail marketed by Bio Delivery Sciences International. Several generic sublingual tablet formulations of buprenorphine similar to Suboxone and Subutex were approved by the FDA and have recently entered the opioid addiction treatment market. Other forms of buprenorphine are also in development by other companies, including intramuscular and intradermal one-week and one-month depot injections which, if approved, will also compete with our product. One additional depot formulation licensed to Braeburn has received tentative FDA approval that restricts marketing of the product in the U.S. until potentially November 2020. Alkermes, Inc. also markets Vivitrol®, a one-month depot injection of naltrexone as a maintenance treatment for opioid dependent patients who have successfully gone through a detoxification process and achieved abstinence.

If successfully developed and approved for commercialization, our ProNeura ropinirole product for PD will face competition primarily from numerous daily dose dopamine agonist treatments currently in use that provide symptom relief from disease related immobility, as well as the complications associated with long-term levodopa therapy (e.g.

dyskinesias, tolerance). Approved products in the U.S. in addition to Requip XL®, which is marketed by GlaxoSmithKline, include Apokyn® (US WorldMeds LLC), Parlodel® (Novartis Pharmaceuticals Inc.), Mirapex ER® (Boehringer Ingelheim Pharmaceuticals Inc.) and Neupro® (UCB Inc.). There is a strong need for products providing continuous, stable, long term delivery of dopamine and dopamine agonists and the FDA recently approved a product called Duodopa®, the first and only treatment delivered via catheters directly into the duodenum that is capable of providing 16 continuous hours of carbidopa and levodopa for treatment of motor fluctuations in advanced PD. Duodopa is marketed globally by Abbvie. Also, we are aware of products in mid-stage clinical development that are capable of short to medium-term subcutaneous and subdermal delivery of levodopa/carbidopa using pumps.

Manufacturing

The manufacturing of Probuphine has primarily been conducted at DPT Laboratories, Inc., or DPT, and we have expanded the manufacturing facility at this contract manufacturer to establish commercial scale capability to support the market launch of Probuphine and ongoing demand. We have entered into a commercial manufacturing agreement with DPT that governs the terms of the production and supply of Probuphine. We are responsible for the manufacture and supply of Probuphine as needed by Knight for Canada and to Molteni for the Molteni Territory.

To date, we have obtained the supply of bupenorphine from Teva Pharmaceuticals, Inc., or Teva, under a commercial supply agreement similar to the one with DPT.

We are in the process of qualifying a new EVA manufacturer which will provide a second source of the material. The vendor that used to sterilize the Probuphine implants indicated that it will no longer sterilize Schedule III controlled substances, including Probuphine. While we have qualified another sterilization vendor and transitioned to a new sterilization process, we cannot guarantee that such services will be available indefinitely. 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.

Sales and Marketing

Prior to Titan’s reacquisition of Probuphine commercialization rights in May 2018, Braeburn had sole responsibility for sales and marketing the product within the United States and, through Knight, in Canada. Commencing in June 2018, we began the process of transitioning to a commercial enterprise by engaging the services of key consultants with expertise in launching and commercializing specialty pharmaceutical products, such as Probuphine. Our goal was to fully understand the hurdles encountered by Braeburn in the prior product launch activities. Based on feedback from key opinion leaders and these consultants, we believe that access to care for patients with Probuphine was 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 restrictive requirements of the REMS program. We also believe that the broad marketing strategy that was initially undertaken reflected an incomplete understanding of the market and did not provide the requisite systems to support the reimbursement process and patient and physician education.

In order to lay the groundwork for increased utilization of Probuphine, we believe it is necessary to streamline the product ordering, distribution and reimbursement processes, to support patients and providers seeking access to treatment, and to develop a more focused commercialization strategy. In October 2018 we engaged the services of Dane Hallberg, who has extensive experience in launching specialty products in the U.S. market, as Chief Commercial Officer. In November 2018, Titan established a promotional review committee (“PRC”) to ensure all Probuphine promotional materials are in compliance with FDA regulations and to support submissions to the FDA’s Office of the Prescription Drug Promotion (OPDP).

Over the last few months we have established pharmaceutical foundational best practices including, but not limited to, sales compliance training and certification; drafting and implementation of company-wide SOPs; Sunshine Act Reporting; federal and state licensing; and sales and promotional materials creation and review. We have also assembled a small sales and marketing team with responsibilities that include regional sales oversight, medical science liaison services, strategic product and brand recognition development, and REMS program management. We have also retained a medical access specialist to address third-party payor coverage and to improve the product distribution system.

Along with establishing the internal team, we have engaged key external services to support these functions, including public relations, product branding and advertising capabilities. We have also engaged AppianRx as our new hub and are working closely with them to establish more efficient systems for product ordering and third party payor pre-approval. We believe that the positive impact of an automated and streamlined product supply chain process will be realized in the second quarter of 2019

We have recently engaged the services of AllianceRx Walgreens Specialty Pharmacy, which we expect to help alleviate bottlenecks in the third-party payor approval and product shipment process, and we hope to add additional large specialty pharmacies to the network in the near future. We have made good progress in establishing a strong foundation for our commercial activities, as well as re-engaging the medical community to consider using Probuphine as an option for the long term maintenance treatment of OUD, all of which lays the ground work for further progress in the market place during the second half of 2019.

While our overall market strategy for the relaunch of Probuphine targets four market segments, we have focused initially on physicians who are already prescribing Probuphine, while in the longer term our plan is to expand our efforts to address three additional market segments.

High Probuphine-prescribing physicians with long-term recovery oriented treatment programs

While there are currently approximately 52,000 buprenorphine certified healthcare providers in the U.S., approximately 90% of prescriptions for treating the 600,000 – 700,000 patients treated with oral buprenorphine are written by approximately 6,000 providers. Moreover, while over 2,500 healthcare providers were previously trained and certified to administer Probuphine, to date less than 200 have prescribed the treatment.

Our initial focus has been on the top tier of Probuphine prescribers to facilitate the growth of their businesses through increased utilization of the product. Utilizing some of the successful Probuphine practices, in the medium to longer term, we plan to establish centers that will provide sites for referrals from other health care providers. In addition, when our new hub, AppianRx, is operational in the second quarter, we expect to see improvement in 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 has the potential to generate new and clinically meaningful data, some of which will help us assess the potential for label expansion. We will also seek to partner with buprenorphine advocacy groups that can facilitate patient-healthcare provider location matching and broaden patient outreach.

Residential Treatment Facilities and Veterans Administration Hospitals

There are currently numerous residential addiction treatment facilities in the U.S. reflecting a large potential patient population who can benefit from Probuphine. 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.

We believe that the Veterans Administration Hospitals present another opportunity for the use of Probuphine. Addiction to opiates is a problem among the veterans, however the ability to treat patients through the VA system is hampered by limited facilities and medical resources. We are exploring programs to train staff at the VA hospitals in the use of Probuphine for long term maintenance treatment which will help in reducing the frequency of visits to the clinic and better utilize available resources.

Academic institutions with addiction treatment and training programs

There are an increasing number of academic addiction medicine training programs that treat OUD patients. At the end of October 2018 we conducted a training seminar for 40+ Nurse Practitioner students at Drexel University who were interested in pursuing careers in addiction medicine and nearing completion of their degree program. This seminar was similar to the Probuphine certification training program and provided these nurses with an opportunity to get familiar with Probuphine. 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 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

It is estimated that of the 2.3 million people currently confined in U.S. correctional facilities, approximately 25% suffer from OUD. Currently, less than 1% of U.S. prisons and jails allow access to medication for OUD due largely to the risk of misuse and diversion of sublingual formulations (pills, film), However, new research published by JAMA Psychiatry has demonstrated benefits of buprenorphine during incarceration and upon release. In Rhode Island, a recent study found that opioid overdose deaths dropped by nearly 2/3 when MAT was provided to all state inmates. A few criminal justice programs have begun to utilize medications in order to address jail overcrowding and recidivism related to OUD.

Our goal 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. The first pilot program has been initiated within the Nevada criminal justice system which has commenced to establish procedures and processes for the introduction of MAT within its system. We will monitor progress and continue to work with the Nevada criminal justice system to introduce Probuphine for maintenance therapy when eligible stable patients are available later in the year.

REMS Program

As a condition to the FDA's approval of Probuphine, we are required to maintain the Probuphine REMS program, with the goal of mitigating the risk of complications of migration, protrusion, expulsion and nerve damage potentially associated with its improper insertion and removal, and also the risks of accidental overdose, misuse and abuse. The REMS program requires training for healthcare providers who prescribe, insert and remove Probuphine implants and provide patient counseling. The distribution of Probuphine is restricted to those healthcare providers who have completed the training and have received certification under the Probuphine REMS. Accordingly, we have established a REMS management team to monitor all aspects of the REMS program requirements along with the medical sales liason, or MSL, team to conduct the REMS training sessions for the certification of health care providers to prescribe and/or insert and remove Probuphine. The MSL team also provides on-going in-market technical support to assist heath care providers developing expertise with the Probuphine insertion and removal procedures.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. drug development

In the United States, the FDA regulates drugs and devices under the Food, Drug and Cosmetics Act, or FDCA. Drugs and devices are also subject to other federal, state and local statutes and regulations. Products composed of both a drug product and device product are deemed combination products. If marketed individually, each component would be subject to different regulatory pathways and reviewed by different centers within the FDA. A combination product, however, is assigned to a center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of some of our product candidates, we expect the primary mode of action to be attributable to the drug component of the product, which means that the FDA's Center for Drug Evaluation and Research would have primary jurisdiction over the premarket development, review and approval. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions,

the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Additionally, a manufacturer may need to recall a product from the market. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of extensive nonclinical laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;

- Submission to the FDA of an IND application, which must become effective before human clinical trials may begin;

- Approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;

- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for each proposed indication;

- Submission to the FDA of an NDA for a new drug;

- A determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;

- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- Potential FDA audit of the nonclinical study and/or clinical trial sites that generated the data in support of the NDA; and

- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

The nonclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

The data required to support an NDA is generated in two distinct development stages: nonclinical and clinical. For new chemical entities, the nonclinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. These nonclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of the nonclinical tests must comply with federal regulations, including GLPs. The sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. Some nonclinical testing may continue even after the IND is submitted, but an IND must become effective before human clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials, including concerns that human research subjects will be exposed to unreasonable health risks, and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other

things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completion. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with GCP and FDA is able to validate the data through an onsite inspection if the agency deems it necessary.

Clinical trials

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.

- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits and provide a preliminary evaluation of efficacy. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks.

- Phase 3 clinical trials generally involve large numbers of patients at multiple sites (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for physician labeling. Phase 3 clinical trials may include comparisons with placebo and/or comparator treatments.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days for serious and unexpected suspected adverse events, finding from other studies or animal or in vitro testing that suggests a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, a sponsor must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within 7 calendar days. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial.

Pursuant to the Cures Act, the manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the later of 60 calendar days after the date of enactment of the Cures Act or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing

process must be capable of consistently producing quality batches of the drug candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA review process

The results of the nonclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under Prescription Drug User Fee Act, or PDUFA, for drugs that do not contain a new chemical entity the FDA has 10 months from the receipt date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the receipt date for a priority NDA. For drugs containing a new chemical entity, these 10 and six month review timeframes are from the filing date of an NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

After the FDA evaluates an NDA, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may resubmit the NDA addressing all of the deficiencies identified in the letter, withdraw the application, or request an opportunity for a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain

contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's safety and efficacy and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA also may place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing. As a condition to the FDA's approval of Probuphine, Braeburn was required to put the Probuphine REMS in place.

505(b)(2) approval process

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments, and permits the filing of an NDA where at least one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. The applicant may rely upon the FDA's prior findings of safety and effectiveness for a previously approved product or on published scientific literature, in support of its application. The FDA may also require 505(b)(2) applicants to perform additional trials to support the changes from the previously approved drug and to further demonstrate the new drug's safety and effectiveness. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Expedited development and review programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Any product submitted to the FDA for marketing, including under the Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or offers a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. Additionally, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinical development. Fast Track designation, priority review, and breakthrough designation do not change the standards for approval but may expedite the development or approval process.

Pediatric trials

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, that includes within 60 days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information.

Post-marketing requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the FDA of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the

internet. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development. Changes in statutes, regulations, or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Orange book listing

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A Section 505(b)(2) NDA is an application in which the applicant, in part, relies on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. Limited changes must be preapproved by the FDA via a suitability petition. ANDAs are termed "abbreviated" because they are generally not required to include nonclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents having claims that cover the applicant's product and method of use. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book. These products may be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Any applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must make patent certifications to the FDA that (1) no patent information on the drug or method of use that is the subject of the application has been submitted to the FDA; (2) the patent has expired; (3) the date on which the patent has expired and approval will not be sought until after the patent expiration; or (4) the patent is invalid or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted. The last certification is known as a paragraph IV certification. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through a paragraph IV certification or if the applicant is not seeking approval of a patented method of use. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients during which ANDAs for generic versions of those drugs cannot be submitted, unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following

the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA based on the approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use; the approval of which was required to be supported by new clinical trials conducted by, or for, the applicant.

U.S. marketing exclusivity

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving abbreviated new drug applications, or ANDAs, for drugs containing the active agent for the original indication or condition of use. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. Three-year and five-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Drug enforcement administration regulation

Because Probuphine is subject to the Controlled Substances Act, or CSA, we must comply with various requirements set forth by that legislation, as amended, its implementing regulations and as enforced by the DEA. The CSA imposes various registration, record-keeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls, prescription and order form requirements and restrictions on prescription refills for certain kinds of pharmaceutical products. A principal factor for determining the particular requirements of the CSA applicable to a product, if any, is its actual or potential abuse profile. A product may be listed as a Schedule I, II, III, IV or V controlled substance, with Schedule I presenting the highest perceived risk of abuse and Schedule V presenting the least. The active ingredient in our product, buprenorphine, is a Schedule III controlled substance and under various restrictions, including, but not limited to, mandatory written prescriptions and a labeling statement informing patients that selling or giving away Probuphine is against the law. In addition, under the Drug Addiction Treatment Act, which amended the CSA, use of Probuphine in the treatment of opioid addiction is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services, or HHS, of their intent to prescribe or dispense the product for the treatment of opioid addiction and have been assigned a unique identification number that must be included on every prescription. The HHS regulates the number of patients that physicians can treat with buprenorphine for opioid addiction and recently increased this number from a maximum of 100 patients to 275 patients for qualified physicians.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized. Separate registrations also are required for separate facilities.

The DEA typically inspects a facility to review its security measures prior to issuing a registration and on a periodic basis. Required security measures include background checks on employees and physical control of inventory through measures such as vaults and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA. Failure to maintain compliance with applicable DEA requirements can result in administrative, civil or criminal enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate administrative proceedings to revoke those registrations. In some circumstances, violations could result in criminal proceedings.

Other regulatory matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services including the Office of the

Inspector General, the United States Department of Justice, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local regulatory authorities. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that any of our product candidates, if approved, are sold in a foreign country, we may be subject to similar foreign laws.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and criminal penalties.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

European Union drug development

In the European Union, our future products may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of nonclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation is currently undergoing a revision process mainly aimed at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials and increasing their transparency.

European Union drug review and approval

In the European Economic Area, or EEA, which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Rest of the world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Reimbursement

Sales of Probuphine and any other product candidates we may successfully develop will depend, in part, on the extent to which such products are covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any products will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require our licensees to provide scientific and clinical support for the use of our product to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Third-party payors are increasingly reducing reimbursements for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our ability to generate sales and royalty revenue. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow our products to be sold on a profitable basis. Decreases in third-party reimbursement for our products or a decision by a third-party payor to not cover our products could reduce physician usage of the products and have a material adverse effect on our results of operations and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices that might otherwise be obtained. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

Reimbursement for injectable and implantable medications that are administered by a healthcare provider generally require a J-Code for the drug itself. Braeburn submitted its application for a permanent J-Code for Probuphine in June 2016. On November 1, 2016, the U.S. Centers for Medicare & Medicaid Services, or CMS, released a final rule that assigned a specific J-Code for Probuphine beginning January 1, 2017. Separate reimbursement codes are required for the Probuphine insertion and removal procedures. Braeburn had also applied for “G” codes for the Probuphine insertion and removal procedures, and in November 2017 the CMS approved specific codes and a reimbursement schedule for the physician office setting and the hospital outpatient setting. These G codes became effective on January 1, 2018. The timeline for the creation of the various procedural reimbursement pathways will vary based on the required governmental process or market needs for accurately tracking and reimbursing for the delivery of Probuphine and related procedural services.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Affordable Care Act and other reform initiatives

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare.

For example, in March 2010, the ACA was enacted in the United States. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. There have been judicial and Congressional challenges to the ACA, and we expect such challenges and amendments to continue in the future. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted and there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates and may affect our overall financial condition and ability to develop product candidates.

Employees

As of December 31, 2018, we had 23 full-time employees.

Item 1A. Risk Factors

Risks Related to Our Business

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

Since we regained the U.S. commercial rights to Probuphine in May 2018 and began our transition to a commercial enterprise, we have been largely dependent on the provision of support services under the Transition Agreement, as well as from advisors and consultants. We have been building the infrastructure necessary to be in a position to relaunch Probuphine, including the retention of a small sales and marketing team. However, we have faced and will continue to face intense competition for sales and marketing personnel with the necessary experience in addiction, reimbursement, specialty pharmacies and our targeted markets. There can be no assurance that the efforts of our sales and marketing personnel will be effective or that we will successfully 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. Probuphine's adoption by physicians has been hindered both by the 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 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 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 revenue from Probuphine, we will be unable to fund the required post-approval clinical studies or 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 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 resources to do so, as the proceeds of the September 2018 financing will only be sufficient to fund start-up costs for two of the required studies. In such 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.

Currently, there is a REMS program in place for Probuphine as required by the FDA. The REMS program 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 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 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 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 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 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, or 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 EVA manufacturer which will provide a second source of the material. The vendor that used to sterilize the Probuphine implants indicated that it will no longer sterilize Schedule III controlled substances, including Probuphine. While we have qualified another sterilization vendor and transitioned to a new sterilization process, we cannot guarantee that such services will be available indefinitely. 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.

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, maintaining our manufacturing equipment, trained personnel at the contract manufacturing vendor, formulation or packaging services, product distribution services, customer service activities and product returns processing. For example, we contract with 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 and SWRI, 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 or Knight 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 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.

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.

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 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 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. Lower priced generic forms of the oral product have also recently come to market. 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.

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.

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, Katherine DeVarney our Executive Vice President and Chief Scientific Officer, and Dane Hallberg, our Executive Vice President and Chief Commercial Officer. The loss of one or more of such individuals could substantially impair ongoing commercial activities and the 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.

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 year ended December 31, 2018 and 2017, we had net losses of approximately $9.3 million and $14.3 million, respectively, and had net cash used in operating activities of approximately $8.4 million and $12.7 million, respectively. 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 and cash equivalents at December 31, 2018, together with the approximately $0.6 million received from the subsequent exercise of warrants, will be sufficient to fund our Probuphine commercial efforts and Phase IV clinical program through the third quarter of 2019. We will be required to demonstrate sufficient progress in commercializing Probuphine in this short period of time in order to be able to raise additional funds to expand commercial activities for Probuphine. We will also require additional funds to advance our ProNeura development programs 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 will also need additional funds to complete the required post-approval clinical trials and there can be no assurance that any source of capital will be available to us on acceptable terms. 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, 2018, 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 and may be affected by numerous factors, including the results of our initial commercialization efforts and future research and development activities. We expect our expenses to increase in connection with our ongoing activities, particularly as we expand our infrastructure and, assuming funding is available, 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 expect to 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. 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, 2018, we had federal net operating loss and tax credit carryforwards of $263.6 million and $8.8 million, respectively, and state net operating loss and tax credit carryforwards of $107.8 million and $9.0 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 agreements contain restrictions on our operations and could result in certain adverse results.

Our Restated Loan Agreement 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 Restated 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. Our Convertible Loan agreement with Molteni contains comparable negative covenants. Subject to certain forbearance provisions in effect through December 31, 2019, upon the occurrence of an event of default under the Restated 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 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:

- sales levels of Probuphine;
- the success of our commercial relaunch;
- 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;
- 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.

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.

We will seek to raise additional funds, and may 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. Following this offering, raising sufficient capital will likely require an amendment to our certificate of incorporation to increase our authorized capital, an action that will require the affirmative vote of holders of a majority of our then outstanding common stock. 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.

Failure to meet the continued listing requirements of Nasdaq could result in a de-listing of our common stock.

If we fail to satisfy the continued listing requirements of Nasdaq, such as the 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.

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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties

Our executive offices are located in approximately 9,255 square feet of office space in South San Francisco, California that we occupy under a five-year operating lease expiring in June 2021. It is our intention to continue to be based in South San Francisco.

Item 3. Legal Proceedings

We are currently not a party to any material legal or administrative proceedings and are not aware of any pending or threatened legal or administrative proceedings against us.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

(a) Price Range of Securities

Our common stock is listed on the NASDAQ Capital Market ("NASDAQ") under the symbol "TTNP". The following table sets forth, for the periods indicated, the high and low sale prices for our common stock as reported by NASDAQ. For current price information, stockholders are urged to consult publicly available sources.

	High	Low
Fiscal 2018		
Fourth Quarter	$3.78	$1.03
Third Quarter	$6.60	$1.20
Second Quarter	$6.90	$3.60
First Quarter	$8.70	$5.64
Fiscal 2017		
Fourth Quarter	$17.10	$6.75
Third Quarter	$12.90	$7.80
Second Quarter	$20.40	$10.80
First Quarter	$28.80	$18.90

(b) Approximate Number of Equity Security Holders

At March 25, 2019, there were 13,413,628 shares of our common stock outstanding held by 121 holders of record. The number of record holders was determined from the records of our transfer agent and does not include beneficial owners of common stock whose shares are held in the names of various security brokers, dealers, and registered clearing agencies.

(c) Dividends

We have never declared or paid any cash dividends on our common stock and we do not anticipate paying any cash dividends to stockholders in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our Board and will be dependent upon our financial condition, results of operations, capital requirements, and such other factors as the Board deems relevant.

(d)

Equity Compensation Plan Information

The following table sets forth aggregate information regarding our equity compensation plans in effect as of December 31, 2018:

Plan category	Number of securities to be issued upon exercise of outstanding options, warrant and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (c)
Equity compensation plans approved by security holders	565,656	$ 16.10	104,304
Equity compensation plans not approved by security holders(1)(2)(3)	99,809	$ 28.34	—
Total	665,465	$ 17.94	104,304

(1) Includes 28,197 shares underlying options granted to employees and consultants who are not officers or directors of Titan under our 2001 Employee Non-Qualified Stock Option Plan.

(2) In May 2009, we granted 18,637 and 9,394 non-qualified stock options outside of our stock option plans to Dr. Rubin and Mr. Bhonsle, respectively, at an exercise price of $26.04 that vested over 48 months from the grant date.

(3) Includes 42,861 non-qualified stock options and restricted share awards granted to employees, directors and consultants under our 2014 Incentive Plan. For a description of the 2014 Plan, see note 12 to the financial statements.

Performance Graph

The information contained in the Performance Graph shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically incorporate it by reference into a document filed under the Securities Act or the Exchange Act.

The following graph compares the cumulative total stockholder return on our common stock with the cumulative total stockholder return of (i) the NASDAQ Composite Index and (ii) the NASDAQ Biotechnology Index. The graph assumes $100 invested on December 31, 2013 and assumes dividends reinvested. Measurement points are at the last trading day of the fiscal years ended December 31, 2014, 2015, 2016, 2017 and 2018. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

COMPARE CUMULATIVE TOTAL RETURN

AMONG TITAN PHARMACEUTICALS, INC., NASDAQ COMPOSITE INDEX AND

NASDAQ BIOTECHNOLOGY INDEX

Item 6. Selected Financial Data.

The selected financial data presented below summarizes certain financial data which has been derived from and should be read in conjunction with our financial statements and notes thereto included in the section beginning on page F-1. See also "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Years Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands, except per share data)				
Statement of Operations Data:					
Total revenue	$6,618	$215	$15,065	$1,671	$3,646
Operating expenses:					
Cost of goods sold	538	—	—	—	—
Research and development	7,478	9,648	6,126	4,675	4,075
General and administrative	6,866	5,069	4,596	3,755	3,046
Other income (expense), net	(759)	195	792	(4,520)	1,072
Net income (loss) and comprehensive income (loss)	(9,023)	(14,307)	5,135	(11,279)	(2,403)
Deemed dividend on trigger of downround provision	(285)	—	—	—	—
Net income (loss) applicable to common stockholders	$(9,308)	$(14,307)	$5,135	$(11,279)	$(2,403)
Basic net income (loss) per common share	$(0.78)	$(4.05)	$1.49	$(3.36)	$(0.84)
Diluted net income (loss) per common share	$(0.79)	$(4.22)	$1.20	$(3.36)	$(1.23)
Shares used in computing:					
Basic net income (loss) per common share	11,960	3,534	3,457	3,343	2,843
Diluted net income (loss) per common share	11,960	3,538	3,577	3,343	2,844

	As of December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	$9,295	$7,522	$14,006	$7,857	$15,470
Working capital	9,849	3,846	12,973	7,391	12,921
Total assets	14,095	8,905	18,667	13,287	20,851
Total stockholders' equity	6,831	857	13,191	6,990	8,611

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Forward-Looking Statements

Statements in the following discussion and throughout this report that are not historical in nature are "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. You can identify forward-looking statements by the use of words such as "expect," "anticipate," "estimate," "may," "will," "should," "in "believe," and similar expressions. Although we believe the expectations reflected in these forward-looking statements are reasonable, such statements are inherently subject to risk and we can give no assurances that our expectations will prove to be correct. Actual results could differ from those described in this report because of numerous factors, many of which are beyond our control. These factors include, without limitation, those described under Item 1A "Risk Factors." We undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date of this report or to reflect actual outcomes. Please see "Note Regarding Forward-Looking Statements" at the beginning of this Annual Report on Form 10-K.

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the related notes thereto and other financial information appearing elsewhere in this Annual Report on Form 10-K.

Overview

We are a pharmaceutical company developing 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 have been transitioning to a commercial stage enterprise since May 25, 2018 when we reacquired Probuphine® (buprenorphine) implant, or Probuphine, from Braeburn Pharmaceuticals, Inc., or Braeburn..Probuphine is the first product based on our ProNeura technology approved in the U.S. and Canada for the maintenance treatment of opioid use disorder, or OUD, in eligible patients. Since the reacquisition, we have been implementing a strategic plan aimed at building the foundation to support an effective U.S. product relaunch targeted at select OUD market segments best suited for a product like Probuphine, including the establishment of a small experienced commercial team and the engagement of new strategic partners in the product order and distribution process.

ProNeura consists 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 short physician office based outpatient 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 diffusion-controlled dissolution, resulting

in a steady rate of release generally similar to intravenous administration thereby avoiding the fluctuating peak and trough levels of oral dosing that pose problems in many disease settings. 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. While our primary focus is on the commercialization of Probuphine, we are also engaged in research and development efforts on a product pipeline based on this platform technology.

We operate in only one business segment, the development of pharmaceutical products. We make available free of charge through our website, www.titanpharm.com, our periodic reports as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Critical Accounting Policies and the Use of Estimates

The preparation of our financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in our financial statements and accompanying notes. Actual results could differ materially from those estimates. We believe the following accounting policies for the years ended December 31, 2018 and 2017 to be applicable:

Revenue Recognition

Beginning January 1, 2018, we have followed the provisions of ASC Topic 606, *Revenue from Contracts with Customers*. The guidance provides a unified model to determine how revenue is recognized.

We generate revenue principally from the sale of Probuphine in the U.S., collaborative research and development arrangements, technology licenses and sales, and government grants. Consideration received for revenue arrangements with multiple components is allocated among the separate performance obligations based upon their relative estimated standalone selling price.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. Our performance obligations include commercialization license rights, development services and services associated with the regulatory approval process.

We have optional additional items in contracts, which are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer’s discretion are generally considered as options. We assess if these options provide a material right to the customer and, if so, such material rights are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any additional payments are recorded in revenue when the customer obtains control of the goods or services.

Transaction Price

We have both fixed and variable consideration. Non-refundable upfront payments are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point they are considered fixed. We allocate the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties or earn-out payments, including milestone payments based on the level of sales, and the license or purchase agreement is deemed to be the predominant item to which the royalties or earn-out payments relate, we recognizes revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty or earn-out payment has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights are calculated using the residual approach. For all other performance obligations, we use a cost-plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under an arrangement and the period over which we expect to complete our performance obligations under an arrangement. We estimate the performance period or measure of progress at the inception of the arrangement and re-evaluate it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these estimates are recorded on a cumulative catch up basis. If we cannot reasonably estimate when our performance obligations either are completed or become inconsequential, then revenue recognition is deferred until we can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for licenses or sales of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that we have incurred to perform the services using the cost-to-cost input method.

Share-Based Payments

We recognize compensation expense for all share-based awards made to employees, directors and consultants. The fair value of share-based awards is estimated at the grant date based on the fair value of the award and is recognized as expense, net of estimated pre-vesting forfeitures, ratably over the vesting period of the award.

We use the Black-Scholes option pricing model to estimate the fair value method of our awards. Calculating stock-based compensation expense requires the input of highly subjective assumptions, including the expected term of the share-based awards, stock price volatility, and pre-vesting forfeitures. We estimate the expected term of stock options granted for the years ended December 31, 2018 and 2017 based on the historical experience of similar awards, giving consideration to the contractual terms of the share-based awards, vesting schedules and the expectations of future employee behavior. We estimate the volatility of our common stock at the date of grant based on the historical volatility of our common stock. The assumptions used in calculating the fair value of stock-based awards represent our best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. In addition, we are required to estimate the expected pre-vesting forfeiture rate and only recognize expense for those shares expected to vest. We estimate the pre-vesting forfeiture rate based on historical experience. If our actual forfeiture rate is materially different from our estimate, our stock-based compensation expense could be significantly different from what we have recorded in the current period.

Income Taxes

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenue and expense for tax and financial statement purposes.

As part of the process of preparing our financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our current tax exposure under the most recent tax laws and assessing temporary differences resulting from differing treatment of items for tax and accounting purposes.

We assess the likelihood that we will be able to recover our deferred tax assets. We consider all available evidence, both positive and negative, expectations and risks associated with estimates of future taxable income and ongoing prudent and feasible tax planning strategies in assessing the need for a valuation allowance. If it is not more likely than not that we will recover our deferred tax assets, we will increase our provision for taxes by recording a valuation

allowance against the deferred tax assets that we estimate will not ultimately be recoverable.

Clinical Trial Accruals

We also record accruals for estimated ongoing clinical trial costs. Clinical trial costs represent costs incurred by CROs and clinical sites. These costs are recorded as a component of research and development expenses. Under our agreements, progress payments are typically made to investigators, clinical sites and CROs. We analyze the progress of the clinical trials, including levels of patient enrollment, invoices received and contracted costs when evaluating the adequacy of accrued liabilities. Significant judgments and estimates must be made and used in determining the accrued balance in any accounting period. Actual results could differ from those estimates under different assumptions. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. The actual clinical trial costs for studies conducted in the past three years have not differed materially from the estimated projection of expenses.

Warrants Issued in Connection with Equity Financing

We generally account for warrants issued in connection with equity financings as a component of equity, unless there is a deemed possibility that we may have to settle warrants in cash. For warrants issued with deemed possibility of cash settlement, we record the fair value of the issued warrants as a liability at each reporting period and record changes in the estimated fair value as a non-cash gain or loss in the Statements of Operations and Comprehensive Income (Loss).

Liquidity and Capital Resources

	2018	2017	2016
	(in thousands)		
As of December 31:			
Cash and cash equivalents	$9,295	$7,522	$14,006
Working capital	$9,849	$3,846	$12,973
Current ratio	3.9:1	1.9:1	3.7:1
Years Ended December 31:			
Cash provided by (used in) operating activities	$(8,431)	$(12,677)	$6,293
Cash used in investing activities	$(416)	$(175)	$(171)
Cash provided by financing activities	$10,620	$6,729	$27

We have funded our operations since inception primarily through the sale of our securities and the issuance of debt, as well as with proceeds from warrant and option exercises, corporate licensing and collaborative agreements, the sale of royalty rights and government-sponsored research grants. In the second quarter or 2018, we began generating revenue from the direct sale of products. At December 31, 2018, we had working capital of approximately $9.8 million compared to working capital of approximately $3.8 million at December 31, 2017.

Our operating activities used approximately $8.4 million of cash during the year ended December 31, 2018. This consisted primarily of the net loss for the period of approximately $9.0 million, approximately $1.3 million related to a non-cash gain on inventory received from the Transition Agreement, approximately $0.4 million related to net changes in other operating assets and liabilities and approximately $0.1 million related to non-cash gains resulting from changes in the fair value of derivatives. This was offset in part by non-cash charges of approximately $1.6 million related to share-based compensation expenses, approximately $0.5 million related to non-cash interest expense and approximately $0.4 million related to depreciation and amortization. Uses of cash in operating activities were primarily to fund product development programs and administrative expenses.

Net cash used in investing activities of approximately $0.4 million during the year ended December 31, 2018 was related to purchases of equipment.

Our financing activities provided approximately $10.6 million during the year ended December 31, 2018, which consisted of approximately $9.7 million related to net proceeds from the sale of stock and warrants, approximately $3.3 million from the exercise of warrants and approximately $0.7 million from the issuance of debt. This was offset in part by $3.0 million related to the repayment of debt.

At December 31, 2018, we had restricted cash of approximately $0.4 million. This represents a cash security deposit for an outstanding letter of credit established to fund upcoming EMA filing fees. The letter of credit was cancelled in March 2019 and the restriction on our cash was removed.

In September 2018, we completed an underwritten public offering of units consisting of stock and warrants pursuant to which we received net proceeds of approximately $9.7 million, after deduction of underwriting fees and other offering expenses. Subsequent to the offering, we received an aggregate of $3.3 million from the exercise of warrants sold in the offering.

In August 2018, we amended the Purchase Agreement to eliminate an aggregate of €2,000,000 of future regulatory milestones in exchange for which Molteni made an immediate payment to us of €950,000 (approximately $1.1 million) and a Convertible Loan to us of €550,000 (approximately $0.6 million) on September 18, 2018 following the submission of our response to the 120-day letter from the European Medicines Agency (“EMA”) before September 14, 2018.

In May 2018, we entered into the Transition Agreement pursuant to which we regained all Probuphine commercialization and clinical development rights we had granted to Braeburn. Braeburn paid us $1.0 million and transferred inventory to us with a value of approximately $1.1 million.

In March 2018, we entered into the Purchase Agreement with Molteni pursuant to which Molteni acquired the European intellectual property related to Probuphine and exclusive commercialization rights in the Molteni Territory. We received an initial payment of €2.0 million (approximately $2.4 million) for the purchased assets and will receive potential additional payments totaling up to €4.5 million (approximately $5.1 million) upon the achievement of certain regulatory and product label milestones. Additionally, we are entitled to receive earn-out payments for up to 15 years on net sales of Probuphine in the Molteni Territory ranging in percentage from the low-teens to the mid-twenties.

In July 2017, we entered into a venture loan and security agreement with Horizon (the "Loan Agreement") pursuant to which we received an initial loan in the principal amount of $7.0 million. In February 2018, we entered into an amendment to the Loan Agreement pursuant to which we prepaid $3.0 million of the outstanding principal amount and agreed to make an additional $1.0 prepayment to Horizon no later than May 14, 2018. In March 2018, the Loan Agreement was amended and restated (the "Restated Loan Agreement") by Titan, Horizon and Molteni. Pursuant to the Restated Loan Agreement, Molteni acquired $2.4 million of the $4.0 million principal balance of the loan and assumed majority and administrative control of the debt obligation and the interest only payment and forbearance periods were extended to December 31, 2019. In addition, Molteni has the right to convert its portion of the debt into shares of our common stock at a conversion price of $7.20 per share and is required to effect this conversion of debt to equity if we complete an equity financing resulting in gross proceeds of at least $10.0 million at a price per share in excess of $7.20 and repay the $1.6 million principal balance of Horizon's loan amount.

At December 31, 2018, we had cash and cash equivalents of approximately $9.3 million, which we believe, along with the $0.6 million received from the subsequent exercise of warrants, are sufficient to fund our planned operations through the third quarter of 2019. Thereafter, we will require additional funds to finance our operations, including the commercialization of Probuphine in the U.S., completion of the Probuphine Phase IV clinical trials mandated by the FDA and advancement of our current ProNeura development programs to later stage clinical studies. Our efforts to obtain additional financing may not be successful.

The following table sets forth the aggregate contractual cash obligations as of December 31, 2018 (in thousands):

	Payments Due by Period				
Contractual obligations	**Total**	**< 1 year**	**1-3 years**	**3-5 years**	**5 years+**
Operating leases	$762	$ 299	$ 463	$ —	$ —
Debt obligations	$5,432	$ 626	$ 4,806	$ —	$ —
Total contractual cash obligations	$6,194	$ 925	$ 5,269	$ —	$ —

Results of Operations

Year Ended December 31, 2018 Compared to Year Ended December 31, 2017

Product revenues for the year ended December 31, 2018 were approximately $0.5 million reflecting net revenues generated from sales of Probuphine by us after reacquiring the product in late May 2018. There were no product revenues in 2017.

License revenues were approximately $5.4 million and $215,000 for the years ended December 31, 2018 and 2017, respectively. Revenues for the year ended December 31, 2018 reflect approximately $2.1 million related to the up-front payment and amortization of deferred revenue related to the sale to Molteni of the European intellectual property rights to our Probuphine product, approximately $1.1 million related to the amendment to our Purchase Agreement with Molteni in August 2018, approximately $2.1 million related to reacquiring the rights to Probuphine and termination of the Braeburn license, and approximately $32,000 related to the recognition of royalties earned on net sales of our Probuphine product by Braeburn prior to termination of the License Agreement in late May 2018. Revenue for the year ended December 31, 2017 reflects the recognition of royalties earned on net sales of Probuphine.

Grant revenues were approximately $0.7 million for the year ended December 31, 2018. We had no grant revenues for the year ended December 31, 2017.

Cost of goods sold for the year ended December 31, 2018 was approximately $0.5 million. Cost of goods sold reflects costs and expenses associated with sales of our Probuphine product by us after reacquiring the product in May 2018.

Research and development expenses for 2018 were approximately $7.5 million compared to approximately $9.6 million in 2017, a decrease of approximately $2.1 million, or 22%. The decrease in research and development costs was primarily associated with decreases in external research and development expenses related to the support of our ProNeura product development programs, including the costs associated with the clinical study of the ropinirole implant and the cost of preparing the Probuphine MAA for submission to the EMA, employee related expenses and other research and development expenses. External research and development expenses include direct expenses such as CRO charges, investigator and review board fees, patient expense reimbursements, expenses for NDA preparation and contract manufacturing expenses. During 2018, external research and development expenses were approximately $3.8 million compared to approximately $5.6 million in 2017. Other research and development expenses include internal operating costs such as research and development personnel-related expenses, non-clinical and clinical product development related travel expenses, and allocation of facility and corporate costs. As a result of the risks and uncertainties inherently associated with pharmaceutical research and development activities described elsewhere in this document, we are unable to estimate the specific timing and future costs of our clinical development programs or the timing of material cash inflows, if any, from our product candidates. However, we anticipate that our research and development expenses will increase in connection with the Probuphine Phase 4 clinical studies commencing in 2019 and our current ProNeura development program and any other ProNeura technology based product development activities we may pursue to the extent these costs are not supported through grants or partners.

Selling, general and administrative expenses for 2018 were approximately $6.9 million compared to approximately $5.1 million in 2017, an increase of approximately $1.8 million, or 35%. The increase in selling, general and administrative expenses was primarily from increases in expenses related to our Probuphine commercial activities, including increases in consulting and other services related costs of approximately $1.0 million, employee related costs of approximately $0.4 million, legal fees of approximately $0.4 million, facilities related costs of approximately $0.1 million, travel costs of approximately $0.1 million. This was offset in part by decreases in non-cash stock-based compensation of approximately $0.2 million.

Net other expense for the year ended December 31, 2018 was approximately $0.8 million, compared to net other income of approximately $0.2 million in 2017. Net other expense in 2018 consisted primarily of $0.1 million related to non-cash gains on changes in the fair value of derivatives offset by approximately $0.9 million consisting of interest expenses related to the Loan Agreement and other expenses. Net other income in 2017 consisted primarily of $0.6 million related to non-cash gains on changes in the fair value of warrant liabilities offset by approximately $0.4 million consisting of interest expenses related to the Loan Agreement and other expenses.

Our net loss applicable to common stockholders for the year ended December 31, 2018 was approximately $9.3 million, or approximately $0.78 per share, compared to our net loss applicable to common stockholders of approximately $14.3 million, or approximately $4.05 per share, for the comparable period in 2017.

Year Ended December 31, 2017 Compared to Year Ended December 31, 2016

License revenues were approximately $215,000 and $15.1 million for the years ended December 31, 2017 and 2016, respectively. 2017 license revenues reflect the recognition of royalties earned on net sales of Probuphine. License revenues for the year ended December 31, 2016 reflect approximately $65,000 from the recognition of royalties earned on net sales of Probuphine and approximately $15.0 million from the recognition of the milestone payment earned upon FDA approval of our Probuphine NDA in May 2016.

Research and development expenses for 2017 were approximately $9.6 million compared to approximately $6.1 million in 2016, an increase of approximately $3.5 million, or 57%. The increase in research and development costs was primarily associated with increases in external research and development expenses related to the support of our ProNeura product development programs, including the costs associated with the IND and commencement of clinical study of the ropinirole implant and the cost of preparing the Probuphine MAA for submission to the EMA, employee related expenses and other research and development expenses. External research and development expenses include direct expenses such as CRO charges, investigator and review board fees, patient expense reimbursements, expenses for NDA preparation and contract manufacturing expenses. During 2017, external research and development expenses relating to our product development programs were approximately $5.6 million compared to approximately $3.5 million in 2016. Other research and development expenses include internal operating costs such as clinical research

and development personnel-related expenses, clinical trials related travel expenses, and allocation of facility and corporate costs. As a result of the risks and uncertainties inherently associated with pharmaceutical research and development activities described elsewhere in this document, we are unable to estimate the specific timing and future costs of our clinical development programs or the timing of material cash inflows, if any, from our product candidates. However, we anticipate that our research and development expenses will increase in connection with our current ProNeura development program and any other ProNeura technology based product development activities we may pursue.

General and administrative expenses for 2017 were approximately $5.1 million compared to approximately $4.6 million in 2016, an increase of approximately $0.5 million, or 11%. The increase in general and administrative expenses was primarily related to increases in non-cash stock-based compensation and employee-related costs of approximately $0.4 million and other expenses of approximately $0.1 million.

Net other income for the year ended December 31, 2017 was approximately $0.2 million, compared to approximately $0.8 million in 2016. Net other income in 2017 consisted primarily of $0.6 million related to non-cash gains on changes in the fair value of warrant liabilities offset by approximately $0.4 million consisting of interest expenses related to our Loan Agreement and other expenses. Net other income in 2016 consisted primarily of $0.8 million related to non-cash gains on changes in the fair value of warrant liabilities.

Our net loss applicable to common stockholders for the year ended December 31, 2017 was approximately $14.3 million, or approximately $4.05 per share, compared to our net income applicable to common stockholders of approximately $5.1 million, or approximately $1.49 per share, for the comparable period in 2016.

Off-Balance Sheet Arrangements

We have never entered into any off-balance sheet financing arrangements and we have never established any special purpose entities. We have not guaranteed any debt or commitments of other entities or entered into any options on non-financial assets.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We held no marketable securities at December 31, 2018 and 2017.

Item 8. Financial Statements and Supplementary Data.

The response to this item is included in a separate section of this Report. See “Index to Financial Statements” on Page F-1.

Item 9. Changes and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

(a) *Evaluation of Disclosure Controls and Procedures* : Our principal executive and financial officers reviewed and evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our principal executive and financial officers concluded that our disclosure controls and procedures are effective in timely providing them with material information relating to the Company, as required to be disclosed in the reports we file under the Exchange Act.

(b) *Management's Annual Report on Internal Control Over Financial Reporting*:

Internal control over financial reporting refers to the process designed by, or under the supervision of, our principal executive officer and principal financial officer, and effected by our Board, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;

(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorization of our management and directors; and

(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisitions, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management overrides. Due to such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk. Management is responsible for establishing and maintaining adequate internal control over financial reporting for the company.

45

Management has used the framework set forth in the report entitled *Internal Control—Integrated Framework* published by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), known as COSO, to evaluate the effectiveness of the Company's internal control over financial reporting. Based on this assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2018.

(c) *Changes in Internal Control Over Financial Reporting* : There were no changes in our internal control over financial reporting (as defined in Rules 13(a)-15(f) and 15(d)-15(f) under the Securities Act) during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors; Executive Officers and Corporate Governance

Set forth below are the name, age and position and a brief account of the business experience of each of our executive officers and directors:

Name	Age	Office	Director Since
Marc Rubin	64	Executive Chairman of the Board	November 2007
Sunil Bhonsle	69	Chief Executive Officer, President and Director	February 2004
Katherine Beebe DeVarney	58	Executive Vice President and Chief Scientific Officer	
Dane Hallberg	50	Executive Vice President and Chief Commercial Officer	
Joseph A. Akers (1)(2)	73	Director	November 2014
Rajinder Kumar (3)	63	Director	January 2017
M. David MacFarlane (1)(2)(3)	78	Director	May 2002
James R. McNab, Jr. (1)(3)	75	Director	November 2014
Federico Seghi Recli	49	Director	May 2018
Scott A. Smith (2)	57	Director	January 2017

(1) Member of Audit Committee
(2) Member of Compensation Committee
(3) Member of Governance Committee

Marc Rubin, M.D. served as our President and Chief Executive from October 2007 until December 2008 and was re-engaged as our Executive Chairman in May 2009. Until February 2007, Dr. Rubin served as Head of Global Research and Development for Bayer Schering Pharma, as well as a member of the Executive Committee of Bayer Healthcare and the Board of Management of Bayer Schering Pharma. Prior to the merger of Bayer Pharmaceuticals and Schering AG in June 2006, Dr. Rubin was a member of the Executive Board of Schering AG since joining the Company in October 2003, as well as Chairman of Schering Berlin Inc. and President of Berlex Pharmaceuticals, a division of Schering AG. From 1990 until August 2003, Dr. Rubin was employed by GlaxoSmithKline where he held positions of increasing responsibility in global clinical and commercial development overseeing programs in the United States, Europe, Asia and Latin America. From 2001 through 2003, he was Senior Vice President of Global Clinical Pharmacology & Discovery Medicine. Dr. Rubin holds an M.D. from Cornell University Medical College. Dr. Rubin currently serves on the board of directors of Curis Inc. and Galectin Therapeutics. Based on Dr. Rubin's position as our Executive Chairman, his extensive senior management experience and service on boards of directors in the biotechnology and pharmaceutical industries and his medical background, our Board believes that Dr. Rubin has the appropriate set of skills to serve as a member of the Board.

Sunil Bhonsle served as our Executive Vice President and Chief Operating Officer from September 1995 until December 2008 and was re-engaged as our President in May 2009. Mr. Bhonsle was appointed as our Chief Executive Officer in November 2015. Mr. Bhonsle served in various positions, including Vice President and General Manager — Plasma Supply and Manager — Inventory and Technical Planning, at Bayer Corporation from July 1975 until April 1995. Mr. Bhonsle holds an M.B.A. from the University of California at Berkeley and a B.Tech. in chemical engineering from the Indian Institute of Technology. Based on Mr. Bhonsle's position as our principal executive officer and his substantial experience in the pharmaceutical industry, particularly in the areas of product development and manufacturing, our Board believes that Mr. Bhonsle has the appropriate set of skills to serve as a member of the Board.

Katherine Beebe DeVarney, Ph.D. joined Titan in February 2007 and currently serves as the Company's Chief Scientific Officer. During her 12 years with the Company, she has served in various scientific and medical research and development capacities, with primary responsibility for oversight of the Company's product research and development, Regulatory Affairs, and Medical Affairs. Dr. DeVarney has 23 years of experience as a Neuroscientist in the pharmaceutical industry, including positions of increasing responsibility with SmithKline Beecham, GlaxoSmithKline, Merck, and Corcept Therapeutics. Prior to her pharmaceutical career, Dr. DeVarney was a hospital-based clinician and worked in academic medicine for 10 years. She received her Ph.D. in Clinical Neuropsychology from George Mason University, and completed a two-year post-doctoral fellowship at Graduate Hospital and the University of Pennsylvania.

Dane Hallberg joined the Company in October 2018 and currently serves as the Company's Chief Commercial Officer. From October 2011 until December 2017, he served as chief executive officer of Able Star L.L.C., a strategic consultancy and full service agency he founded for market access, pharmaceutical and biotechnology companies. From June 2018 until he began consulting with Titan in September 2018, Mr. Hallberg, served as a strategic consultant to Bristol-Myers Squibb. Mr. Hallberg, who has over 20 years of experience in the healthcare industry, received a B.S. and M.A. from Western Illinois University, and completed the Executive Leadership Program at Cornell University.

Joseph A. Akers was employed in various capacities by Bayer Corporation, Bayer Healthcare and certain related entities, including as president of the Hematology/Cardiology Business Unit from 2004 to 2007, president and chief executive officer of Bayer Business and Corporate Services from July 2002 through 2003 and executive vice president and chief administrative and financial officer from 1999 to July 2002. Mr. Akers received a B.S. in marketing and an M.B.A. in finance from the University of California at Berkeley. Based on Mr. Akers' extensive management experience in the pharmaceutical industry, particularly in the areas of administration and finance, our Board believes that Mr. Akers has the appropriate set of skills to serve as a member of the Board.

Rajinder Kumar, Ph.D. has served as the Chairman and Chief Executive Officer of MeRaD Pharmaceutical Ltd. in Cambridge U.K. since May 2009. He has also served as President and Chief Medical Officer of Vitas Pharma in Hyderabad, India since he founded such company in 2010. For the decade prior to joining MeRaD, he served in various executive capacities with Dr. Reddy's Labs, Ranbaxy Laboratories Limited, Synaptic Pharmaceutical LLP and Glaxo SmithKline Beecham. Dr. Kumar is a member of scientific advisory boards in neuroscience, anti-infectives and metabolic disorders He received a B.S. in Human Biology from the University of London, a Masters in Ethology from the University of Birmingham, a MBChB in Medicine from the University of Dundee and an advanced diploma in Psychological Medicine from The Royal College of Surgeons and Physicians in Ireland. Based on Dr. Kumar's management experience in the pharmaceutical industry, our Board believes that Dr. Kumar has the appropriate set of skills to serve as a member of the Board.

M. David MacFarlane, Ph.D. served as Vice President and Responsible Head of Regulatory Affairs of Genentech, Inc. from 1989 until his retirement in August 1999. Prior to joining Genentech, Inc., he served in various positions with Glaxo Inc., last as Vice President of Regulatory Affairs. Based on Dr. MacFarlane's management experience in the pharmaceutical industry, particularly in the area of clinical and regulatory affairs, our Board believes that Dr. MacFarlane has the appropriate set of skills to serve as a member of the Board.

James R. McNab, Jr. has served since June 2014 as chief executive officer of JT Pharmaceuticals, Inc., a privately-held drug discovery company he founded. Since 2009, Mr. McNab has served as executive chairman of FirstString Research, Inc., a privately-held biopharmaceutical company. Mr. McNab has co-founded several privately-held companies, including Sontra Medical Corporation, a drug delivery company, and Parker Medical Associates, a manufacturer and worldwide supplier of orthopedic and sports-related products. He received a B.A. in economics from Davidson College and an M.B.A. from the University of North Carolina at Chapel Hill. Based on Mr.

McNab’s extensive management experience in the pharmaceutical industry, our Board believes that Mr. McNab has the appropriate set of skills to serve as a member of the Board.

Federico Seghi Recli has been vice president of Molteni Farmaceutici Polska SP zo.o, since July 1994. From October 2005 until May 2017, he served as chief executive officer of L. Molteni & C. Dei Fratelli Alitti Società di Esercizio S.p.a. (“Molteni”) and was a member of the board of directors of Molteni’s parent holding company until its merger with Molteni effective December 2018. He has also been director of P2-Molteni Pharma Limited (UK) since September 2016 and vice president Business Development of Molteni Therapeutics Srl since September 2018. Mr. Seghi Recli's career experience also includes senior roles with Merck S.p.A, including President and CEO from 2002 until 2005. Mr. Seghi Recli holds a degree in economics from the University of Florence. Based on Mr. Seghi Recli’s management experience in the pharmaceutical industry, our Board believes that Mr. Seghi Recli has the appropriate set of skills to serve as a member of the Board.

Scott A. Smith has served since September 2018 as President of BioAlta, LLC. Prior to this he served in various management capacities with Celgene Corporation since 2008, including President and Chief Operating Officer from 2017 to 2018 and as President, Inflammation and Immunology since August 2014. From 2003 to 2008, he served in various executive capacities with Biovail Pharmaceuticals, Inc. and prior thereto spent 16 years Pharmacia & Upjohn Company. Mr. Smith holds a BSc in Chemistry and Biology and an HBSc in Pharmacology and Toxicology from the University of Western Ontario and a Masters in International Management from the American Graduate School of International Management in Arizona. Based on Mr. Smith’s extensive management experience in the pharmaceutical industry, our Board believes that Mr. Smith has the appropriate set of skills to serve as a member of the Board.

As indicated above, each of our directors has extensive management and operational experience in one or more facets of the pharmaceutical industry, including research, product development, clinical and regulatory affairs, manufacturing and sales and marketing, providing our company with the leadership needed by a biotechnology company in all stages of its development.

Directors serve until the next annual meeting or until their successors are elected and qualified. Officers serve at the discretion of the Board, subject to rights, if any, under contracts of employment. See “Item 6. Executive Compensation—Employment Agreements.”

Board Leadership Structure

Currently, our principal executive officer and chairman of the Board positions are held separately by Sunil Bhonsle and Marc Rubin, respectively.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act, requires our executive officers, directors and persons who beneficially own more than 10% of a registered class of our equity securities to file with the Securities and Exchange Commission initial reports of ownership and reports of changes in ownership of our common stock and other equity securities. Such executive officers, directors, and greater than 10% beneficial owners are required by SEC regulation to furnish us with copies of all Section 16(a) forms filed by such reporting persons.

Based solely on our review of such forms furnished to us and written representations from certain reporting persons, we believe that all filing requirements applicable to our executive officers, directors and greater than 10% beneficial owners were complied with during 2018.

Code of Ethics

We adopted a Code of Business Conduct and Ethics (the “Code”) in February 2013 that applies to all directors, officers and employees. The Code was filed as an exhibit to our Annual Report on Form 10-K for the year ended December 31, 2012 and is available on our website at *www.titanpharm.com.* A copy of our code of ethics will also be provided to

any person without charge, upon written request sent to us at our offices located at 400 Oyster Point Blvd, Suite 505, South San Francisco, California 94080.

Changes in Director Nomination Process for Stockholders

None.

Item 11. Executive Compensation

Overview

During 2018, the compensation packages of Dr. Rubin, our Executive Chairman, and Sunil Bhonsle, our Chief Executive Officer and President continued to reflect our current level of operations and resources. The key objectives for 2018 were to support our ProNeura product development programs, the submission of our Probuphine product for approval with the EMA in Europe and its potential licensing with a European partner and the reacquisition of Probuphine commercial rights and subsequent efforts toward relaunch. This compensation discussion describes the material elements of compensation awarded to, earned by, or paid to each of our executive officers who served as named executive officers during the year ended December 31, 2018. This compensation discussion focuses on the information contained in the following tables and related footnotes and narrative for primarily the last completed fiscal year; however, we also describe compensation actions taken before or after the last completed fiscal year to the extent it enhances the understanding of our executive compensation disclosure.

Compensation Program Objectives and Philosophy

Our Compensation Committee currently oversees the design and administration of our executive compensation program. It reviews and approves all elements of compensation for each of our named executive officers taking into consideration recommendations from our principal executive officer (for compensation other than his own), as well as competitive market guidance. We define our competitive markets for executive talent to be the pharmaceutical and biotechnology industries in northern California. To date, we have utilized the Radford Biotechnology Surveys, a third party market specific compensation survey, and, when applicable, other independent third-party compensation consultants to benchmark our executive compensation.

The principal elements of our executive compensation program have historically been base salary, long-term equity incentives in the form of stock options or restricted stock awards, eligibility for bonus, post-termination severance and acceleration of stock option vesting for certain named executive officers upon termination and/or a change in control. We also provide other benefits and perquisites have consisting of life, health and disability insurance benefits, and a qualified 401(k) savings plan. Our philosophy has been to position the aggregate of these elements at a level that is competitive within the industry and commensurate with our size and performance recognizing operational needs and limited financial resources during this period.

Base Salaries

During 2018, the base salary of our named executives was based on their respective employment agreements and was reflective of the availability of resources and level of continuing operations at the time the agreements were entered into. Dr. Rubin received an annual salary of $295,000 and Mr. Bhonsle received an annual salary of $395,000. The current employment agreements expire on March 31, 2019 and the Compensation Committee has retained the services of a compensation consultant to advise it in connection with our entry into new agreements with such individuals that reflects the time commitment necessary and the roles such executives will play in implementing our strategic plans.

Long-term Equity Incentives

We provide the opportunity for our named executive officers and other executives to earn a long-term equity incentive award. Long-term incentive awards provide employees with the incentive to stay with us for longer periods of time, which in turn, provides us with greater stability. Equity awards also are less costly to us in the short term than cash compensation. We review long-term equity incentives for our named executive officers and other executives annually.

Historically, for our named executive officers, our stock option grants were of a size and term determined and approved by the Compensation Committee in consideration of the range of grants in the Radford Survey, generally falling within the 50-75% range outlined in the survey. We have traditionally used stock options as our form of equity compensation because stock options provide a relatively straightforward incentive for our executives, result in less immediate dilution of existing stockholders' interests and, prior to our adoption of FAS 123(R), resulted in less compensation expense for us relative to other types of equity awards. All grants of stock options to our employees are granted with exercise prices equal to or greater than the fair market value of our common stock on the respective grant dates. For a discussion of the determination of the fair market value of these grants, see "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and the Use of Estimates."

We do not time stock option grants to executives in coordination with the release of material non-public information. Our stock option grants have a 10-year contractual exercise term. In general, the option grants are also subject to the following post-termination and change in control provisions:

Event	Award Vesting	Exercise Term
• Termination by us for Reason Other than Cause, Disability or Death	• Forfeit Unvested Options	• Earlier of: (1) 90 days or (2) Remaining Option Period
• Termination for Disability, Death or Retirement	• Forfeit Unvested Options	• Earlier of: (1) 2 years or (2) Remaining Option Period
• Termination for Cause	• Forfeit Vested and Unvested Options	• Expire
• Other Termination	• Forfeit Unvested Options	• Earlier of: (1) 90 days or (2) Remaining Option Period
• Change in Control	• Accelerated*	• *

* The Compensation Committee may provide that, in the event of a change in control, any outstanding awards that are unexercisable or otherwise unvested will become fully vested and immediately exercisable. If there is a termination of employment, the applicable termination provisions regarding exercise term will apply.

In March 2018, Dr. Rubin and Mr. Bhonsle were each granted options to purchase 28,334 shares of common stock which vested 25% on the grant date and 25% on each of the three month, six month and nine month anniversaries of the grant date.

Compensation Committee Interlocks and Insider Participation

Members of our Compensation Committee of the board of directors are Joseph A. Akers, M. David MacFarlane and Scott A. Smith. No member of our Compensation Committee was, or has been at any time in the last 10 years, an officer or employee of Titan or any of our former subsidiaries.

No member of the Compensation Committee has a relationship that would constitute an interlocking relationship with executive officers or directors of the Company or another entity.

SUMMARY COMPENSATION TABLE

The following table shows information concerning the annual compensation for services provided to us by our named executive officers for the periods set forth.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Options Awards ($) (1)	Stock Awards ($) (1)	All Other Compensation ($)(2)	Total Compensation ($)
Marc Rubin, M.D.	2018	$295,000	$—	$125,079	$ —	$ —	$ 420,079
Executive Chairman	2017	295,000	—	207,100	—	—	502,100
	2016	295,000	73,000	245,311	—	—	613,311
Sunil Bhonsle	2018	$395,000	$—	$125,079	$ —	$ —	$ 520,079
Chief Executive Officer, President	2017	395,000	—	236,686	—	91,881	723,567
and Principal Financial Officer	2016	395,000	96,000	276,323	—	—	767,323

(1) Amounts shown represent the grant date fair value computed in accordance with FASB ASC 718. The assumptions used by us with respect to the valuation of option grants and stock awards are set forth in "Titan Pharmaceuticals, Inc. Financial Statements—Notes to Financial Statements—Note 12—Stock Plans."

(2) Amounts shown represent the payment of accrued vacation compensation.

GRANTS OF PLAN-BASED AWARDS

The following table shows information concerning grants of plan based awards to named executive officers during the year ended December 31, 2018**.**

Name	Grant Date	Approval Date(1)	Number of Shares of Common Stock Underlying Awards (#)		Exercise or Base Price of Option Awards ($/Sh)	Grant Date Fair Value of Stock and Option Awards($)(2)
Marc Rubin, M.D.	3/7/2018	3/6/2018	28,334	(3)	$ 5.82	$ 125,079
Sunil Bhonsle	3/7/2018	3/6/2018	28,334	(3)	$ 5.82	$ 125,079

(1) All grants were approved by the Compensation Committee on the dates indicated.

(2) Valuation assumptions are found under “Titan Pharmaceuticals, Inc. Financial Statements—Notes to Financial Statements—Note 12—Stock Plans.”

(3) These option grants vested as follows: 25% on the grant date and 25% on each of the three month, six month and nine month anniversaries of the grant date.

Employee Benefits Plans

The principal purpose of our stock incentive plans is to attract, motivate, reward and retain selected employees, consultants and directors through the granting of stock-based compensation awards. The stock option plans provides for a variety of awards, including non-qualified stock options, incentive stock options (within the meaning of Section 422 of the Code), stock appreciation rights, restricted stock awards, performance-based awards and other stock-based awards.

2001 Stock Option Plan

In August 2001, we adopted the 2001 Employee Non-Qualified Stock Option Plan, or the 2001 NQ Plan, pursuant to which 53,031 shares of common stock were authorized for issuance for option grants to employees and consultants who are not officers or directors of Titan. The 2001 NQ Plan expired by its terms in August 2011. On December 31, 2018, options to purchase an aggregate of 28,917 shares of our common stock were outstanding under the 2001 NQ Plan.

2002 Stock Incentive Plan

In July 2002, we adopted the 2002 Stock Incentive Plan, or the 2002 Plan. Under the 2002 Plan, as amended, a total of approximately 217,000 shares of our common stock were authorized for issuance to employees, officers, directors, consultants, and advisers. The 2002 Plan expired by its terms in July 2012. On December 31, 2018, options to purchase an aggregate of 86,626 shares of our common stock were outstanding under the 2002 Plan.

2014 Incentive Plan

In February 2014, our Board adopted the 2014 Incentive Plan, or the 2014 Plan, pursuant to which 75,758 shares of our common stock were authorized for issuance to employees, directors, officers, consultants and advisors. On December 31, 2018, options to purchase 42,861 shares of our common stock were outstanding under the 2014 Plan.

2015 Omnibus Equity Incentive Plan

In August 2015, our stockholders approved the 2015 Omnibus Equity Incentive Plan, or the 2015 Plan. The 2015 Plan, as amended in August 2018, authorized a total of 583,334 shares of our common stock for issuance to employees, directors, officers, consultants and advisors. On December 31, 2018, options to purchase 479,030 shares of our common stock were outstanding under the 2015 Plan. Subsequent to year end, the 2015 Plan was further amended to increase the number of authorized shares eligible for awards thereunder to 1,666,667.

OUTSTANDING EQUITY AWARDS AT FISCAL YEAR-END

The following table summarizes the number of securities underlying outstanding plan awards for each named executive officer as of December 31, 2018.

Name	Option Awards				
	Number of Securities Underlying Unexercised Awards (#) Exercisable	Number of Securities Underlying Unexercised Awards (#) Unexercisable		Exercise Price ($)	Expiration Date
Marc Rubin, M.D.	3,031	—		26.04	5/17/2019
	455	—		26.04	5/17/2019
	8,637	—		26.04	5/17/2019
	18,637	—		26.04	5/17/2019
	4,546	—		46.20	4/15/2021
	7,576	—		37.92	1/3/2022
	6,061	—		19.80	3/16/2025
	15,150	—		30.60	12/14/2025
	13,184	—		30.60	02/02/2026
	10,695	973	(1)	23.40	02/13/2027
	28,334	—		5.82	03/07/2028
Sunil Bhonsle	3,031	—		26.04	5/17/2019
	304	—		26.04	5/17/2019
	11,819	—		26.04	5/17/2019
	9,394	—		26.04	5/17/2019
	6,061	—		46.20	4/15/2021
	9,091	—		37.92	1/3/2022
	7,273	—		19.80	3/16/2025
	15,150	—		30.60	12/14/2025
	14,850	—		30.60	2/02/2026
	12,223	1,112	(1)	23.40	02/13/2027
	28,334	—		5.82	03/07/2028

(1) These option grants vest monthly over 24 months from the grant date.

There were no option exercises by our named executive officers during 2018.

Pension Benefits

We do not sponsor any qualified or non-qualified defined benefit plans.

Nonqualified Deferred Compensation

We do not maintain any non-qualified defined contribution or deferred compensation plans. The Compensation Committee, which is comprised solely of "outside directors" as defined for purposes of Section 162(m) of the Code, may elect to provide our officers and other employees with non-qualified defined contribution or deferred compensation benefits if the Compensation Committee determines that doing so is in our best interests. We sponsor a tax qualified defined contribution 401(k) plan in which Dr. Rubin and Mr. Bhonsle participated.

Employment Agreements

In September 2016, we entered into employment agreements, as amended on August 9, 2018, with Dr. Rubin and Mr. Bhonsle providing for base annual salaries of $295,000 and 395,000, respectively. The employment agreements contain the following terms:

- Bonuses. The executive may, at the sole discretion of the board of directors or the compensation committee, be considered for an annual bonus of up to 50% of his then base salary, payable in cash or awards under the Company's equity incentive plan.

- Term; Termination. The Employment Agreements have a 30 month term expiring on March 31, 2019 but may be terminated by the Company for any reason at any time. In the event of termination by the Company without cause or by the executive for good reason not in connection with a change of control, as those terms are defined in such agreements, the executive is entitled to (i) severance for the greater of 12 months or the balance of the term, (ii) a pro rata portion of any annual bonus, (iii) 12 months of COBRA payments, and (iv) the immediate accelerated vesting of any unvested restricted shares and stock options. In the event such a termination is within 30 days prior to or six months following a change of control, the executive is entitled to an additional six months of COBRA payments.

- Restrictive Covenants. The Employment Agreements contain one-year post-termination noncompetition and non-solicitation provisions.

- Clawback. The Employment Agreements contain a two-year post-termination clawback of benefits provision in the event of a restatement of financial results upon which such benefits were based.

DIRECTOR COMPENSATION

Summary of Director Compensation

The following table summarizes compensation that our directors earned during 2018 for services as members of our Board.

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)	Options Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)	Nonqualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
Joseph A. Akers (2)	$ 57,500	$ —	$ —	$ —	$ —	$ —	$ 57,500
Rajinder Kumar (3)	50,000	—	—	—	—	—	50,000
M. David MacFarlane, Ph.D. (4)	60,000	—	—	—	—	—	60,000
James R. McNab, Jr. (5)	57,500	—	—	—	—	—	57,500
Federico Seghi Recli (6)	28,125	—	3,242	—	—	—	31,367
Scott A. Smith (7)	52,500	—	—	—	—	—	52,500

(1) Valuation assumptions are found under “Titan Pharmaceuticals, Inc. Financial Statements—Notes to Financial Statements—Note 12—Stock Plans.”

(2) The aggregate number of option awards held at December 31, 2018 was 6,138.
(3) The aggregate number of option awards held at December 31, 2018 was 2,501.
(4) The aggregate number of option awards held at December 31, 2018 was 9,551.
(5) The aggregate number of option awards held at December 31, 2018 was 6,138.
(6) The aggregate number of option awards held at December 31, 2018 was 835.
(7) The aggregate number of option awards held at December 31, 2018 was 2,501.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth as of March 25, 2019, the number of shares of our common stock beneficially owned by (i) each person who is known by us to be the beneficial owner of more than five percent of our common stock; (ii) each director and director nominee; (iii) each of the named executive officers in the Summary Compensation Table; and (iv) all directors and executive officers as a group. As of March 25, 2019, we had 13,413,628 shares of common stock issued and outstanding.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission (the "SEC") and generally includes voting or investment power with respect to securities. Unless otherwise indicated, the stockholders listed in the table have sole voting and investment power with respect to the shares indicated.

Name and Address of Beneficial Owner [1]	**Shares Beneficially Owned** [2]		Percent of Shares Beneficially Owned	
Joseph A. Akers	74,974	(3)	*	
Sunil Bhonsle	225,821	(4)	1.7	%
Rajinder Kumar, Ph.D.	2,501	(5)	*	
M. David MacFarlane, Ph.D.	39,327	(6)	*	
James R. McNab, Jr.	89,475	(7)	*	
Marc Rubin, M.D.	245,916	(8)	1.8	%
Federico Seghi Recli	134,310	(9)	1.0	%
Scott A. Smith	2,501	(10)	*	
All executive officers and directors as a group (8) persons	814,825		5.9	%

*Less than one percent.

(1) Unless otherwise indicated, the address of such individual is c/o Titan Pharmaceuticals, Inc., 400 Oyster Point Boulevard, Suite 505, South San Francisco, California 94080.

(2) In computing the number of shares beneficially owned by a person and the percentage ownership of a person, shares of our common stock subject to options held by that person that are currently exercisable or exercisable within 60 days of March 25, 2019 are deemed outstanding. Such shares, however, are not deemed outstanding for purposes of computing the percentage ownership of each other person. Except as indicated in the footnotes to this table and pursuant to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock.

(3) Includes (i) 6,138 shares issuable upon exercise of outstanding options and (ii) 33,334 shares issuable upon exercise of outstanding warrants.

(4) Includes (i) 94,059 shares issuable upon exercise of outstanding options, (ii) 50,000 shares issuable upon exercise of outstanding warrants and (iii) 9,117 shares held in a family trust for which he serves as trustee.

(5) Includes 2,501 shares issuable upon exercise of outstanding options.

(6) Includes 8,944 shares issuable upon exercise of outstanding options and (ii) 13,334 shares issuable upon exercise of outstanding warrants.

(7) IncludesN,138 shares issuable upon exercise of outstanding options and (ii) 33,334 shares issuable upon exercise of outstanding warrants.

(8) Includes 86,521 shares issuable upon exercise of outstanding options and (ii) 66,667 shares issuable upon exercise of outstanding warrants.

(9) Includes 834 shares issuable upon exercise of outstanding options. Does not include 777,743 shares issuable upon conversion of notes and exercise of warrants held by Molteni. Mr. Seghi Recli does not have voting or dispositive power over, and disclaims beneficial ownership of, such underlying shares, except to the extent of his direct pecuniary interest therein. The shares attributed to Molteni are subject to a 4.99% exercise limitation.

(10) Includes 2,501 shares issuable upon exercise of outstanding options.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Certain Relationships and Related Transactions.

None.

Independence of Directors

The following members of our Board meet the independence requirements and standards currently established by the NYSE MKT: Joseph A. Akers, Rajinder Kumar, M. David MacFarlane, James R. McNab, Jr., Federico Seghi Recli and Scott A. Smith.

Board Committees

Our Board has established the following three standing committees: audit committee; compensation committee; and nominating and governance committee, or nominating committee.

The audit committee was formed in compliance with Section 3(a)(58)(A) of the Exchange Act and consists of Joseph A. Akers, M. David MacFarlane and James R. McNab, Jr., each of whom meets the independence requirements and standards currently established by the NYSE MKT and the SEC. In addition, the Board has determined that Messr. Akers is an “audit committee financial expert” and “independent” as defined under the relevant rules of the SEC and the NYSE MKT. The audit committee assists the Board by overseeing the performance of the independent auditors and the quality and integrity of Titan’s internal accounting, auditing and financial reporting practices. The audit committee is responsible for retaining (subject to stockholder ratification) and, as necessary, terminating, the independent auditors, annually reviews the qualifications, performance and independence of the independent auditors and the audit plan, fees and audit results, and pre-approves audit and non-audit services to be performed by the auditors and related fees. During the fiscal year ended December 31, 2018, the audit committee met four times.

The compensation committee makes recommendations to the Board concerning salaries and incentive compensation for our officers, including our Principal Executive Officer, and employees and administers our stock option plans. The compensation committee consists of Joseph A. Akers, M. David MacFarlane and Scott A. Smith, each of whom meets the independence requirements and standards currently established by the NYSE MKT. The compensation committee did not meet as a separate committee, but took action by written consent two times during the fiscal year ended December 31, 2018.

The purpose of the governance committee is to assist the Board in identifying qualified individuals to become Board members, in determining the composition of the Board and in monitoring the process to assess Board effectiveness. The governance committee consists of James R. McNab, Jr., Rajinder Kumar and M. David MacFarlane who meet the independence requirements and standards currently established by the NYSE MKT. The governance committee did not meet as a separate committee or take action by written consent during the fiscal year ended December 31, 2018.

The charters for the audit, compensation and governance committees, which have been adopted by our Board, contain detailed descriptions of the committees' duties and responsibilities and are available in the Investor Relations section of our website at *www.titanpharm.com.*

Role of the Board in Risk Oversight

Our audit committee is primarily responsible for overseeing our risk management processes on behalf of the full Board. The audit committee receives reports from management at least quarterly regarding our assessment of risks. In addition, the audit committee reports regularly to the full Board, which also considers our risk profile. The audit committee and the full Board focus on the most significant risks we face and our general risk management strategies. While the Board oversees our risk management, management is responsible for day-to-day risk management processes. Our Board expects management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the audit committee and the Board. We believe this division of responsibilities is the most effective approach for addressing the risks we face and that our Board leadership structure, which also emphasizes the independence of the Board in its oversight of its business and affairs, supports this approach.

Board Meetings

Our business and affairs are managed under the direction of our Board, which is currently composed of eight members. The primary responsibilities of the Board are to provide oversight, strategic guidance, counseling and direction to our management. During the fiscal year ended December 31, 2018, the Board met 18 times and no director attended fewer than 75% of the meetings of the Board and Board committees of which the director was a member.

Item 14. Principal Accounting Fees and Services.

Aggregate fees billed by OUM & Co. LLP, an independent registered public accounting firm, during the fiscal years ended December 31, 2018 and 2017 were as follows:

	2018	2017
Audit Fees	$302,204	$210,824
Audit-Related Fees	3,159	6,693

Tax Fees	43,500	15,000
All Other Fees	—	—
Total	$348,863	$232,517

Audit Fees —This category includes aggregate fees billed by our independent auditors for the audit of our annual financial statements, audit of management's assessment and effectiveness of internal controls over financial reporting, review of financial statements included in our quarterly reports on Form 10-Q and services that are normally provided by the auditor in connection with statutory and regulatory filings for those fiscal years.

Audit-Related Fees —This category consists of services by our independent auditors that, including accounting consultations on transaction related matters, are reasonably related to the performance of the audit or review of our financial statements and are not reported above under Audit Fees.

Tax Fees —This category consists of professional services rendered for tax compliance and preparation of our corporate tax returns and other tax advice.

All Other Fees —During the years ended December 31, 2018 and 2017, OUM & Co. LLP did not incur any fees for other professional services.

The audit committee reviewed and approved all audit and non-audit services provided by OUM & Co. LLP and concluded that these services were compatible with maintaining its independence. The audit committee approved the provision of all non-audit services by OUM & Co. LLP. Of the total number of hours expended during OUM & Co. LLP's engagement to audit our financial statements for the year ended December 31, 2018, none of the hours were attributed to work performed by persons other than permanent, full-time employees of OUM & Co. LLP.

Pre-Approval Policies and Procedures

In accordance with the SEC's auditor independence rules, the audit committee has established the following policies and procedures by which it approves in advance any audit or permissible non-audit services to be provided to us by our independent auditor.

Prior to the engagement of the independent auditors for any fiscal year's audit, management submits to the audit committee for approval lists of recurring audit, audit-related, tax and other services expected to be provided by the independent auditors during that fiscal year. The audit committee adopts pre-approval schedules describing the recurring services that it has pre-approved, and is informed on a timely basis, and in any event by the next scheduled meeting, of any such services rendered by the independent auditor and the related fees.

The fees for any services listed in a pre-approval schedule are budgeted, and the audit committee requires the independent auditor and management to report actual fees versus the budget periodically throughout the year. The audit committee will require additional pre-approval if circumstances arise where it becomes necessary to engage the independent auditor for additional services above the amount of fees originally pre-approved. Any audit or non-audit service not listed in a pre-approval schedule must be separately pre-approved by the audit committee on a case-by-case basis.

Every request to adopt or amend a pre-approval schedule or to provide services that are not listed in a pre-approval schedule must include a statement by the independent auditors as to whether, in their view, the request is consistent with the SEC's rules on auditor independence.

The audit committee will not grant approval for:

- any services prohibited by applicable law or by any rule or regulation of the SEC or other regulatory body applicable to us;
- provision by the independent auditors to us of strategic consulting services of the type typically provided by management consulting firms; or
- the retention of the independent auditors in connection with a transaction initially recommended by the independent auditors, the tax treatment of which may not be clear under the Internal Revenue Code and related regulations and

which it is reasonable to conclude will be subject to audit procedures during an audit of our financial statements.

Tax services proposed to be provided by the auditor to any director, officer or employee of Titan who is in an accounting role or financial reporting oversight role must be approved by the audit committee on a case-by-case basis where such services are to be paid for by us, and the audit committee will be informed of any services to be provided to such individuals that are not to be paid for by us.

In determining whether to grant pre-approval of any non-audit services in the "all other" category, the audit committee will consider all relevant facts and circumstances, including the following four basic guidelines:

- whether the service creates a mutual or conflicting interest between the auditor and us;
- whether the service places the auditor in the position of auditing his or her own work;
- whether the service results in the auditor acting as management or an employee of our company; and
- whether the service places the auditor in a position of being an advocate for our company.

PART IV

Item 15. Exhibits and Financial Statements Schedules.

(a) 1. Financial Statements

An index to Financial Statements appears on page F-1.

2. Schedules

All financial statement schedules are omitted because they are not applicable, not required under the instructions or all the information required is set forth in the financial statements or notes thereto.

57

TITAN PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors

Titan Pharmaceuticals, Inc.

South San Francisco, California

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Titan Pharmaceuticals, Inc. (the “Company”) as of December 31, 2018 and 2017, the related statements of operations and comprehensive income (loss), stockholders’ equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2018**,** in conformity with accounting principles generally accepted in the United States of America.

Going Concern Uncertainty

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has an accumulated deficit that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (“PCAOB”) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ OUM & CO. LLP

San Francisco, California
March 30, 2019
We have served as the Company's auditor since 2004.

TITAN PHARMACEUTICALS, INC.

BALANCE SHEETS

	December 31,	
	2018	2017
	(in thousands, except share and per share data)	
Assets		
Current assets:		
Cash and cash equivalents	$ 9,295	$ 7,522
Restricted cash	361	361
Receivables	1,737	65
Inventory	1,262	—
Contract assets	99	—
Prepaid expenses and other current assets	547	362
Total current assets	13,301	8,310
Property and equipment, net	794	595
Total Assets	$ 14,095	$ 8,905
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,526	$ 821
Accrued clinical trials expenses	620	289
Other accrued liabilities	466	354
Deferred revenue	313	—
Current portion of long-term debt, net of debt discount of $123,000	527	3,000
Total current liabilities	3,452	4,464
Long-term debt, net of debt discount of $543,000 and $497,000	3,787	3,584
Derivative liability	25	—
Total Liabilities	7,264	8,048
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value per share; 5,000,000 shares authorized, none issued and outstanding at December 31, 2018 and 2017.	—	—
Common stock, at amounts paid-in, $0.001 par value per share; 125,000,000 shares authorized, 13,010,292 and 3,533,958 shares issued and outstanding at December 31, 2018 and 2017, respectively.	13	4
Additional paid-in capital	339,397	324,124
Accumulated deficit	(332,579)	(323,271)
Total stockholders' equity	6,831	857
Total Liabilities and Stockholders' Equity	$ 14,095	$ 8,905

See accompanying notes to financial statements.

F-3

TITAN PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)

	Years ended December 31,		
	2018	2017	2016
	(in thousands, except per share amount)		
Revenue:			
License revenue	$ 5,376	$ 215	$ 15,065
Product revenue	535	—	—
Grant revenue	707	—	—
Total revenue	6,618	215	15,065
Operating expenses:			
Cost of goods sold	538	—	—
Research and development	7,478	9,648	6,126
Selling, general and administrative	6,866	5,069	4,596
Total operating expenses	14,882	14,717	10,722
Income (loss) from operations	(8,264)	(14,502)	4,343
Other income (expense):			
Interest income (expense), net	(887)	(369)	37
Other expense, net	(6)	(55)	(70)
Non-cash gain on changes in the fair value of warrants	—	619	825
Non-cash gain on changes in the fair value of derivatives	134	—	—
Other income (expense), net	(759)	195	792
Net income (loss) and comprehensive income (loss)	(9,023)	(14,307)	5,135
Deemed dividend on trigger of down round provision	(285)	—	—
Net income (loss) applicable to common stockholders	$ (9,308)	$ (14,307)	$ 5,135
Basic net income (loss) per common share	$ (0.78)	$ (4.05)	$ 1.49
Diluted net income (loss) per common share	$ (0.79)	$ (4.22)	$ 1.20
Weighted average shares used in computing basic net income (loss) per common share	11,960	3,534	3,457
Weighted average shares used in computing diluted net income (loss) per common share	11,960	3,538	3,577

See accompanying notes to financial statements.

TITAN PHARMACEUTICALS, INC

STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands)

	Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balances at December 31, 2015	—	$ —	3,344	$ 3	$ 321,086	$ (314,099)	$ —	$ 6,990
Net income						5,135		5,135
Issuance of common stock upon exercise of warrants, net			188					—
Issuance of common stock upon exercise of options, net			2	1	26			27
Stock-based compensation					1,039			1,039
Balances at December 31, 2016	—	—	3,534	4	322,151	(308,964)	—	13,191
Net loss						(14,307)		(14,307)
Issuance of warrants to purchase common stock, net					286			286
Stock-based compensation					1,687			1,687
Balances at December 31, 2017	—	—	3,534	4	324,124	(323,271)	—	857
Net loss						(9,023)		(9,023)
Issuance of warrants to purchase common stock, net					527			527
Issuance of common stock, net			1,815	2	2,435			2,437
Issuance of preferred stock, net	8				7,214			7,214
Issuance of common stock upon conversion of preferred stock, net	(8)		5,483	5	(11)			(6)
Issuance of common stock upon exercise of warrants, net			2,178	2	3,266			3,268
Stock-based compensation					1,557			1,557
Deemed dividend resulting from downround provision					285	(285)		—
Balances at December 31, 2018	—	$ —	13,010	$ 13	$ 339,397	$ (332,579)	$ —	$ 6,831

See accompanying notes to financial statements.

TITAN PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

	Years ended December 31,		
	2018	2017	2016
	(in thousands)		
Cash flows from operating activities:			
Net income (loss)	$(9,023)	$(14,307)	$5,135
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Non-cash gain on inventory received from termination of license agreement	(1,293)	—	—
Depreciation and amortization	380	417	377
Non-cash interest expense	490	141	—
Non-cash gain on changes in fair value of warrants	—	(619)	(825)
Non-cash gain on changes in fair value of derivatives	(134)	—	—
Stock-based compensation	1,557	1,687	1,039
Changes in operating assets and liabilities:			
Receivables	(1,672)	3,522	626
Inventory	31	—	—
Contract assets	120	—	—
Prepaid expenses and other assets	(185)	(125)	(63)
Accounts payable	542	(2,194)	(1,143)
Other accrued liabilities	443	(1,199)	1,147
Deferred revenue	313	—	—
Net cash provided by (used in) operating activities	(8,431)	(12,677)	6,293
Cash flows from investing activities:			
Purchases of furniture and equipment	(416)	(175)	(171)
Net cash used in investing activities	(416)	(175)	(171)
Cash flows from financing activities:			
Sale of common & preferred stock	9,651	—	—
Issuance of warrants	51	—	—
Proceeds from issuance of common stock from the exercise of stock options	—	—	27
Proceeds from the exercise of warrants	3,268	—	—
Proceeds from the issuance of debt	650	6,729	—
Payments on long-term debt	(3,000)	—	—
Net cash provided by financing activities	10,620	6,729	27
Net increase (decrease) in cash	1,773	(6,123)	6,149
Cash, cash equivalents and restricted cash at beginning of period	7,883	14,006	7,857
Cash, cash equivalents and restricted cash at end of period	$9,656	$7,883	$14,006
Supplemental disclosure of cash flow information			
Interest paid	$471	$298	$—
Warrants issued	$6,348	$287	$—
Derivatives issued	$159	$—	$—
Deemed dividend on trigger of down round provision	$285	$—	$—
Purchases of property and equipment in accounts payable	$163	$—	$—

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the balance sheets that sum to the total of the same such amounts shown in the statement of cash flows (in thousands):

	2018	2017	2016
Cash and cash equivalents	$9,295	$7,522	$14,006
Restricted cash	361	361	—
Cash, cash equivalents and restricted cash shown in the statement of cash flows	$9,656	$7,883	$14,006

See accompanying notes to financial statements.

TITAN PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

The Company

We are a pharmaceutical company developing therapeutics for the treatment of select chronic diseases utilizing our proprietary long-term drug delivery platform, ProNeura™, and we are currently transitioning to a commercial stage enterprise having re-acquired Probuphine® in May 2018, our first product approved in the U.S. for the maintenance treatment of opioid dependence. We operate in only one business segment, the development and commercialization of pharmaceutical products. All share and per share amounts give retroactive effect to a 1 for 6 reverse stock split effected in January 2019. See Note 14 “Subsequent Events.”

The accompanying financial statements have been prepared assuming we will continue as a going concern.

At December 31, 2018, we had cash and cash equivalents of approximately $9.3 million, which we believe, along with the $0.6 million received from the subsequent exercise of warrants, are sufficient to fund our planned operations through the third quarter of 2019. Thereafter, we will require additional funds to finance our operations, including the commercialization of Probuphine in the U.S., completion of the Probuphine Phase IV clinical trials mandated by the FDA and advancement of our current ProNeura development programs to later stage clinical studies. Our efforts to obtain additional financing may not be successful.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Going concern assessment

We assess going concern uncertainty in our financial statements to determine if we have sufficient cash on hand and working capital, including available borrowings on loans, to operate for a period of at least one year from the date the financial statements are issued or available to be issued, which is referred to as the "look-forward period" as defined by Accounting Standard Update ASU No. 2014-15. As part of this assessment, based on conditions that are known and reasonably knowable to us, we will consider various scenarios, forecasts, projections, estimates and will make certain key assumptions, including the timing and nature of projected cash expenditures or programs, and its ability to delay or curtail expenditures or programs, if necessary, among other factors. Based on this assessment, as necessary or applicable, we make certain assumptions around implementing curtailments or delays in the nature and timing of programs and expenditures to the extent we deem probable those implementations can be achieved and we have the proper authority to execute them within the look-forward period in accordance with ASU No. 2014-15.

Based upon the above assessment, we concluded that, at the date of filing the financial statements in this Annual Report on Form 10-K for the year ended December 31, 2018, we did not have sufficient cash to fund our operations for the next 12 months without additional funds and, therefore, there was substantial doubt about our ability to continue as a going concern within 12 months after the date the financial statements were issued.

Stock-Based Compensation

We recognize compensation expense using a fair-value based method, for all stock-based payments including stock options and restricted stock awards and stock issued under an employee stock purchase plan. These standards require companies to estimate the fair value of stock-based payment awards on the date of grant using an option pricing model. See Note 12 "Stock Plans," for a discussion of our stock-based compensation plans. Our non-cash stock-based compensation expense related to employees, non-employee members of our Board and consultants totaled approximately $1.6 million, $1.7 million and $1.0 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Warrants Issued in Connection with Equity Financing

We generally account for warrants issued in connection with equity financings as a component of equity, unless there is a deemed possibility that we may have to settle the warrants in cash. For warrants issued with deemed possibility of cash settlement, we record the fair value of the issued warrants as a liability at each reporting period and record changes in the estimated fair value as a non-cash gain or loss in the Statements of Operations and Comprehensive Income (Loss).

Cash, Cash Equivalents and Marketable Securities

Our investment policy emphasizes liquidity and preservation of principal over other portfolio considerations. We select investments that maximize interest income to the extent possible given these two constraints. We satisfy liquidity requirements by investing excess cash in securities with different maturities to match projected cash needs and limit concentration of credit risk by diversifying our investments among a variety of high credit-quality issuers and limit the amount of credit exposure to any one issuer. The estimated fair values have been determined using available market information. We do not use derivative financial instruments in our investment portfolio.

All investments with original maturities of three months or less are considered to be cash equivalents. Marketable securities, consisting primarily of high-grade debt securities, U.S. government and corporate notes and bonds, and commercial paper, are classified as available-for-sale at time of purchase and carried at fair value. If the fair value of a security is below its amortized cost and we plan to sell the security before recovering its cost, the impairment is considered to be other-than-temporary. Other-than-temporary declines in fair value of our marketable securities are charged against interest income. We had money market funds of approximately $8.9 million and $7.4 million as of December 31, 2018 and 2017, respectively, included in our cash and cash equivalents. We did not hold any marketable securities as of December 31, 2018 and 2017.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets ranging from three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the assets.

Revenue Recognition

Beginning January 1, 2018, we have followed the provisions of ASC Topic 606, *Revenue from Contracts with Customers*. The guidance provides a unified model to determine how revenue is recognized.

We generate revenue principally from the sale of Probuphine in the U.S., collaborative research and development arrangements, technology licenses and sales, and government grants. Consideration received for revenue arrangements with multiple components is allocated among the separate performance obligations based upon their relative estimated standalone selling price.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. Our performance obligations include commercialization license rights, development services and services associated with the regulatory approval process.

We have optional additional items in contracts, which are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer’s discretion are generally considered as options. We assess if these options provide a material right to the customer and, if so, such material rights are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any additional payments are recorded in revenue when the customer obtains control of the goods or services.

Transaction Price

We have both fixed and variable consideration. Non-refundable upfront payments are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point they are considered fixed. We allocate the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties or earn-out payments, including milestone payments based on the level of sales, and the license or purchase agreement is deemed to be the predominant item to which the royalties or earn-out payments relate, we recognizes revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty or earn-out payment has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights are calculated using the residual approach. For all other performance obligations, we use a cost-plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under an arrangement and the period over which we expect to complete our performance obligations under an arrangement. We estimate the performance period or measure of progress at the inception of the arrangement and re-evaluate it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these

estimates are recorded on a cumulative catch up basis. If we cannot reasonably estimate when our performance obligations either are completed or become inconsequential, then revenue recognition is deferred until we can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for licenses or sales of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that we have incurred to perform the services using the cost-to-cost input method.

Research and Development Costs and Related Accrual

Research and development expenses include internal and external costs. Internal costs include salaries and employment related expenses, facility costs, administrative expenses and allocations of corporate costs. External expenses consist of costs associated with outsourced clinical research organization activities, sponsored research studies, product registration, patent application and prosecution, and investigator sponsored trials. We also record accruals for estimated ongoing clinical trial costs. Clinical trial costs represent costs incurred by CROs and clinical sites. These costs are recorded as a component of research and development expenses. Under our agreements, progress payments are typically made to investigators, clinical sites and CROs. We analyze the progress of the clinical trials, including levels of patient enrollment, invoices received and contracted costs when evaluating the adequacy of accrued liabilities. Significant judgments and estimates must be made and used in determining the accrued balance in any accounting period. Actual results could differ from those estimates under different assumptions. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

Net Income (Loss) Per Share

Basic net income (loss) per share excludes the effect of dilution and is computed by dividing net income (loss) by the weighted-average number of shares outstanding for the period. Diluted net income (loss) per share reflects the potential dilution that could occur if securities or other contracts to issue shares were exercised into shares. In calculating diluted net income (loss) per share, the numerator is adjusted for the change in the fair value of the warrant liability (only if dilutive) and the denominator is increased to include the number of potentially dilutive common shares assumed to be outstanding during the period using the treasury stock method.

The following table sets forth the reconciliation of the numerator and denominator used in the computation of basic and diluted net income (loss) per common share for the years ended December 31, 2018, 2017 and 2016:

	Years ended December 31,		
(in thousands, except per share amounts)	2018	2017	2016
Numerator:			
Net income (loss) used for basic earnings per share	$(9,308)	$(14,307)	$5,135
Less change in fair value of warrant liability	—	619	825
Less change in fair value of derivatives	134	—	—
Net income (loss) used for diluted earnings per share	$(9,442)	$(14,926)	$4,310
Denominator:			
Basic weighted-average outstanding common shares	11,960	3,534	3,457
Effect of dilutive potential common shares resulting from options	—	—	24
Effect of dilutive potential common shares resulting from warrants	—	4	96
Weighted-average shares outstanding—diluted	11,960	3,538	3,577
Net income (loss) per common share:			
Basic	$(0.78)	$(4.05)	$1.49
Diluted	$(0.79)	$(4.22)	$1.20

The table below presents common shares underlying stock options and warrants that are excluded from the calculation of the weighted average number of shares of common stock outstanding used for the calculation of diluted net income (loss) per common share. These are excluded from the calculation due to their anti-dilutive effect for the years ended December 31, 2018, 2017 and 2016:

	Years ended December 31,		
(in thousands)	2018	2017	2016
Weighted-average anti-dilutive common shares resulting from options and awards	588	393	214
Weighted-average anti-dilutive common shares resulting from warrants	264	203	—
	852	596	214

Comprehensive Income (Loss)

Comprehensive income and loss for the periods presented is comprised solely of our net income and loss. Comprehensive loss for the years ended December 31, 2018 and 2017 were $ 9.0 million and 14.3 million, respectively. Comprehensive income for the year ended December 31, 2016 was $ 5.1 million.

Recent Accounting Pronouncements

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* . ASU No. 2016-18 is intended to reduce diversity in practice in the classification and presentation of changes in restricted cash on the Statements of Cash Flows. The ASU requires that the Statements of Cash Flows explain the change in total cash, cash equivalents and amounts generally described as restricted cash or restricted cash equivalents when reconciling the beginning-of-period and end-of-period total amounts. The ASU also requires a reconciliation between the total of cash, cash equivalents and restricted cash presented on the Statements of Cash Flows and the cash and cash equivalents balance presented on the Balance Sheets. We adopted ASU No. 2016-18, and the guidance has been retrospectively applied to all periods presented. The adoption of the guidance did not have an impact on our Balance Sheets or Statements of Operations and Comprehensive Income (Loss).

In July 2017, the FASB issued a two-part Accounting Standards Update, or ASU, No. 2017-11, *I. Accounting for Certain Financial Instruments With Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests With a Scope Exception* amending guidance in FASB ASC 260, Earnings Per Share, FASB ASC 480, Distinguishing Liabilities from Equity, and FASB ASC 815, Derivatives and Hedging. The amendments in Part I of ASU 2017-11 change the classification analysis of certain equity-linked financial instruments (or embedded features) with down round features. The amendments in Part II of ASU 2017-11 re-characterize the indefinite deferral of certain provisions of Topic 480 that now are presented as pending content in the Codification, to a scope exception. Those amendments do not have an accounting effect. ASU 2017-11 is effective for public business entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018. Early adoption is permitted. We adopted ASU 2017- 11 for the year ended December 31, 2017, and retrospectively applied ASU 2017-11 as required. There was no retrospective impact as a result of the adoption of ASU 2017-11 on the financial statements. See Note 8, “Debt Agreements.”

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments,* addressing eight specific cash flow issues in an effort to reduce diversity in practice. The amended guidance is effective for fiscal years beginning after December 31, 2017, and for interim periods within those years. The adoption of ASU No. 2016-15 did not have a material impact on our statements of cash flows.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation - Stock Compensation: Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 addresses several aspects of the accounting for share-based payment award transactions, including: (a) income tax consequences; (b) classification of awards as either equity or liabilities; (c) classification on the statement of cash flows; and (d) accounting for forfeitures. We adopted the provisions of ASU 2016-09 in the first quarter of 2017. We have elected to continue to estimate forfeitures based on the estimated number of awards expected to vest. In addition, the adoption of ASU 2016-09 resulted in the recognition of $12.0 million of previously unrecognized excess tax benefits in deferred tax assets, fully offset by a valuation allowance. All tax-related cash flows resulting from stock-based compensation, including the excess tax benefits related to the settlement of stock-based payment awards, are now classified as cash flows from operating activities on our Statements of Cash Flows. The adoption of ASU 2016-09 did not have a material impact on our results of operations or financial condition.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements* which provides an optional transition method that allows entities to elect to apply the standard prospectively at its effective date, versus recasting the prior periods presented. We are currently in the process of evaluating the transition method. Unlike current GAAP which requires only capital leases to be recognized on the balance sheet, the new guidance will require both types of leases (i.e. operating and capital leases) to be recognized on the balance sheet. The FASB lessee accounting model will continue to account for both types of leases. The capital lease will be accounted for in substantially the same manner as capital leases are accounted for under existing GAAP. The operating lease will be accounted for in a manner similar to operating leases under existing GAAP, except that lessees will recognize a lease liability and a lease asset for all of those leases. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018, with early adoption permitted. We expect to adopt this standard beginning in 2019 and do not expect that this standard will have a material impact on our statements of operations and comprehensive loss; however, we expect that upon adoption, this standard will impact the carrying value of our assets and liabilities on our balance sheets as a result of the requirement to record right-of-use assets and corresponding lease obligations for current operating leases. We are still evaluating whether there are other existing contracts that may become leases under the new lease standard, and the impact of the adoption of this standard on our financial statements and disclosures. We will continue to monitor additional modifications, clarifications or interpretations undertaken by the FASB that may impact our current conclusions, and will expand our analysis to include any new lease arrangements initiated prior to adoption.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* and has subsequently issued several supplemental or clarifying ASUs (collectively, "ASC 606"), ASC 606 supersedes nearly all existing revenue recognition guidance under U.S. GAAP. The core principle of ASC 606 is to recognize revenues when

promised goods or services are transferred to customers in an amount that reflects the consideration to which an entity expects to be entitled for those goods or services. ASC 606 defines a five step process to achieve this core principle and, in doing so, more judgment and estimates may be required within the revenue recognition process than are required under existing U.S. GAAP.

The standard is effective for annual periods beginning after December 15, 2017, and interim periods therein, using either of the following transition methods: (i) a full retrospective approach reflecting the application of the standard in each prior reporting period with the option to elect certain practical expedients, or (ii) a retrospective approach with the cumulative effect of initially adopting ASC 606 recognized at the date of adoption.

We adopted the new standard effective January 1, 2018 under the modified retrospective transition method, applying the new guidance to the most current period presented. Upon adoption, there was no change to the units of accounting previously identified under legacy GAAP, which are now considered performance obligations under the new guidance, and there was no change to the revenue recognition pattern for each performance obligation. Therefore, the adoption of the new standard resulted in no cumulative effect to the opening accumulated deficit balance.

We assessed the impact that the adoption of ASC 606 would have on our financial statements by analyzing our current portfolio of customer contracts, including a review of historical accounting policies and practices to identify potential differences in the application of ASC 606. Additionally, we performed a comprehensive review of our current processes and systems to determine and implement changes required to support the adoption of ASC 606 on January 1, 2018.

Subsequent Events

We have evaluated events that have occurred subsequent to December 31, 2018 and through the date that the financial statements are issued.

Fair Value Measurements

We measure the fair value of financial assets and liabilities based on authoritative guidance which defines fair value, establishes a framework consisting of three levels for measuring fair value, and requires disclosures about fair value measurements. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. There are three levels of inputs that may be used to measure fair value:

Level 1 – quoted prices in active markets for identical assets or liabilities;

Level 2 – quoted prices for similar assets and liabilities in active markets or inputs that are observable;

Level 3 – inputs that are unobservable (for example cash flow modeling inputs based on assumptions).

Financial instruments, including receivables, accounts payable and accrued liabilities are carried at cost, which we believe approximates fair value due to the short-term nature of these instruments. The $8.9 million and $7.4 million fair values of money market funds as of December 31, 2018 and 2017 included in our cash and cash equivalents, are classified as Level 1 and were derived from quoted market prices as active markets for these instruments exists. Our warrant liabilities are classified within level 3 of the fair value hierarchy because the value is calculated using significant judgment based on our own assumptions in the valuation of these liabilities.

As a result of the fair value adjustment of the warrant liabilities, we recorded no gains or losses on changes in the fair value during the year ended December 31, 2018. We recorded a non-cash gain on decreases in the fair value of approximately $619,000 during the year ended December 31, 2017 in our Statements of Operations and Comprehensive Income (Loss). See Note 7, “Warrant Liability” for further discussion on the calculation of the fair value of the warrant liability.

We recorded non-cash gains of approximately $134,000 related to decreases in the fair value of our derivative liability for the year ended December 31, 2018. See Note 5 “Molteni Purchase Agreement” for further discussion on the calculation of the fair value of the derivative liability.

The following table rolls forward the fair value of the Company’s warrant liability, the fair value of which is determined by Level 3 inputs for the years ended December 31, 2018 and 2017 (in thousands):

	December 31,	
	2018	2017
Fair value, beginning of period	$—	$619
Issuance of derivatives	159	—
Change in fair value	(134)	(619)
Fair value, end of period	$25	$—

2. Property and Equipment

Property and equipment consisted of the following at December 31, 2018 and 2017 (in thousands):

	2018	2017
Furniture and office equipment	$388	$388
Leasehold improvements	408	408
Laboratory equipment	3,249	2,690
Computer equipment	1,188	1,168
	5,233	4,654
Less accumulated depreciation and amortization	(4,439)	(4,059)
Property and equipment, net	$794	$595

Depreciation and amortization expense was $380,000, $417,000 and $377,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

3. Research and License Agreements

We have entered into various agreements with research institutions, universities, clinical research organizations and other entities for the performance of research and development activities and for the acquisition of licenses related to those activities.

We have no annual payment requirements to maintain our current licenses. Certain licenses provide for the payment of royalties by us on future product sales, if any. In addition, in order to maintain these licenses and other rights during product development, we must comply with various conditions including the payment of patent-related costs.

4. Braeburn License

Until its termination in May 2018, we were party to a license agreement (as amended, the "License Agreement") pursuant to which we had granted Braeburn the exclusive commercialization rights to Probuphine in the United States and its territories and Canada. Under the License Agreement, we received certain milestone payments, as well as royalties on net sales of Probuphine. The License Agreement provided for us to be reimbursed by Braeburn for any development services and activities undertaken at Braeburn's request. Under ASC 606, there was no change in the amount or timing of revenue recognized under the License Agreement. In February 2016, Braeburn sublicensed rights to develop and commercialize Probuphine in Canada to Knight.

On May 25, 2018, we entered into the Transition Agreement with Braeburn pursuant to which we regained all rights to the commercialization and clinical development of Probuphine in the United States and Canada. Braeburn paid us $1.0 million, transferred inventory to us with a value of approximately $1.1 million and agreed to provide support services through December 28, 2018. In addition, the Transition Agreement provided for the immediate transfer to us of all regulatory documentation and development data related to Probuphine. The estimated fair value of the inventory received was determined using available inputs such as existing supply agreements, prior selling prices and remaining life to expiration. We recognized approximately $2.1 million of license related revenue related to this transaction during the three month period ended June 30, 2018. The sublicense to Knight was assigned to Titan as part of the Transition Agreement.

As of December 31, 2018, we have recognized approximately $15.0 million in license revenue related to the up-front payment we received upon execution of the License Agreement. In addition, we received a $15.0 million milestone payment from Braeburn following the achievement of FDA approval of the product NDA. As such, upon receipt of FDA approval our obligation was fulfilled and we recognized the $15.0 million regulatory milestone payment from Braeburn in accordance with the milestone method of revenue recognition. We have recognized approximately $312,000 of royalty revenue on net sales of Probuphine prior to termination of the License Agreement. Internal and external research and development costs related to this product have been expensed in the period incurred.

5. Molteni Purchase Agreement

On March 21, 2018, we entered into the Purchase Agreement with Molteni pursuant to which Molteni acquired the European intellectual property related to Probuphine, including the MAA under review by the EMA, and will have the exclusive right to commercialize the Probuphine product supplied by us in the Molteni Territory.

We received an initial payment of €2.0 million (approximately $2.4 million) for the purchased assets and will receive additional potential payments upon the achievement of certain regulatory and product label milestones. Additionally, we are entitled to receive earn-out payments for up to 15 years on net sales of Probuphine in the Molteni Territory ranging in percentage from the low-teens to the mid-twenties.

We concluded that the performance obligations identified in the Purchase Agreement included the transfer of the intellectual property and our efforts towards the approval by the EMA and other regulatory bodies. The initial closing payment was allocated between the property transfer and our EMA efforts as set forth below.

We used the expected cost-plus approach to estimate the standalone selling price of approximately $1.4 million related to our efforts towards the approval by the EMA and other regulatory bodies. This includes employee related expenses as well as other manufacturing, regulatory and clinical costs which will be incurred as part of our efforts. At the time of the agreement, we believed that the services would be at a consistent rate and would be substantially complete as of December 31, 2018. As such, we recognized the revenue ratably at an amount equal to approximately $157,000 per month through June 30, 2018. We currently estimate that the services will likely extend until March 31, 2019 and we will recognize the revenue ratably at an amount equal to approximately $104,000 per month over the period from July 1, 2018 through March 31, 2019. If the facts and circumstances change, we will reassess these assumptions. The costs associated with these services will be expensed over the same period.

We used the residual approach to value the transfer of the intellectual property at approximately $1.0 million as we had not established and had no reliable way to establish a standalone selling price for the intellectual property.

As a result of the outcome of the milestone and earn-out payments being unpredictable due to the involvement of third parties, we believe that using the most likely amount method is appropriate. Any subsequent revenue related to milestone and earn-out payments will be recognized at the time the milestones are achieved or when the related net sales have occurred.

The Purchase Agreement provides that we will supply Molteni with semi-finished product (i.e., the implant, the applicator and related technology) on an exclusive basis at a fixed price through December 31, 2019, with subsequent price increases not to exceed annual cost increases to us for the active pharmaceutical ingredient and under our current manufacturing agreement. Revenue will be recognized when the semi-finished product has been transferred to Molteni.

Molteni will be prohibited from marketing a Competitor Product (as defined in the Purchase Agreement) in the Molteni Territory for the five year period following approval of the MAA. Thereafter, Molteni will be required to pay us a low single digit royalty on net sales of any Competitor Product.

The following table presents changes in contract assets and liabilities during the year ended December 31, 2018:

(in thousands)	Beginning Balance	Additions	Deductions	Ending Balance
Year ended December 31, 2018				
Contract assets	$ —	$ 291	$ (192)	$ 99
Contract liabilities:				

Deferred revenue	$ —	$ 2,448	$ (2,135)	$ 313

On August 3, 2018, we entered into an amendment (the "Amendment") to the Purchase Agreement with Molteni. Under the Amendment, Molteni made an immediate payment to us of €950,000 (approximately $1.1 million) and committed to make a convertible loan to us of €550,000 (approximately $0.6 million) provided we have submitted our response to the 120-day letter from the EMA on or prior to September 14, 2018 in accordance with the Amendment, both in exchange for the elimination of an aggregate of €2.0 million (approximately $2.3 million) of regulatory milestones provided for in the Purchase Agreement that are potentially payable in 2019, at the earliest. The loan (the "Convertible Loan") was made on September 18, 2018 and will convert automatically into shares of our common stock upon the issuance by the EMA of marketing approval for Probuphine at a conversion price per share equal to the lower of (i) the closing price on the loan funding date ($3.42 per share) or (ii) the closing price on the conversion date. In the event the EMA has not granted marketing approval by December 31, 2019, the Convertible Loan will become due and payable, together with accrued interest at the rate of one-month LIBOR (to the extent in excess of 1.10%) plus 9.50% per annum. We concluded that the approximately $1.1 million immediate payment by Molteni reflected a milestone payment with no additional obligations to us and therefore was recognized as revenue during the three month period ended September 30, 2018. Due to the conversion provision of the Convertible Loan, ASC 815, *Derivatives and Hedging* required that we classify this as an embedded derivative and changes in the fair value were recorded in the Statements of Operations and Comprehensive Loss. The Convertible Loan contains other covenants and events of default substantially consistent with the Restated Loan Agreement described in Note 8. "Debt Agreements."

The key assumptions used to value the Convertible Loan embedded derivative were as follows:

Assumption		
Date of issuance	September 18, 2018	
Expected price volatility	87	%
Expected term (in years)	0.75	
Risk-free interest rate	2.32	%
Dividend yield	0.00	%
Fair value of conversion provision	$158,530	

Assumption		
Valuation date	December 31, 2018	
Expected price volatility	135	%
Expected term (in years)	0.50	
Risk-free interest rate	2.51	%
Dividend yield	0.00	%
Fair value of conversion provision	$25,064	

6. Commitments and Contingencies

Lease Commitments

We lease our facilities under an operating lease that expires in June 2021. Rent expense was $286,000, $293,000, and $257,000 for years ended December 31, 2018, 2017, and 2016, respectively.

The following is a schedule of future minimum lease payments at December 31, 2018 (in thousands):

2019	$299
2020	308
2021	155
2022 and thereafter	—
	$762

Legal Proceedings

There are no ongoing legal proceedings against our company.

7. Warrant Liability

Until they expired by their terms on April 18, 2018, we had warrants outstanding to purchase an aggregate of 163,900 shares of common stock at an exercise price of $29.10 per share. The warrants contained a provision where the warrant holder had the option to receive cash equal to the Black Scholes fair value of the remaining unexercised portion of the warrant as cash settlement in the event that there was a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, *Distinguishing Liabilities from Equity* required that these warrants be classified as liabilities. The fair value of these warrants was determined using the Lattice valuation model, and the changes in the fair value were recorded in the Statements of Operations and Comprehensive Loss.

8. Debt Agreements

In July 2017, we entered into a venture loan and security agreement ("Loan Agreement") with Horizon Technology Finance Corporation ("Horizon"), which provides for up to $10.0 million in loans, including an initial loan in the amount of $7.0 million funded upon signing of the Loan Agreement. An additional $3.0 million loan is subject to our achievement of the following milestones on or prior to March 31, 2018:

- Revenue resulting from royalty payments of not less than $750,000;
- Execution of a partnership or similar agreement for the marketing and sale of Probuphine in Europe; and
- Market capitalization of not less than $50.0 million.

Repayment of the loans is on an interest-only basis through December 31, 2018, followed by monthly payments of principal and accrued interest for the balance of the 46-month term. The loans bear interest at a floating coupon rate of one-month LIBOR (floor of 1.10%) plus 8.40%. A final payment equal to 5.0% of each loan tranche will be due on the scheduled maturity date for such loan. In addition, if we repay all or a portion of the loan prior to the applicable maturity date, we will pay Horizon a prepayment penalty fee, based on a percentage of the then outstanding principal balance, equal to 4% if the prepayment occurs during the interest-only payment period, 3% if the prepayment occurs during the 12 months following such period, and 2% thereafter.

Our obligations under the Loan Agreement are secured by a first priority security interest in all of our assets, with the exception of our intellectual property. We agreed not to pledge or otherwise encumber our intellectual property assets, subject to certain exceptions.

The Loan Agreement includes customary affirmative and restrictive covenants, excluding any covenants to attain or maintain certain financial metrics, and also includes customary events of default, including for payment failures, breaches of covenants, change of control and material adverse changes. Upon the occurrence of an event of default and following any applicable cure periods, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and Horizon may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement.

In connection with the Loan Agreement, we issued Horizon seven-year warrants to purchase an aggregate of 46,770 shares of our common stock ("Horizon Warrants"). The per share exercise price of the Horizon Warrants was the lower of (i) $11.76 or (ii) the price per share of any securities that may be issued by the Company in an equity financing during the next 18 months. We issued Horizon an additional warrant that will only become exercisable upon the funding of the second tranche of the loan, the number of shares and exercise price to be calculated at such time. We agreed to file a registration statement covering the resale of the shares underlying the Horizon Warrants. In accordance with ASC 480, *Distinguishing Liabilities from Equity*, as amended by ASU, No. 2017-11, which we early adopted during 2017, these warrants have been classified as equity. The fair value of these warrants at the time of issuance was determined using a Lattice valuation model and was recorded in the Balance Sheet.

The key assumptions used to value the Horizon Warrants were as follows:

Assumption		
Date of issuance	July 27, 2017	
Expected price volatility	47	%
Expected term (in years)	7.00	
Risk-free interest rate	2.12	%
Dividend yield	0.00	%
Weighted-average fair value of warrants	$6.12	

In connection with the closing of the Offering on September 25, 2018, the Horizon Warrants became exercisable to purchase an aggregate of 366,668 shares of common stock at an exercise price of $1.50 per share.

In accordance with the guidance in ASU 2017-11, we recognized the effect of triggering the down round feature as a dividend in our Balance Sheets at December 31, 2018 and as an addition to net loss attributable to common

stockholders and in our calculation of basic and fully diluted earnings per share in our Statements of Operations and Comprehensive Loss for the year ended December 31, 2018. We calculated the dividend of approximately $0.3 million resulting from the trigger of the down round provision on September 25, 2018 using the Black Scholes Option Pricing Model and the assumptions indicated in the table below:

Assumption	Pre-reset		Post-reset	
Exercise price per share	$ 11.76		$ 1.50	
Expected price volatility	71	%	71	%
Expected term (in years)	5.84		5.84	
Risk-free interest rate	3.02	%	3.02	%
Dividend yield	0.00	%	0.00	%
Weighted-average fair value of warrants	$ 0.30		$ 0.84	

On February 2, 2018, we entered into an amendment to the Original Loan Agreement (the “Amended Loan Agreement”) pursuant to which we prepaid $3.0 million of the outstanding $7.0 million principal amount and provided Horizon with a lien on our intellectual property. The other terms of the Original Loan Agreement remained unchanged.

On March 21, 2018, we entered into an Amended and Restated Venture Loan and Security Agreement (the “Restated Loan Agreement”) with Horizon and Molteni pursuant to which Horizon assigned approximately $2.4 million of the $4.0 million outstanding principal balance of the loan to Molteni and Molteni was appointed collateral agent and assumed majority and administrative control of the debt. Under the Restated Loan Agreement, the interest only payment and forbearance periods were extended to December 31, 2019. In addition, Molteni has the right to convert its portion of the debt into shares of our common stock at a conversion price of $7.20 per share and is required to effect this conversion of debt to equity if we complete an equity financing resulting in gross proceeds of at least $10.0 million at a price per share of common stock in excess of $7.20 and repay the $1.6 million balance of Horizon’s loan amount. The lien on our intellectual property remains in place at this time. As the present value of the cash flows under the terms of the Restated Loan Agreement is less than 10% different from the remaining cash flows under the terms of the Amended Loan Agreement prior to being amended and restated, the Restated Loan Agreement was accounted for as a debt modification. Accordingly, expenses incurred as a result of the modification were expensed as incurred and the previously deferred fees and costs related to the debt will continue to be amortized over the remaining term along with the related warrants issued as part of the agreement described in Note 9 “Rights Agreement.”

In connection with the Restated Loan Agreement, we issued Horizon seven-year warrants to purchase 6,667 shares of our common stock at an exercise price of $7.20 per share. The new Horizon warrants have been classified as equity and their fair value at the time of issuance was determined using a Black Scholes valuation model and was recorded in the Balance Sheets as a discount to the debt obligation.

The key assumptions used to value the new Horizon warrants were as follows:

Assumption		
Date of issuance	March 21, 2018	
Expected price volatility	86	%
Expected term (in years)	7.00	
Risk-free interest rate	2.82	%
Dividend yield	0.00	%
Weighted-average fair value of warrants	$4.86	

9. Rights Agreement

In consideration of Molteni's entry into the Restated Loan Agreement and the Purchase Agreement, on March 21, 2018, we entered into an agreement (as amended in May 2018, the "Rights Agreement") with Molteni pursuant to which we agreed to (i) issue Molteni seven-year warrants to purchase 90,000 shares of our common stock at an exercise price of $7.20 per share (the "Molteni Warrants"), (ii) provide Molteni customary demand and piggy-back registration rights with respect to the shares of common stock issuable upon conversion of its loan and exercise of the Molteni Warrants, (iii) appoint one member of our board of directors following conversion of its loan to equity and (iv) provide board observer rights to Molteni if it has not designated a board nominee as well as certain information rights. The board designation, observer and information rights will terminate at such time as Molteni ceases to beneficially own at least one percent of our outstanding capital stock (inclusive of the shares issuable upon conversion of debt under the Restated Loan Agreement and exercise of the Molteni Warrants). The Molteni Warrants have been classified as equity and their fair value at the time of issuance was determined using a Black Scholes valuation model. The amount was allocated equally between the Restated Loan Agreement and the Purchase Agreement and was recorded in the Balance Sheets as a discount to the debt obligation and a contract asset, respectively.

The key assumptions used to value the Molteni Warrants were as follows:

Assumption		
Date of issuance	March 21, 2018	
Expected price volatility	86	%

Expected term (in years)	7.00	
Risk-free interest rate	2.82	%
Dividend yield	0.00	%
Weighted-average fair value of warrants	$4.86	

10. Guarantees and Indemnifications

As permitted under Delaware law and in accordance with our Bylaws, we indemnify our officers and directors for certain events or occurrences while the officer or director is or was serving at our request in such capacity. The term of the indemnification period is for the officer's or director's lifetime. The maximum amount of potential future indemnification is unlimited; however, we have a director and officer insurance policy that limits our exposure and may enable us to recover a portion of any future amounts paid. We believe the fair value of these indemnification agreements is minimal. Accordingly, we have not recorded any liabilities for these agreements as of December 31, 2018.

In the normal course of business, we have commitments to make certain milestone payments to various clinical research organizations in connection with our clinical trial activities. Payments are contingent upon the achievement of specific milestones or events as defined in the agreements, and we have made appropriate accruals in our financial statements for those milestones that were achieved as of December 31, 2018. We also provide indemnifications of varying scope to our CROs and investigators against claims made by third parties arising from the use of our products and processes in clinical trials. Historically, costs related to these indemnification provisions were immaterial. We also maintain various liability insurance policies that limit our exposure. We are unable to estimate the maximum potential impact of these indemnification provisions on our future results of operations.

11. Stockholders' Equity (Deficit)

Common Stock

On September 20, 2018, we entered into an underwriting agreement (the "Underwriting Agreement") with A.G.P./Alliance Global Partners, as representative (the "Representative") of the underwriters (the "Underwriters") pursuant to which we sold to the Underwriters in a public offering (the "Offering") an aggregate of (i) 850,000 Class A Units at a public offering price of $1.50 per unit, with each unit consisting of one share of common stock and a Warrant to purchase one share of common stock, and (ii) 8,225 Class B Units at a public offering price of $1,000 per unit, with each unit consisting of one share of Series A Convertible Preferred Stock (the "Preferred Shares") and Warrants to purchase 667 shares of common stock. The Warrants have an exercise price of $1.50 and will expire five years from the date of issuance. The Preferred Shares, which were convertible into an aggregate of 5,483,334 shares of common stock, included a beneficial ownership blocker but had no dividend rights (except to the extent that dividends were also paid on the common stock), liquidation preference or other preferences over common stock, and had no voting rights. In September and October 2018, the Preferred Shares were converted in full into 5,483,334 shares of common stock..

Pursuant to the Underwriting Agreement, the Underwriters were granted a 45-day option to purchase up to an additional 950,000 shares of common stock and/or additional Warrants to purchase up to 950,000 shares of common stock. We also agreed to issue to the Representative and its designees warrants to purchase an aggregate of 253,334 shares of Common Stock at an exercise price of $1.68 per share.

The Offering closed on September 25, 2018. At the closing, the Underwriters exercised their option to purchase 950,000 additional Warrants at a price of $0.06 per warrant. On October 3, 2018, we completed the sale of 633,334 shares of common stock at a purchase price of $1.44 per share in connection with an exercise of the over-allotment option by the Underwriters. On October 22, 2018, we completed the sale of 316,667 shares of common stock at a

purchase price of $1.44 per share in connection with the final exercise of the Underwriter's over-allotment option.

From October 1, 2018 through November 9, 2018, Warrants to purchase an aggregate of 2,178,484 shares of common stock were exercised, resulting in proceeds to us of approximately $3.3 million.

As of December 31, 2018, the following warrants to purchase shares of our common stock were outstanding (in thousands, except per share price):

Date Issued	Expiration Date	Exercise Price	Outstanding
10/08/2014	10/08/2020	$ 19.80	141
07/27/2017	07/27/2024	$ 1.50	367
03/21/2018	03/21/2025	$ 7.20	7
03/21/2018	03/21/2025	$ 7.20	90
09/25/2018	09/25/2023	$ 1.50	5,105
09/25/2018	09/25/2023	$ 1.68	253
			5,963

Shares Reserved for Future Issuance

As of December 31, 2018, shares of common stock reserved by us for future issuance consisted of the following (in thousands):

Stock options outstanding	665
Shares issuable upon the exercise of warrants	5,963
	6,628

12. Stock Plans

In August 2015, our stockholders approved the 2015 Omnibus Equity Incentive Plan, or the 2015 Plan. The 2015 Plan, as amended in August 2018, authorized a total of 583,334 shares of our common stock for issuance to employees, directors, officers, consultants and advisors. On December 31, 2018, options to purchase 479,030 shares of our common stock were outstanding under the 2015 Plan. See Note 14 - “Subsequent Events.”

In February 2014, our Board adopted the 2014 Incentive Plan, or the 2014 Plan, pursuant to which 75,758 shares of our common stock were authorized for issuance to employees, directors, officers, consultants and advisors. On December 31, 2018, options to purchase 42,861 shares of our common stock were outstanding under the 2014 Plan. Upon receipt of stockholder approval of the 2015 Plan, the 2014 Plan was terminated.

In May 2009, we granted 18,637 and 9,394 non-qualified stock options outside of our stock option plans to Dr. Rubin and Mr. Bhonsle, respectively, at an exercise price of $26.04 that vested over 48 months from the grant date.

In October 2007, we granted 13,258 non-qualified stock options outside of our stock option plans to Dr. Rubin, at an exercise price of $79.20 per share that vested over 48 months from the grant date. These options expired by their terms in October 2017.

In July 2002, we adopted the 2002 Stock Incentive Plan (“2002 Plan”). The 2002 Plan, as amended in 2005, authorized a total of approximately 217,000 shares of our common stock for issuance to employees, officers, directors, consultants, and advisers. The exercise prices of options granted under the 2002 Plan were 100% of the fair market value of our common stock on the date of grant. The 2002 Plan expired by its terms in July 2012. On December 31, 2018, options to purchase an aggregate of 86,626 shares of our common stock were outstanding under the 2002 Plan.

In August 2001, we adopted the 2001 Employee Non-Qualified Stock Option Plan (“2001 NQ Plan”) pursuant to which 53,031 shares of common stock were authorized for issuance for option grants to employees and consultants who are not officers or directors of Titan. The exercise prices of options granted under the 2001 NQ Plan were 100% of the fair market value of our common stock on the date of grant. The 2001 Stock Option Plan expired by its terms in August 2011. On December 31, 2018, options to purchase an aggregate of 28,917 shares of our common stock were outstanding under the 2001 NQ Plan.

The option exercise prices in the following tables do not give effect to the option repricing approved by our stockholders in January 2019. See Note 14 - “Subsequent Events.”

Activity under our stock plans, as well as non-plan activity, is summarized below (shares in thousands):

	Shares or Awards Available For Grant	Number of Options and Awards Outstanding	Weighted Average Exercise Price
Balance at December 31, 2015	152	314	$ 34.98
Increase in shares reserved	190	—	—
Options granted	(28)	28	$ 30.60
Options exercised	—	(1)	$ 20.22
Options expired	—	(7)	$ 65.10
Balance at December 31, 2016	314	334	$ 34.02
Options granted	(158)	158	$ 15.30
Options cancelled	10	(19)	$ 31.62
Options expired	—	(18)	$ 78.66
Balance at December 31, 2017	166	455	$ 25.91
Increase in shares reserved	167	—	—
Options granted	(245)	245	4.23
Options cancelled	16	(32)	23.31
Options expired	—	(3)	50.16
Balance at December 31, 2018	104	665	$ 17.94

Options to purchase approximately 0.6 million shares were exercisable at December 31, 2018 and 2017. The options outstanding at December 31, 2018 have been segregated into five ranges for additional disclosure as follows (options in thousands):

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$1.26 - $5.46	87	9.78	$ 1.38	3	$ 1.97
$5.52 - $6.66	154	9.18	$ 5.82	154	$ 5.82
$6.72 - $23.10	125	5.22	$ 12.68	125	$ 12.68
$23.16 - $28.32	125	4.15	$ 24.76	120	$ 24.82
$28.38 - $77.88	174	4.85	$ 35.88	174	$ 35.88
$1.26 - $77.88	665	6.44	$ 17.94	576	$ 20.34

We use the Black-Scholes-Merton option-pricing model with the following assumptions to estimate the stock-based compensation expense for the years ended December 31, 2018, 2017 and 2016:

	Years Ended December 31,		
	2018	2017	2016
Weighted-average risk-free interest rate	2.84 %	2.13 %	1.53 %
Expected dividend payments	—	—	—
Expected holding period (years)(1)	6.39	5.90	6.53
Weighted-average volatility factor(2)	0.88	0.90	0.92
Estimated forfeiture rates for options granted	26 %	27 %	29 %

(1) Expected holding period is based on historical experience of similar awards, giving consideration to the contractual terms of the stock-based awards, vesting schedules and the expectations of future employee behavior.

(2) Weighted average volatility is based on the historical volatility of our common stock.

(3) Estimated forfeiture rates are based on historical data.

During the year ended December 31, 2018, options to purchase 245,010 shares were granted to employees, directors and consultants. Based upon the above methodology, the weighted-average fair value of options and awards granted during the years ended December 31, 2018, 2017 and 2016 was $3.21, $11.58 and $18.60, respectively.

The following table summarizes the stock-based compensation expense and impact on our basic and diluted loss per share for the years ended December 31, 2018, 2017 and 2016:

	Years Ended December 31,		
(in thousands, except per share amounts)	2018	2017	2016
Research and development	$ 575	$ 519	$ 386
General and administrative	982	1,168	653
Total stock-based compensation expenses	$ 1,557	$ 1,687	$ 1,039
Increase in basic net income (loss) per share	$ (0.27)	$ (0.08)	$ (0.05)
Increase in diluted net income (loss) per share	$ (0.27)	$ (0.08)	$ (0.05)

The following table summarizes option activity for the year ended December 31, 2018:

(in thousands, except per share amounts)	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2018	455	$ 25.91	5.75	$ 30
Granted	245	4.23		
Cancelled	(32)	23.31		
Expired	(3)	50.16		
Outstanding at December 31, 2018	665	$ 17.94	6.44	$ 4
Exercisable at December 31, 2018	576	$ 20.34	5.93	$ —

As of December 31, 2018, there was approximately $103,000 of total unrecognized compensation expense related to non-vested stock options. This expense is expected to be recognized over a weighted-average period of 2.3 years.

There were no outstanding stock awards at December 31, 2018.

13. Income Taxes

As of December 31, 2018, we had federal net operating loss carryforwards of approximately $256.1 million that expire at various dates through 2037 and $7.5 million which do not expire but are subject to 80% taxable income limitations. As of December 31, 2018, we had federal research and development tax credits of approximately $8.8 million that expire at various dates through 2038. We also had net operating loss carryforwards for California income tax purposes of approximately $107.8 million that expire at various dates through 2038 and state research and development tax credits of approximately $9.0 million which do not expire.

Current federal and California tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change of a corporation under Internal Revenue Code Section 382 and 383. We have performed a change in ownership analysis through December 31, 2018 and expect our net operating loss and tax credit carryforwards to be available to offset future taxable income, if any.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and operating loss and credit carryforwards. Significant components of our deferred tax assets are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$62,863	$62,295
Research credit carryforwards	15,886	15,873
Other, net	1,321	1,705
Total deferred tax assets	80,070	79,873
Valuation allowance	(80,070)	(79,873)
Net deferred tax assets	$—	$—

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $0.2 million during 2018, decreased by $24.4 million during 2017 and decreased by $4.4 million during 2016.

The provision for income taxes consists of state minimum taxes due. The effective tax rate of our provision (benefit) for income taxes differs from the federal statutory rate as follows (in thousands):

	Year Ending December 31,		
	2018	2017	2016
Computed at 21%	$(1,879)	$(4,832)	$1,758
State taxes	(167)	(157)	(187)
Change in valuation allowance	197	(28,555)	(4,439)
Other	121	388	659
Revaluation of warrant liability	(30)	(210)	(280)
Research and development credits	144	(250)	(252)
Net operating loss carryforward expirations	975	1,007	2,741
Impact of 2017 Tax Act	—	32,609	—
Impact of IRC 162m	639	—	—
Total	$—	$—	$—

We had no unrecognized tax benefits or any amounts accrued for interest and penalties for the three year period ended December 31, 2018. Our policy is to recognize interest and penalties related to income taxes as a component of income tax expense. We do not expect the amount of unrecognized tax benefits will materially change in the next twelve months.

We file tax returns in the U.S. federal jurisdiction and some state jurisdictions. We are subject to the U.S. federal and state income tax examination by tax authorities for such years 1999 through 2018, due to net operating losses that are being carried forward for tax purposes.

The Tax Cuts and Jobs Act ("2017 Tax Act") was enacted in December 2017. The 2017 Tax Act, among other things, reduces the U.S. federal corporate tax rate from 35% to 21%, effective January 1, 2018, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign earnings. We revalued our deferred tax assets as of December 31, 2018 based on a U.S. federal tax rate of 21%, which resulted in a reduction to our deferred tax assets of $32.6 million fully offset by a reduction to the valuation allowance.

14. Subsequent Events

Reverse Stock Split

On January 24, 2019, pursuant to prior stockholder authorization, our Board effected the Reverse Split of the outstanding shares of our common stock at a ratio of one (1) share for every six (6) shares outstanding, so that every six (6) outstanding shares of common stock before the Reverse Split represents one (1) share of common stock after the Reverse Split. Pursuant to their respective terms, the number of shares underlying our outstanding options and warrants was reduced by the Reverse Split ratio.

All share and per share amounts in the accompanying financial statements have been restated for all periods presented to give retroactive effect to the Reverse Split. The shares of common stock retained a par value of $0.001 per share.

From January 1, 2019 through March 25, 2019, Warrants to purchase an aggregate of 403,335 shares of common stock were exercised, resulting in proceeds to us of approximately $0.6 million.

On January 23, 2019, our stockholders approved an amendment to the Titan Pharmaceuticals, Inc. 2015 Omnibus Equity Incentive Plan to increase the number of shares authorized for awards thereunder from 583,334 to 1,666,667.

On January 23, 2019, our stockholders approved a repricing of 122,115 options with exercise prices in excess of $21.00 (post-Reverse Split) held by employees and consultants other than the named executive officers or members of the Board. The effected options were repriced to $1.55 (post-Reverse Split).

15. Quarterly Financial Data (Unaudited)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
	(in thousands, except per share amount)			
2018				
Total revenue	$1,064	$ 2,668	$ 1,650	$ 1,236
Net loss	$(2,605)	$ (869)	$ (2,330)	$ (3,504)
Basic net loss per share	$(0.74)	$ (0.25)	$ (0.64)	$ (0.62)
Diluted net loss per share	$(0.74)	$ (0.25)	$ (0.68)	$ (0.62)
2017				
Total revenue	$40	$ 77	$ 40	$ 58
Net loss	$(3,005)	$ (3,451)	$ (4,191)	$ (3,660)
Basic net loss per share	$(0.85)	$ (0.98)	$ (1.19)	$ (1.04)
Diluted net loss per share	$(0.96)	$ (1.03)	$ (1.19)	$ (1.04)

(b) Exhibits

No.	Description
1.1	Underwriting Agreement between Titan Pharmaceuticals, Inc. and A.G.P./Alliance Global Partners (25)
3.1.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended (5)
3.1.2	Certificate of Amendment to the Restated Certificate of Incorporation dated September 24, 2015 (14)
3.1.3	Certificate of Amendment to the Restated Certificate of Incorporation dated January 23, 2019 (26)
3.2	By-laws of the Registrant (1)
3.3	Certificate of Designation of Series A Convertible Preferred Stock (25)
4.1	Form of 2014 Class A Warrant(13)
4.3	Form of 2014 Underwriter Warrant (13)
4.4	Form of Lender Warrant (18)
4.5	Form of Rights Agreement Warrant (20)
4.6	Warrant Agency Agreement between Titan Pharmaceuticals, Inc. and Continental Stock Transfer & Trust Company and Form of Offering Warrant (25)
4.7	Representative's Purchase Warrant(25)
10.1	2001 Non-Qualified Employee Stock Option Plan (2)
10.2	2002 Stock Option Plan (3)
10.3	Lease for the Registrant's facilities, amended as of October 1, 2004(4)
10.4	Amendments to lease for Registrant's facilities dated May 21, 2007 and March 12, 2009(5)
10.5	Amendment to lease for Registrant's facilities dated June 15, 2010(6)
10.6±	License Agreement by and between Titan Pharmaceuticals, Inc. and Braeburn Pharmaceuticals Sprl, dated December 14, 2012 (8)
10.7	Amendment dated May 28, 2013 to License Agreement by and between Titan Pharmaceuticals, Inc. and Braeburn Pharmaceuticals Sprl (9)
10.8	Second Amendment dated July 2, 2013 to License Agreement by and between Titan Pharmaceuticals, Inc. and Braeburn Pharmaceuticals Sprl (10)
10.9	Third Amendment dated November 12, 2013 to License Agreement by and between Titan Pharmaceuticals, Inc. and Braeburn Pharmaceuticals Sprl(11)
10.10	Titan Pharmaceuticals, Inc. 2014 Incentive Plan (12)
10.11	Titan Pharmaceuticals, Inc. Third Amended and Restated 2015 Omnibus Equity Incentive Plan(26)
10.12	Controlled Equity Offering SM Sales Agreement, dated September 1, 2016, between Titan Pharmaceuticals, Inc. and Cantor Fitzgerald & Co. (16)
10.13	Employment Agreement between Titan Pharmaceuticals, Inc. and Titan Pharmaceuticals, Inc. and Sunil Bhonsle (17)
10.14	Employment Agreement between Titan Pharmaceuticals, Inc. and Titan Pharmaceuticals, Inc. and Marc Rubin (17)
10.15	Venture Loan and Security Agreement, dated July 27, 2017, by and between Titan Pharmaceuticals, Inc. and Horizon Technology Finance Corporation (18)
10.16	Amendment of Venture Loan and Security Agreement, dated February 2, 2018, by and between Titan Pharmaceuticals, Inc. and Horizon Technology Finance Corporation (19)
10.17	Amended and Restated Venture Loan and Security Agreement, dated March 21, 2018, by and between Titan Pharmaceuticals, Inc., Horizon Technology Finance Corporation and L. Molteni & C. Dei Frattelli Alitti Società Di Esercizio S.P.A. (20)

10.18±	Asset Purchase, Supply and Support Agreement dated March 21, 2018, by and between Titan Pharmaceuticals, Inc. and L. Molteni & C. Dei Frattelli Alitti Società Di Esercizio S.P.A. (20)
10.19	Rights Agreement dated March 21, 2018, by and between Titan Pharmaceuticals, Inc. and L. Molteni & C. Dei Frattelli Alitti Società Di Esercizio S.P.A. (20)
10.20±	Termination and Transition Services Agreement dated May 25, 2018 by and between Titan Pharmaceuticals, Inc. and Braeburn Pharmaceuticals, Inc. (21)
10.21±	Amendment to Asset Purchase, Supply and Support Agreement dated August 3, 2018, by and between Titan Pharmaceuticals, Inc. and L. Molteni & C. Dei Frattelli Alitti Società Di Esercizio S.P.A (22)
10.22±	Distribution and Sublicense Agreement dated February 1, 2016 as amended by agreement dated August 2, 2018 between Titan Pharmaceuticals, Inc. and Knight Therapeutics Inc. (23)
10.23	Amendment to lease for Registrant's facility dated March 21, 2016(23)
10.24	Amendment to Employment Agreement with Sunil Bhonsle dated August 9, 2018 (23)
10.25	Amendment to Employment Agreement with Marc Rubin dated August 9, 2018(23)

10.26	Unsecured Convertible Loan Agreement dated September 18, 2018 (24)
10.27	Employment Agreement between the Registrant and Katherine Beebe DeVarney
10.28	Employment Agreement between the Registrant and Dane Hallberg
14.1	Code of Business Conduct and Ethics (12)
23.1	Consent of OUM & Co., LLP, Independent Registered Public Accounting Firm
31.1	Certification of the Principal Executive and Financial Officer pursuant to Rule 13(a)-14(a) of the Securities Exchange Act of 1934
32.1	Certification of the Principal Executive and Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

± Confidential treatment has been granted as to certain portions of this exhibit.

(1) Incorporated by reference from the Registrant's Registration Statement on Form S-3 (File No. 333-221126).

(2) Incorporated by reference from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2001.

(3) Incorporated by reference from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2002.

(4) Incorporated by reference from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2005.

(5) Incorporated by reference from the Registrant's Registration Statement on Form 10 filed on January 14, 2010.

(6) Incorporated by reference from the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2010.

(7) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on April 10, 2012.

(8) Incorporated by reference from the Registrant's Current Report on Form 8-K/A filed on February 28, 2013.

(9) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on May 29, 2013.

(10) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on July 5, 2013.

(11) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on November 13, 2013.

(12) Incorporated by reference from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2013.

(13) Incorporated by reference from the Registrant's Registration Statement on Form S-1/A dated September 30, 2014.

(14) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on September 28, 2015.

(15) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on August 3, 2016.

(16) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on September 1, 2016.

(17) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on September 30, 2016.

(18) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on July 27, 2017.

(19) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on February 7, 2018.

(20) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on March 26, 2018.

(21) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on May 30, 2018.

(22) Incorporated by reference from the Registrant's Current Report on Form 8-K filed on August 3, 2018.

(23) Incorporated by reference from the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2018.

(24) Incorporated by reference from the Registrant's Current Report on Form 8-K dated September 20, 2018.
(25) Incorporated by reference from the Registrant's Current Report on Form 8-K dated September 25, 2018.
(26) Incorporated by reference from the Registrant's Current Report on Form 8-K dated January 25, 2019.

SIGNATURES

Pursuant to the requirements of Section 12 of the Securities Exchange Act of 1934, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 31, 2019 TITAN PHARMACEUTICALS, INC.

By: /S/ SUNIL BHONSLE
Name: **Sunil Bhonsle**
Title: **President and Chief Executive Officer**

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons in the capacities and on the dates stated.

Signature	**Title**	**Date**
/s/ Marc Rubin, M.D. Marc Rubin, M.D.	Executive Chairman	March 30, 2019
/s/ Sunil Bhonsle Sunil Bhonsle	President, Chief Executive Officer and Director (principal executive officer and principal financial officer)	March 31, 2019
/s/ Joseph A. Akers Joseph A. Akers	Director	March 31, 2019
/s/ Rajinder Kumar, Ph.D. Rajinder Kumar, Ph.D.	Director	March 30, 2019
/s/ M. David MacFarlane, Ph.D. M. David MacFarlane, Ph.D.	Director	March 29, 2019
/s/ James R. McNab, Jr. James R. McNab, Jr.	Director	March 30, 2019
/s/ Federico Seghi Recli Federico Seghi Recli	Director	March 30, 2019
/s/ Scott A. Smith Scott A. Smith	Director	March 29, 2019

/s/ Brian E. Crowley Brian E. Crowley	Vice President, Finance (principal accounting officer)	March 31, 2019