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

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the Fiscal Year Ended December 31, 2017
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: 000-29959

Pain Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**91-1911336**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*

7801 N. Capital of Texas Highway, Suite 260, Austin, TX 78731
(512) 501-2444
(Address, including zip code, of registrant's principal executive offices and telephone number, including area code)

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: None

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 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 such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☑ No ☐.

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. ☐

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 ☐	Smaller reporting company ☑
(Do not check if a smaller reporting company)	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 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 Act). Yes ☐ No ☑

The aggregate market value of the voting and non-voting common equity held by non-affiliates was $22,840,436 computed by reference to the last sales price of $4.15 as reported on the Nasdaq Global Select Market, as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2017. The number of shares outstanding of the Registrant's common stock on January 19, 2018 was 6,595,509, as adjusted to reflect a ratio of 7-for-1 reverse stock split effective May 10, 2017.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2018 Annual Meeting of Stockholders (the "Proxy Statement"), to be filed with the Securities and Exchange Commission, are incorporated by reference to Part III of this Form 10-K Report.

PAIN THERAPEUTICS, INC.

FORM 10-K
INDEX

PART I

This annual report contains certain statements that are considered forward-looking statements within the meaning of the Private Securities Reform Act of 1995. We intend that such statements be protected by the safe harbor created thereby. Forward-looking statements relate to expectations, beliefs, projections, future plans and strategies, anticipated events or trends and similar expressions concerning matters that are not historical facts. In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “should,” “will” and “would” or the negatives of these terms or other comparable terminology.

The forward-looking statements are based on our beliefs, assumptions and expectations of our future performance, taking into account all information currently available to us. Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to statements about:

- The timing and topics of discussions with the U.S. Food and Drug Administration, or FDA, regarding the New Drug Application, or NDA, for REMOXY® ER (oxycodone capsules CII), or REMOXY;
- the timing of the planned resubmission of the NDA for REMOXY;
- development activities to potentially support obtaining approval of REMOXY by the FDA;
- the ability of REMOXY to capture a share of the market for extended release opioid drugs;
- the status of products and potential products which are competitive with REMOXY and the implications of the FDA requirements for approval of such competitive products;
- our plans to rely on third parties, including Durect Corporation, or Durect, and Noramco, Inc., or Noramco, to supply us with excipients and active pharmaceutical ingredients and to manufacture REMOXY;
- discussions with potential strategic partners for the development and commercialization of REMOXY;
- the outcome of research and development activities, including, without limitation, development activities for FENROCK™ and potential formulation of additional dosage forms of our drug candidates;
- the potential benefits of our product candidates such as REMOXY, FENROCK, PTI-125 or PTI-125DX including the potential ability of PTI-125 to prevent or reverse amyloid-related Alzheimer’s damage or PTI-125DX to diagnose Alzheimer’s disease;
- the utility of protection of our intellectual property;
- expected future sources of revenue and capital and increasing cash needs;
- potential competitors or competitive products;
- market acceptance of our drug candidates and potential drug candidates;
- expectations regarding trade secrets, technological innovations, licensing agreements and outsourcing of certain business functions;
- expenses increasing, interest income decreasing or fluctuations in our operating results;
- operating losses and anticipated operating and capital expenditures;
- expected uses of capital resources;
- expectations regarding the issuance of shares of common stock to employees pursuant to equity compensation awards net of employment taxes;
- anticipated hiring and development of our internal systems and infrastructure;
- the sufficiency of our current resources to fund our operations over the next twelve months; and
- assumptions and estimates used for our disclosures regarding stock-based compensation.

Such forward-looking statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to:

- difficulties or delays in the preparation and filing of the NDA for REMOXY and in potentially obtaining regulatory approval of the NDA for REMOXY, including the potential for requests by the FDA for additional data which may require an extended period of time to obtain and submit;
- unexpected adverse side effects or inadequate therapeutic efficacy or manufacturing or stability issue of our drug candidates that could slow or prevent product approval (including the risk that current and past results of clinical trials are not indicative of future results of clinical trials) or potential post-approval market acceptance;
- having or obtaining sufficient resources for the successful development, manufacture and commercialization of REMOXY;
- the quantity, quality or sufficiency of the data, materials and information transferred to us by Pfizer, Inc., or Pfizer regarding the REMOXY development program;
- discussions with potential strategic partners for the development and commercialization of REMOXY;
- the successful development of other drug candidates, independently as well as pursuant to our other collaboration agreements, and the continuation of such agreements;
- difficulties or delays in development, testing, clinical trials (including patient enrollment), regulatory authorization or approval, production and commercialization of our drug candidates;
- the uncertainty of protection of our intellectual property rights or trade secrets;
- potential infringement of the intellectual property rights of third parties;
- pursuing in-license and acquisition opportunities;
- maintenance or third party funding of our collaboration and license agreements;
- legislation or regulatory actions affecting product pricing, reimbursement or access;
- significant breakdown or interruption of our information technology and infrastructure;
- significant issues that may arise related to outsourcing certain preclinical studies, clinical trials and formation and manufacturing activities;
- hiring and retaining personnel; and
- our financial position and our ability to obtain additional financing if necessary.

In addition, such statements are subject to the risks and uncertainties discussed in the "Risk Factors" section and elsewhere in this document.

All information in this Annual Report on Form 10-K has been retroactively adjusted to reflect the ratio of a 7-for-1 reverse stock split that took effect on May 10, 2017, except as otherwise described or as required by law. See "*Part II-Item 1 Management's Discussion and Analysis of Financial Condition and Results of Operations-Recent developments*."

Item 1. *Business*

Overview

Pain Therapeutics, Inc. develops proprietary drugs that offer significant improvements to patients and healthcare professionals. We generally focus our drug development efforts on disorders of the nervous system.

Our expertise consists of developing new drug candidates and guiding these through various regulatory and development pathways in preparation for their eventual commercialization. By necessity, the conduct of drug development is complex, lengthy, expensive and risky. The FDA has not yet established the safety or efficacy of our drug candidates.

Reverse Stock Split

On May 4, 2017, following stockholder approval, our board of directors approved a reverse stock split at a ratio of 7-for-1. On May 4, 2017, we filed with the Secretary of State of the State of Delaware a Certificate of Amendment to the Company's Amended and Restated Certificate of Incorporation to effect the 7-for-1 reverse stock split of our outstanding shares of common stock. The number of outstanding shares of common stock on the date of the reverse split was reduced from 46.1 million to 6.6 million shares. Our common stock began trading on the Nasdaq Global Market on a split-adjusted basis when the market opened for trading on May 10, 2017. As a result, all common stock share amounts included in this Annual Report on Form 10-K have been retroactively reduced by a factor of seven, and all common stock per share amounts have been increased by a factor of seven, with the exception of our common stock par value.

The following is a summary of our pipeline of drug assets:

REMOXY ER (extended-release oxycodone capsules CII) – REMOXY, our lead drug candidate, is a proprietary abuse-deterrent, twice-daily, oral oxycodone to treat severe chronic pain. We plan to resubmit the REMOXY NDA to the FDA, with Priority Review in Q1 2018. We own exclusive rights to develop and commercialize REMOXY worldwide, with a sales royalty obligation to one of our technology partners.

FENROCK™ (transdermal fentanyl patch CII) – FENROCK is a proprietary, abuse-deterrent fentanyl skin patch to treat severe pain. This is an early-stage program that is substantially funded by a competitive research grant award from the National Institute on Drug Abuse (NIDA), the primary agency of the U.S. government for research on drug abuse. We own exclusive, worldwide rights to FENROCK, with no royalty obligations to any third party.

PTI-125 – PTI-125 is a proprietary small molecule drug for the treatment of Alzheimer's disease (AD). In 2017, we completed a first-in-human Phase I study with PTI-125. This program is substantially funded by competitive research grant awards from the National Institutes of Health (NIH), the primary agency of the U.S. government for biomedical research. We own exclusive, worldwide rights to PTI-125, with no royalty obligations to any third party.

PTI-125DX – PTI-125 is a proprietary, blood-based diagnostic/biomarker to detect Alzheimer's disease (AD). This clinical-stage program is substantially funded by competitive research grant awards from the NIH. We own exclusive, worldwide rights to PTI-125DX, with no royalty obligations to any third party.

REMOXY ER - *a drug candidate for severe chronic pain*

Our lead drug candidate is called REMOXY ER (extended-release). REMOXY is a proprietary, abuse-deterrent, twice-daily, capsule formulation of oral oxycodone, a strong opioid drug. REMOXY is intended to meet the needs of healthcare professionals who appropriately prescribe extended-release oxycodone and who seek to minimize the risks of drug diversion, abuse or accidental patient misuse. In particular, REMOXY's thick, sticky, high viscosity formulation may deter unapproved routes of drug administration, such as injection, snorting or smoking. The proposed indication for REMOXY is for "*the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate*."

We own exclusive, worldwide rights to REMOXY.

Opioid drugs, such as oxycodone, are an important treatment option for patients with severe chronic pain. However, misuse, abuse and diversion of these prescription drugs remains a serious, persistent problem. For over a decade, we have pioneered technology, tools and techniques that enable the development of Abuse-Deterrent Formulations (ADFs). ADFs are intended to make opioid drugs difficult to abuse yet provide steady pain relief when used appropriately by patients. ADFs are intended to help in the fight against prescription drug abuse.

In March 2016, we resubmitted to the FDA a New Drug Application (NDA) for REMOXY. In September 2016, we received a Complete Response Letter, or CRL, from the FDA for the REMOXY NDA. The CRL informed us that REMOXY could not be approved in its present form and specified additional actions and data needed for drug approval. The CRL substantially focused on the need to conduct a clinical abuse-deterrent study via the nasal route of administration, and additional in vitro (non-clinical) studies to further characterize the abuse-deterrent properties of REMOXY. The 2016 CRL

made no mention of clinical safety, drug efficacy, manufacturing, stability, bioequivalence or any other issues from a prior CRL.

In February 2017, we met with the FDA regarding REMOXY. During this meeting, we reached written agreement with the FDA on a roadmap to resubmit the NDA for REMOXY. Final minutes of our FDA meeting confirmed two key requirements needed for the resubmission of the REMOXY NDA:

- To support a potential drug label claim against abuse by injection: Repeat an injectability/syringeability study using thin films of drug, smaller volumes of solvents, additional mixed solvents and alternative extraction methods and syringe filter.
- To support a potential drug label claim against abuse by snorting: Conduct an intranasal abuse potential study in human volunteers.

During 2017, we conducted these mandated studies with REMOXY. We believe positive results from these studies support label claims against abuse by injection and abuse by snorting. In November 2017, we concluded a pre-NDA meeting with the FDA. The purpose of this pre-NDA meeting was to agree on submission requirements for the REMOXY NDA under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. During the pre-NDA meeting, we received comments and clarification from the FDA on the acceptability of the data to be included in the REMOXY NDA resubmission, including a recent intranasal study. All questions were addressed and summarized in official minutes of the meeting issued by the FDA. There are no discrepancies or requests for clarifications following receipt of final meeting minutes.

As a result, we intend to resubmit the REMOXY NDA in Q1 2018 with Priority (six-month) Review.

Background on Uses and Abuse of Opioid Drugs

Opioid drugs are primarily used to relieve pain. They are among the world's oldest known drugs. The term 'opioid' refers to an entire class of analgesic substances that are derived from the opium poppy plant. Drugs that fall within this class include oxycodone, hydrocodone, fentanyl, heroin, morphine and many other related substances.

In recent decades, oxycodone, a semi-synthetic opium derivative, has become a standard of care to treat severe chronic pain. Oxycodone is in Schedule II of the federal Controlled Substances Act of 1970, which means it has accepted medical use with severe restrictions, a high potential for abuse and regulations around its manufacture, possession, storage, use and distribution.

Oxycodone can provide significant therapeutic benefits for patients in pain when used as prescribed. In recent years, patients with severe chronic pain have benefited from oxycodone in long-acting formulations. Long-acting formulations contain a very high dose of oxycodone that is intended to release evenly over 12 hours. Long-acting oxycodone offers the convenience of less-frequent dosing intervals and improved compliance, a potential win-win for prescribers and for patients with severe chronic pain.

However, the emergence of long-acting oxycodone has also corresponded with a dramatic increase in opioid drug abuse. Drug abuse is the use of opioid drugs for reasons other than what the drug was prescribed for, and often via unapproved routes of administration, such as injection, snorting or smoking. Opioids such as oxycodone are primarily abused due to their ability to produce a strong, if fleeting, euphoric high.

Drug abusers have learned effective ways to tamper with, and defeat, long-acting oxycodone formulations. Defeating the long-acting properties of an oxycodone formulation can be as easy as crushing or grinding tablets, then swallowing, injecting, snorting or smoking the crushed substance. This release high levels of oxycodone faster than intended (called "dose-dumping"), resulting in an immediate and powerful euphoric high, as compared to swallowing an intact tablet as prescribed.

Misuse of oxycodone is not always intentional. According to a medical publication, about two-thirds of surveyed patients with chronic pain did not think that cutting, crushing, or grinding their medication would change the way it worked (Pergolizzi et al., 2014).

In addition, the pain-relieving effects of OxyContin® (oxycodone HCI), a widely used abuse-deterrent extended-release formulation of oxycodone, often wears off early, according to a lengthy investigation published by the *Los Angeles Times* in 2016. The *Los Angeles Times* investigation reports that a single dose of twice-daily oxycodone often does not last for the intended 12 hours and performs more like "an 8-hour drug." This makes some patients take extra doses or stronger ones, raising the risk of abuse and addiction. An additional problem for physicians and patients alike can arise when insurance plans will not reimburse, and pharmacists will not dispense, more than two doses of OxyContin per day.

Opioid abuse is extremely dangerous. Opioid abuse can lead to drug-seeking behavior, tolerance and physical or psychological dependence. Even a single episode of opioid abuse can also lead to overdose, respiratory depression or death.

The Role of Abuse-deterrent Formulations

Policy makers have developed a multi-pronged approach aimed at combating opioid misuse, abuse and addiction. One targeted effort has been to encourage the pharmaceutical industry to develop ADFs. In April 2015, the FDA issued a final guidance to assist the pharmaceutical industry in developing ADF opioid drug products.

ADFs attempt to raise the bar on opioid abuse by making it more difficult, longer or aversive to tamper with a long-acting formulation, while recognizing that no drug or drug formulation can be made abuse-proof. In particular, an ADF drug can still be misused and result in overdose simply by ingesting the drug in higher than recommended doses. ADFs are not designed to prevent opioid-induced euphoria. ADF technology aims to decrease the likelihood that a long-acting opioid formulation will dose-dump under conditions of abuse or accidental misuse. By mitigating dose-dumping, the likelihood of overdose and death associated may decrease.

The intention of ADFs is to displace non-abuse-deterrent drug products. First-generation ADFs were introduced into the marketplace in 2010. However, we believe the relative weakness of first generation ADFs means opioid abuse continues to be a serious public health issue. In 2016, over 64,000 people died in the United States from opioid overdose, increasing from over 33,000 in 2015, according to the Centers for Disease Control Prevention. According to the FDA, "for each death [due to narcotic pain relievers], there are an additional ten treatment admissions, 32 emergency department visits and 825 nonmedical users of these drugs." (Source: *FDA's Efforts to Address the Misuse and Abuse of Opioids*, 2/6/2013).

As a pioneer in the design and development of ADFs, we believe a robust design for a novel ADF for twice-daily oxycodone revolves around four basic objectives: (i) safety and clinical efficacy over the entire 12-hours when used as prescribed; ii) abuse-deterrent when abused; (iii) ease of large scale manufacturing; and (iv) novel, non-infringing intellectual property. Many ADF programs may achieve three of these four objectives but the practical reality is that few ADFs achieve all four. We believe this is reflected in the industry's relatively high failure rate with regards to ADFs developments for long-acting opioid formulations.

Market Opportunity for REMOXY ER

REMOXY targets the market for opioid therapy. The global opioid market has been estimated by third-parties to be valued at nearly $35 billion in 2015. North America dominates the global market, with about 60-65% market share, or about $20 billion. We estimate extended-release opioid drugs are an approximately $4 billion market in the United States.

We believe REMOXY can capture a share of the approximately $4 billion market in the United States for extended-release opioid drugs, including a portion of the existing multi-billion OxyContin (Purdue Pharma L.P.) franchise. OxyContin remains the largest selling extended-release opioid in the United States by dollars. Despite OxyContin's commercial success, we believe the drug carries a stigma due to widespread, well-documented cases of abuse and overdose; the persistence of negative media reports around this drug; the magnitude of the opioid epidemic and the sheer number of deaths associated with this problem; and on-going legal actions against Purdue by government agencies and private parties.

In addition to targeting the oxycodone market, REMOXY targets the approximately 10-15 million additional prescriptions for non-abuse-deterrent extended-release opioids annually in the United States. Many of these opioids include active pharmaceutical ingredients, such as morphine, that may be perceived as having greater side effects than oxycodone-based formulations.

Opioid prescriptions in the United States peaked in 2010 and have decreased each year through 2017. The reasons for this erosion are complex, but center around the fact that opioid abuse remains a serious, pervasive and persistent problem for physicians and patients alike. In particular, prescriptions for non-abuse deterrent opioids are likely to continue to drop significantly in the years ahead.

In addition, government actions serve to materially limit the market for opioid therapy to only those patients who have an appropriate need for such drugs. For example, in response to an epidemic of opioid overdoses, in 2017 the Center for Disease Control (CDC) released important new clinical guidelines for physicians treating adult patients for chronic pain. The CDC guidelines provide specific recommendations to clinicians about the appropriate prescribing of opioids to improve pain management and patient safety, including: *"When opioids are started, the lowest possible effective dosage should be prescribed to reduce risks of opioid use disorder and overdose."* (Source: *CDC Guideline for Prescribing Opioids for Chronic Pain*). We believe these and other actions will continue to restrict the approvability, use, promotion and distribution of opioid drugs in the United States, and may serve to eliminate the market for non-abuse-deterrent opioids.

We own exclusive, worldwide rights to REMOXY. If approved and granted appropriate label claims, we believe REMOXY may have potential to distinguish itself from competitors with:

- ü best-in-class abuse-deterrent properties;
- ü true twice-daily dosing;
- ü lowest initial starting dose;
- ü minimal food effect;
- ü lack of generic drug substitution; and
- ü over 15 years of intellectual property protection.

We believe direct competitors to REMOXY will include the two ADFs of twice-daily oxycodone that are commercially available in the United States:

- OxyContin ER (oxycodone HCI) from Purdue Pharma L.P. - A reformulated version of the original OxyContin OC, this drug received FDA approval in April 2010. According to its package insert, "OxyContin is formulated with inactive ingredients intended to make the tablet more difficult to manipulate for misuse and abuse." Some patients have complained that the new formulation is not as effective or causes gastrointestinal problems, according to *Pain News Network* (2016).
- Xtampza® ER (oxycodone) from Collegium Pharmaceuticals, Inc. - *Xtampza ER* received FDA approved in April 2016 and is available in capsules containing microspheres formulated with oxycodone base and inactive ingredients that make the formulation more difficult to manipulate for the purpose of abuse. Each capsule contains 9, 13.5, 18, 27, or 36 mg of oxycodone (equivalent to 10, 15, 20, 30 or 40 mg of oxycodone HCl, respectively).

The FDA has approved two other extended-release, ADFs of oxycodone. However, neither of these two drugs were ever launched into the marketplace in the United States: a) in 2016, the FDA approved *Troxyca® ER* (Pfizer, Inc), a capsule combination of oxycodone HCL and naltrexone, an opioid antagonist; and b) in 2014, the FDA approved *Targiniq® ER* (Purdue Pharma LP), a tablet combination of oxycodone HCL and naloxone, an opioid antagonist.

REMOXY will compete against all extended-release opioids, including generic drug products. In November 2017, the FDA issued final guidance on the regulatory pathway for generic abuse-deterrent opioid products. Among other requirements, the new FDA guidance emphasizes that sponsors of generic abuse-deterrent oxycodone must ensure that a generic opioid drug is no less abuse deterrent than the original opioid and must also evaluate all potential routes of abuse, even those routes of abuse for which a generic sponsor does not seek a label-claim. We believe these new FDA requirements represents a high bar for generic drug developers in terms of added development time, expenses, technical expertise and regulatory risks.

Currently we have no capability to launch or to commercialize REMOXY. We continue to review potential launch and commercialization strategies for REMOXY. Options include a potential strategic transaction around all of our drug candidates; a commercial collaboration for REMOXY; or establishing commercial capabilities in-house to launch REMOXY on our own.

Chronology of REMOXY ER

We initiated the development of REMOXY over a decade ago, before any formal guidance was in place with regards to regulatory pathways for ADFs. As a result of our pioneering efforts with REMOXY, we have developed a foundation of practical and scientific experience with regard to regulatory and development pathways for ADFs.

The following is a top-line reverse chronology of the development of REMOXY:

- As a result of our pre-NDA meeting, we intend to resubmit the REMOXY NDA to the FDA in Q1 2018 with Priority (six-month) Review.
- In November 2017, we concluded a pre-NDA meeting with the FDA.
- In February 2017, we met with the FDA regarding REMOXY.
- In September 2016, we received a CRL from the FDA regarding the NDA for REMOXY.
- In March 2016, we resubmitted the NDA for REMOXY with the FDA.
- In 2015, we generated additional abuse-deterrent data, continued an on-going stability study and made other preparations necessary to resubmit the NDA for REMOXY with the FDA.
- In 2015, we and Pfizer concluded the transfer of the REMOXY program. We believe Pfizer has transferred to us its data, materials, capital equipment and other assets related to REMOXY.
- In 2014, Pfizer provided us with written notice of termination of its development of REMOXY. We and Pfizer agreed on an orderly transfer of all rights, data, IP, etc.
- From 2011-2014, Pfizer conducted fundamental investigations of the REMOXY formulation and its manufacture. As a result, Pfizer modified the REMOXY formulation and conducted successful studies to establish bioequivalence of the current formulation to the original formulation of REMOXY, to generate additional abuse-deterrent data and to provide manufacturing stability.
- In 2011, Pfizer received a CRL on the REMOXY NDA filed by King. Once again, FDA cited manufacturing issues (specifically, *in vitro* drug stability). Once again, the CRL did not question REMOXY's safety, clinical efficacy, abuse-deterrent properties or use of the reference listed drug.
- In 2010, King resubmitted the REMOXY NDA with the FDA. In early 2011, Pfizer acquired King. References to Pfizer include references to Pfizer's subsidiary King.
- In 2009, King assumed sole control and responsibility for REMOXY.
- In 2008, we filed an NDA for REMOXY with the FDA. Later that year, we received a CRL over manufacturing issues (specifically, *in vitro* drug stability). However, the CRL did not question REMOXY's safety, clinical efficacy, abuse-deterrent properties or use of the reference listed drug.
- In 2005, we and King Pharmaceuticals, Inc., or King, entered into an exclusive agreement to develop and commercialize REMOXY.
- In 2003, we filed an Investigational New Drug application, or IND, for REMOXY with the FDA.

FENROCK™ - *a drug candidate for severe pain*

FENROCK is a proprietary transdermal patch that contains the prescription drug fentanyl to manage pain and incorporates novel abuse-deterrent technology. This is an early-stage, pre-IND program that is substantially funded by a competitive research grant award from the NIH's NIDA.

Fentanyl is an opioid drug that is up to 100 times more potent than morphine. When used properly by patients under the care of a qualified physician, a fentanyl patch releases the drug slowly over 72 hours. This helps to manage pain that is severe enough to require daily around-the-clock, long-term treatment. However, fentanyl is also abused by non-patients for its euphoric effects. Abusers can chew on a fentanyl patch, or simply extract the fentanyl from a patch, then inject or ingest the contents. This practice is illicit and highly dangerous. It can quickly introduce into the body a massive amount of fentanyl, which can lead to addiction, overdose and death.

In November 2017, we announced a research and development grant from NIDA following a competitive, in-depth evaluation of FENROCK technology for scientific and technical merit. The grant of approximately $2.2 million provides us with funding to develop FENROCK.

We developed in-house the technology for FENROCK and own all development and commercial rights, without royalty or milestone obligations to any third-parties.

Fentanyl is a schedule II substance under the U.S. Controlled Substance Act.

PTI-125 - *a drug candidate to treat Alzheimer's Disease*

PTI-125 is a proprietary, experimental drug for the treatment of Alzheimer's disease (AD). AD is a progressive brain disorder that slowly destroys memory and thinking skills, and eventually the ability to carry out the simplest tasks. Damage to the brain starts a decade or more before problems appear. During this early stage of disease, people seem to be symptom-free, but toxic changes are taking place in the brain. Eventually, brain damage becomes widespread and affected people are often unable to care for themselves. Currently, AD cannot be detected until symptoms appear. Over five million Americans live with AD, a number that is expected to increase significantly in the coming years.

PTI-125 is a small molecule drug candidate that was designed by us and characterized by outside collaborators. PTI-125 has been shown to significantly improve AD neuropathologies in mouse models of the disease and in post-mortem brain tissue from AD patients, including receptor dysfunctions, neuroinflammation, tau hyperphosphorylation, insulin resistance and plaques and tangles that are hallmarks of AD.

PTI-125 works by binding to filamin A (FLNA), a protein critical to beta amyloid's toxicity. Beta amyloid exerts multiple toxic effects, eventually causing the plaques and tangles found in the brains of people with AD. By binding to FLNA, PTI-125 may prevents and even reverse amyloid-related AD damage.

To date, the underlying science for PTI-125 has been published in *Journal of Neuroscience*, *Neurobiology of Aging*, *Journal of Biological Chemistry*, *PLOS-One* and other peer-reviewed scientific journals.

In June 2017, we announced that the NIH's *National Institute on Aging* awarded us a $1.7 million research grant following a competitive, in-depth evaluation of PTI-125 for scientific and technical merit. This NIH research grant enabled us to begin testing PTI-125 in human subjects. Subsequently, an Investigational New Drug (IND) application for PTI-125 was submitted and accepted by the FDA.

In October 2017, we announced the successful completion of a Phase I clinical study for PTI-125. This study investigated for the first time the safety, dosing and pharmacokinetic profile of PTI-125 in healthy human volunteers.

In this first-in-human study, PTI-125 was evaluated in 24 healthy human volunteers in a single-site in the United States for safety, tolerability and pharmacokinetics. Study subjects were administered a single oral dose of 50, 100 or 200 mg of PTI-125. The drug was well-tolerated in all subjects. Importantly, PTI-125 showed no treatment-related adverse effects and no dose-limiting safety findings. Pharmacokinetic measurements showed PTI-125, a small molecule, was rapidly absorbed. Dose-proportionality outcomes were observed over the entire dose range of 50 to 200 mg. There were two key findings for this Phase I Study:

- PTI-125 was safe and well-tolerated at all doses studied; and
- PTI-125 demonstrated favorable pharmacokinetics for further drug development.

Given the absence of dose-limiting effects in healthy adults, an excellent non-clinical safety database, a strong scientific rationale, and multiple peer-reviewed publications and research grant awards, we believe there is significant merit to move this drug program to the next level of development.

We own exclusive, worldwide rights to PTI-125, with no royalty obligations to any third party.

PTI-125DX - *a blood-based diagnostic to detect Alzheimer's Disease*

We are developing innovative technology to diagnose AD with a simple blood test. We believe finding a way to diagnose AD at an early-stage is vitally important. A blood test may help detect AD before symptoms occur, or rule out other possible causes of memory problems, or might be used as a biomarker to measure the efficacy of drug candidates during clinical trials, or to define new potential therapies for AD.

Our diagnostic technology is related to PTI-125, our clinical-stage drug candidate for AD, whose underlying science has been published in *Journal of Neuroscience*, *Neurobiology of Aging*, *Journal of Biological Chemistry*, *PLOS-One* and other peer-reviewed scientific journals. PTI-125DX is not a genetic based assay, nor does it rely on neuroimaging markers. PTI-125DX highlights critical changes that occur in the brain by detecting biochemical markers that are found in blood during the course of the disease.

The PTI-125DX assay is relatively quick, easy, non-hazardous and inexpensive, and can be repeated as necessary without contraindications. If successful, we believe the data generated by PTI-125DX can be used by clinicians or algorithms to classify patients at different stages of AD and/or to distinguish AD from other related diseases with better specificity or reliability than current methodologies.

PTI-125DX is an early-stage program. We have generated data from hundreds of blood samples using PTI-125DX. Results have not been published to date in order to better protect the intellectual property around this technology.

In September 2017, we announced a $1.8 million research grant from the NIH for PTI-125DX. The NIH's *National Institute on Aging* awarded us this research grant following a confidential, competitive and in-depth evaluation of PTI-125DX technology for scientific and technical merit. The research grant is a technical-milestone based award that will enable us to work collaboratively with leaders in the field to develop and test on clinical samples a blood-based diagnostic for AD.

PTI-125DX was designed by us and characterized by outside collaborators. We own worldwide commercial rights to PTI-125DX and related technology, without royalty or milestone obligations to any third parties.

Strategy

Our corporate strategy has changed little over the years: to spend carefully but to keep innovation at the top of our agenda. Elements of our corporate strategy include:

Focus on Clinical Development Stage Products. We believe this focus will enable us to generate product revenues earlier than if we were focused on early-stage research and discovery activities.

Retain Significant Rights to Our Drugs. We currently retain worldwide commercialization rights to all of our technology and drug candidates in all markets and indications, including REMOXY. In general, we intend to independently develop our drug candidates through late-stage clinical trials.

Outsource Key Functions. We intend to continue to outsource preclinical studies, clinical trials and formulation and manufacturing activities. We believe outsourcing permits significant time savings and allows for more efficient deployment of our resources.

We also conduct basic research and development in collaboration with academic and other partners. Our research and development expenses were $7.6 million and $9.2 million for the year ended December 31, 2017 and 2016, respectively. See "*Item 7 Management's Discussion and Analysis of Financial Condition and Results of Operations*" for additional details regarding our research and development activities.

Our Intellectual Property

The protection of patents, designs, trademarks and other proprietary rights that we own or license is critical to our success and competitive position. We own or license a number of U.S. and foreign patents, patent applications and rights to patents covering our products and technology. We consider the overall protection of our patents and other intellectual property rights to be of material value and act to protect these rights from infringement.

We seek to protect our technology by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. The focus of our patent strategy is to secure and maintain intellectual property rights to technology for the following categories of our business:

- the technology that forms the basis of REMOXY and FENROCK, our other abuse-deterrent drug candidates;
- the technologies related to PTI-125 and PTI-125DX product candidates; and
- the manufacture and use of our product candidates.

However, we may rely on certain proprietary technologies and know-how that are not patentable. We protect our proprietary information, in part, by the use of confidentiality agreements with our employees, consultants, and certain of our contractors.

We plan to prosecute and defend our patent applications, allowed patents, issued patents and proprietary information. Our competitive position and potential future revenues will depend in large part upon our ability to protect our intellectual property from challenges and to enforce our patent rights against potential infringements.

Patents expire, on a country by country basis, at various times depending on various factors, including the filing date of corresponding patent applications. Our patents and the patents we license from third parties include the following issued U.S. Patents: 8,168,217; 8,153,152; 8,147,870; 8,133,507; 8,354,124; 8,415,401; 8,420,120; 8,974,821; 8,945,614; 8,951,556; 9,233,160; 9,517,271; 9,555,113; 9,592,204; 9,855,333; and 9,572,885.

Our issued U.S. patent for REMOXY with the longest patent term extends to March 2034. Outside the United States, our granted patent with the longest patent term for REMOXY extends to 2028. Patents may have their term extended for various reasons including the grant of patent term adjustments, patent term extensions, or supplemental protection certificates, or may have their term shortened for various reasons including by terminal disclaimers. Certain United States patent applications and patent applications outside the United states are pending.

In addition, we use a unique and complex process to manufacture REMOXY. We also protect as trade secrets the significant pharmaceutical know-how and detailed knowledge of a complex supply chain to manufacture REMOXY.

REMOXY, REMOXY ER and FENROCK are trademarks of Pain Therapeutics, Inc.

Formulation Agreement with Durect Corporation

We have an exclusive, worldwide Development and License Agreement, or the Durect Agreement, with Durect to use a patented controlled-release technology that forms the basis for REMOXY.

Under the terms of the Durect Agreement, we are solely responsible for clinical development, Durect is responsible for furnishing suitable laboratory facilities, equipment and personnel during pre-clinical phases of development and we and Durect are jointly responsible for certain pre-clinical activities. We reimburse Durect's expenses and have made milestone payments based on the achievement of certain clinical or regulatory milestones. We paid Durect approximately $40.4 million from the inception of the Durect Agreement to December 31, 2017. We could pay another $1.5 million milestone payment to Durect under the Durect Agreement.

We are obligated to pay Durect royalties on commercial sales of REMOXY. These royalties range from 6.0% to 11.5% of net sales, depending on the volume of sales of REMOXY in a given calendar year. There are no minimum payments, and the royalty rate resets back to 6.0% at the beginning of each calendar year.

The Durect Agreement terminates on a country-by-country basis upon the later of the expiration of the last to expire of the patents licensed under such agreement or a certain number of years following first commercial sale in such country. Currently, the last to expire patent covered by such agreement expires in 2034. However, such date may be extended by the issuance of any additional patents pursuant to pending patent applications. We can terminate the Durect Agreement with notice to Durect, and we and Durect can terminate such agreement under certain circumstances, including material breach and insolvency.

Prior Agreements with Pfizer

Between 2005 and 2014, Pfizer paid us a total of $290 million, including $155 million in upfront fees, $30 million in milestone payments and $105 million to reimburse expenses we incurred under the agreements we had with Pfizer. Pfizer has no further obligations to us. We have no further obligations to Pfizer, except that we will owe Pfizer a one-time payment of $200,000, payable at the time REMOXY is approved by the FDA, related to certain commercial manufacturing equipment we purchased from Pfizer.

Manufacturing

We do not own or lease any manufacturing facilities. We outsource formulation, manufacturing and related activities to third parties.

Our suppliers must comply with current good manufacturing practices, or GMP, enforced by the FDA and other government agencies such as the U.S. Drug Enforcement Administration, or DEA. Our suppliers are subject to unannounced inspection by regulators, including pre-approval inspections by the FDA and the DEA, to ensure they are in strict compliance with government regulations and standards. Our suppliers may be forced to stop producing, storing, shipping or testing our drug products if they fall out of compliance with government regulations and standards.

We have no control over our suppliers' compliance, or lack thereof, with the multitude of regulations and standards that affect our drug products. We cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers will be expensive and time consuming. Further, if REMOXY is approved, our commercial suppliers may encounter difficulties in achieving high volumes of production to satisfy commercial demands. Failure by any of our suppliers to perform as expected could delay or prevent commercialization of REMOXY or result in shortages, cost overruns, or other problems and would materially harm our business.

Commercial supply of certain excipients from Durect

We will rely on Durect as the sole source of certain excipients in REMOXY. Durect has limited experience manufacturing pharmaceutical products and maintaining GMP-compliant operations. A Pre-Approval Inspection, or PAI, by the FDA officials is often integral to the FDA approval process. A PAI is an unannounced evaluation of a manufacturing or test site for readiness for commercial scale manufacturing, conformance with commitments made in an NDA and data integrity. To our knowledge, the FDA has never conducted a PAI of any Durect facility. We do not and cannot know whether Durect's manufacturing or test facilities could pass a PAI inspection related to REMOXY, or whether Durect has invested in the necessary systems to pass a PAI inspection.

We rely on Durect to supply to us certain excipients for the REMOXY formulation. Under the Durect Agreement, these excipients are supplied to us at Durect's cost, plus thirty (30) percent. We currently do not have a long-term commercial supply agreement in place with Durect. We expect that we and Durect will negotiate a supply agreement for these excipients. We may not be able to establish a commercial supply agreement on acceptable terms. Until a commercial supply agreement is in place with Durect, we expect to obtain excipients from Durect via individual purchase orders.

If we receive marketing approval for REMOXY, Durect may need to materially expand its manufacturing capacity. Durect may not be able to increase its manufacturing capacity for REMOXY in a timely or economic manner, or at all. Moreover,

significant scale up of manufacturing will require additional validation studies, which are subject to the FDA review and approval.

C*ommercial supply of oxycodone with Noramco*

We expect to rely on Noramco as the sole source of the oxycodone base used in REMOXY. We currently do not have a long-term commercial supply agreement in place with Noramco. We expect to negotiate with Noramco a commercial supply agreement to supply us with oxycodone base. We may not be able to establish a commercial supply agreement on acceptable terms, or at all. Until we have a commercial supply agreement in place with Noramco, we expect to obtain oxycodone base from Noramco via individual purchase orders.

C*ommercial drug supply agreement with Mallinckrodt*

Our sole supplier for commercial supplies of REMOXY is Mallinkcrodt Pharmaceuticals, or Mallinckrodt. In October 2007, we and Mallinckrodt entered into a long-term supply agreement, or the Mallinckrodt Agreement when Pfizer was responsible for commercialization of REMOXY. Pfizer assigned the Mallinckrodt Agreement to us upon the termination of the Pfizer Agreements. In March 2010, we and Mallinckrodt entered into an amended and restated long-term supply agreement. In a letter dated February 21, 2017, Mallinckrodt alleged a breach of contract because REMOXY had not yet been approved by the FDA. However, since then we and Mallinkcrodt have continued to work towards the approvability of REMOXY and commercial readiness. We continue to rely on our agreement with Mallinkcrodt to move forward with the REMOXY program.

We expect to continue to rely on Mallinckrodt as the sole-source drug product manufacturer of REMOXY pursuant to the Mallinckrodt Agreement. In addition to drug product manufacturing, Mallinckrodt is responsible for sourcing excipients in REMOXY other than those provided by the Durect Agreement.

Commercial manufacturing and supply agreements

We will rely on third parties to conduct certain quality control and assurance testing, shipping or storage of REMOXY.

Government Regulation

Regulation by governmental authorities in the United States and other countries is a significant factor in the manufacture and marketing of pharmaceuticals and in our ongoing research and development activities. All of our products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical testing and clinical trials and other pre-marketing approval requirements by the FDA and regulatory authorities in other countries. In the United States, various federal, and in some cases state, statutes and regulations also govern or impact the manufacturing, safety, labeling, storage, record keeping and marketing of our products. The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require us to spend substantial resources. Regulatory approval, when and if obtained, may be limited in scope which may significantly limit the indicated uses for which our products may be marketed. Further, approved drugs, as well as their manufacturers, are subject to ongoing review and discovery of previously unknown problems with such products that may result in restrictions on their manufacture, sale or use or in their withdrawal from the market.

Applicable FDA regulations require the filing of an NDA or a Biologic License Application, or BLA and approval by the FDA prior to commercialization of any of our drug candidates in the United States.

The Drug Approval Process

We will be required to complete several activities before we can market any of our drug candidates for human use in the United States, including:

- preclinical studies;
- submission to the FDA of an IND which must become effective before human clinical trials commence;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate;
- submission to the FDA of an NDA; and
- FDA approval of the NDA prior to any commercial sale or shipment of the drug.

Preclinical tests include laboratory evaluation of product chemistry and formulation, as well as animal studies to assess the potential safety of the product. Preclinical safety tests must be conducted by laboratories that comply with the FDA regulations regarding Good Laboratory Practice. We submitted the results of preclinical tests to the FDA as part of our INDs prior to commencing clinical trials. We may be required to conduct additional toxicology studies.

Based on preclinical testing, an IND is filed with the FDA to begin human testing of the drug in the United States. The IND becomes effective if not rejected by the FDA within 30 days. The IND must indicate the results of previous experiments, how, where and by whom the new clinical trials will be conducted, the chemical structure of the compound, the method by which it is believed to work in the human body, any toxic effects of the compound found in the animal studies and how the compound is manufactured. All clinical trials must be conducted in accordance with Good Clinical Practice. In addition, an Institutional Review Board, or IRB, generally comprised of physicians at the hospital or clinic where the proposed clinical trials will be conducted, must review and approve the IND. The IRB also continues to monitor the clinical trial. We must submit progress reports detailing the results of the clinical trials to the FDA at least annually. In addition, the FDA may, at any time during the 30-day period or at any time thereafter, impose a clinical hold on proposed or ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials under the IND cannot commence or recommence without the FDA authorization and then only under terms authorized by the FDA. An FDA imposed clinical hold on an IND application can result in substantial delay and large, unforeseen expenses, and it may cancel the viability of developing a new drug candidate in the United States.

Clinical trials are typically conducted in three sequential phases that may overlap. Phase I clinical trials typically study a drug's safety profile and may include the safe dosage range. Phase I clinical trials also determine how a drug is absorbed, distributed, metabolized and excreted by the body, and the duration of its action. In addition, we may, to the extent feasible, assess early indicators of a drug's efficacy in our Phase I clinical trials. In Phase II clinical trials, controlled studies are conducted on volunteer patients with the targeted disease or condition. The primary purpose of these tests is to evaluate the effectiveness of the drug on the volunteer patients as well as to determine a drug's side effect profile. These clinical trials may be conducted concurrently with Phase I clinical trials. In addition, Phase I/II clinical trials may be conducted to evaluate not only the efficacy of the drug on the patient population, but also its safety. During Phase III clinical trials, the drug is studied in an expanded patient population and in multiple sites. Physicians monitor the patients to determine efficacy and to observe and report adverse events that may result from use of the drug.

Our clinical trials are designed to produce clinical information about how our drugs perform compared to placebo or compared to existing drugs where appropriate. We have designed most Phase II and Phase III clinical trials to date as randomized, double-blind, placebo-controlled, dose-ranging studies. A randomized clinical trial is one in which patients are randomly assigned to the various study treatment arms. A double-blind clinical trial is one in which the patient, the physician and our trial monitor are unaware if the patient is receiving placebo or study drug in order to preserve the integrity of the clinical trial and reduce bias. A placebo-controlled clinical trial is one in which a subset of patients is purposefully given inactive medication.

We may not successfully complete Phase I, Phase II or Phase III clinical trials within any specified time period, or at all, with respect to any of our drug candidates. Furthermore, we or the FDA may suspend clinical trials at any time in response to concerns that participants are exposed to an unacceptable health risk.

After the completion of clinical trials, if there is substantial evidence that the drug is safe and effective, an NDA is filed with the FDA. The NDA must contain all of the information on the drug gathered to that date, including data from the clinical trials. NDAs often exceed 100,000 pages in length.

The FDA may request additional information before accepting an NDA. In such an event, the NDA must be resubmitted with the additional information and, again, is subject to review before filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Federal Food, Drug and Cosmetic Act, the FDA reviews the NDA and responds to the applicant. The review process is typically extended for significant amounts of time by the FDA's requests for additional information or clarification regarding information already provided in the submission.

It is FDA policy to convene an expert Advisory Committee meeting during the review cycle for opioid drug products. The purpose of an Advisory Committee is to provide third-party input on key regulatory decisions, including approval and labeling of abuse-deterrent products, and whether the totality of the data submitted by a sponsor is sufficient to support marketing approval in the United States and labeling of the product with claims on abuse-deterrence. Advisory Committee meetings are non-binding, that is, the FDA is not legally bound to follow any recommendation, vote or input of an Advisory Committee on any matter.

If the FDA's evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue either a CRL indicating either an approval or may identify conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. If the FDA's evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter.

If the FDA approves the NDA, the drug becomes available for physicians to prescribe. Periodic reports must be submitted to the FDA, including descriptions of any reported adverse reactions. The FDA may request additional post-marketing studies, or Phase IV clinical trials, to evaluate long-term effects of the approved drug.

Risk Evaluation and Mitigation Strategy (REMS)

The FDA requires a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of the approval of an NDA or after approval to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the FDA considers the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary for a new drug, the drug sponsor must submit a proposed REMS plan as part of its NDA prior to approval. A REMS for a newly approved drug can include medication guides, communication plans for healthcare professionals, and Elements To Assure Safe Use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. In addition, the REMS must include a timetable to periodically assess the strategy, at a minimum, at 18 months, three years, and seven years after the REMS approval. The requirement for a REMS can materially affect the potential market and profitability of a drug.

The FDA has initiated efforts to develop a standardized REMS for opioid medications to ensure their safe use. In July 2012, the FDA approved a class-wide REMS for extended-release formulations of oxycodone. Manufacturers subject to this class-wide REMS must work together to implement the REMS as part of a single shared system to reduce the burden of the REMS on the healthcare system. The central component of the extended release/long acting opioid REMS program is an education program for prescribers and patients. REMS include a Medication Guide available for distribution to patients who are dispensed the drug, as well as ETASU. ETASU include training for healthcare professionals who prescribe the drug; information provided to prescribers that they can use to educate patients in the safe use, storage, and disposal of opioids; and information provided to prescribers of the existence of the REMS and the need to successfully complete the necessary training. Prescriber training required as part of the REMS is conducted by accredited, independent continuing education providers, without cost to healthcare professionals, under unrestricted grants funded by opioid analgesic manufacturers. Moreover, REMS assessments must be submitted on an annual basis to assess the extent to which ETASU are meeting the goals of the REMS and whether the goals or elements should be modified.

Advertising and Promotion

The FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. Our lead drug candidate, REMOXY, cannot be commercially promoted before receiving FDA approval. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses — that is, uses not approved by the FDA and therefore not described in the drug's labeling — because the FDA does not regulate the practice of medicine. However, FDA

regulations impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements and restrictions in this area may subject us to adverse publicity and enforcement action by the FDA, the U.S. Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject us to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which we promote or distribute REMOXY.

Post-Approval Requirements

Once an NDA is approved, REMOXY will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug listing and registration, recordkeeping, periodic reporting, product sampling and distribution, adverse event reporting and advertising, marketing and promotion restrictions.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-market testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to Current Good Manufacturing Practices (cGMPs) after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration subjects entities to periodic announced or unannounced inspections by the FDA or these state agencies, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered. In addition, other regulatory actions may be taken, including, among other things, warning letters, the seizure of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, refusal to approve pending applications or supplements to approved applications, civil penalties, and criminal prosecution.

The FDA may require post-approval studies and clinical trials if the FDA finds that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for REMOXY through an NDA, we will be required to list with the FDA each patent whose claims cover the drug product. Upon approval of REMOXY, each of the patents listed in the application for this drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the "Orange Book". Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated NDA, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredient in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or efficacy of their drug product. However, in November 2017, the FDA issued final guidance on the regulatory pathway for generic abuse-deterrent opioid products. Among other requirements, the new FDA guidance emphasizes that sponsors of generic abuse-deterrent oxycodone must ensure that a generic opioid drug is no less abuse deterrent than the original opioid and must also evaluate all potential routes of abuse, even those routes of abuse for which a generic sponsor does not seek a label-claim. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to make certain certifications to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not

been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than make certifications concerning a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant. The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA seeking approval of a generic version of that drug or any Section 505(b)(2) NDA that relies on the FDA's findings regarding that drug. A drug may obtain a three-year period of exclusivity for a change to the drug, such as the addition of a new indication to the labeling or a new formulation, during which the FDA cannot approve an ANDA or any Section 505(b)(2) NDA, if the supplement includes reports of new clinical trials (other than bioavailability clinical trials) essential to the approval of the supplement.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Section 505(b)(2) NDAs

Generally, drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on data not developed by the applicant, such as the FDA's findings of safety and efficacy in the approval of a similar product or published literature in support of its application.

Section 505(b)(2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from clinical trials not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and efficacy is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical trials of the new product. The FDA may also require companies to perform additional clinical trials or provide additional materials to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on the FDA's findings of safety and effectiveness for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Therefore, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired; until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired; and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant. In the interim period, the FDA may grant tentative approval. Tentative approval indicates that the FDA has determined that the applicant meets the standards for approval as of the date that the tentative approval is granted. Final regulatory approval can

only be granted if the FDA is assured that there is no new information that would affect final regulatory approval. As with traditional NDAs, a Section 505(b)(2) NDA may be eligible for three-year marketing exclusivity, assuming the NDA includes reports of new clinical trials (other than bioavailability clinical trials) essential to the approval of the NDA.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, clinical trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to post certain information regarding the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

DEA Regulatory Requirements

Our lead drug candidate, REMOXY, is regulated as a controlled substance under the Controlled Substances Act, or CSA. CSA establishes registration, security, recordkeeping, reporting, storage, distribution, importation, exportation and other requirements administered by the DEA. The DEA regulates the handling of controlled substances through a closed chain of distribution. This control extends to the equipment and raw materials used in their manufacture and packaging of REMOXY, in order to prevent loss and diversion into illicit channels of commerce.

REMOXY, an abuse-deterrent oral formulation of oxycodone, is listed by the DEA as a Schedule II controlled substance under the CSA. Consequently, the manufacturing, shipping, storing, selling and use of the products is subject to a high degree of regulation. Schedule II drugs are subject to the strictest requirements for registration, security, recordkeeping and reporting. Also, distribution and dispensing of these drugs are highly regulated. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

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.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special permits and notification requirements apply to imports and exports of narcotic drugs.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. Because REMOXY is regulated as a Schedule II controlled substance, it will be subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for how much oxycodone may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. The limited aggregate amount of opioids that the DEA allows to be produced in the United States each year is allocated among individual companies, who must submit applications annually to the DEA for individual production and procurement quotas. We and our contract manufacturers must receive an annual quota from the DEA in order to produce or procure any Schedule I or Schedule II substance, including oxycodone base for use in manufacturing REMOXY. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments.

To enforce these requirements, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in administrative, civil or criminal enforcement action that could have a material adverse effect on our business, results of operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate administrative proceedings to revoke those registrations. In certain circumstances, violations could result in criminal proceedings. In addition, individual states also independently regulate controlled substances. We and our contract manufacturers will be subject to state regulation on distribution of these products.

Other Regulatory Requirements

We may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, national restrictions on technology transfer, and import, export, and customs regulations. It is possible that any portion of the regulatory framework under which we operate may change and that such change could have a negative impact on our current and anticipated operations. Failure to comply with these requirements could result, among other things, in suspension of regulatory approval, recalls, injunctions or civil or criminal sanctions.

Third-Party Payor Coverage and Reimbursement

The commercial success of REMOXY, if approved, will depend, in part, upon the availability of coverage and adequate reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for REMOXY in whole or in part if they determine that our drug product is not medically appropriate or necessary. Also, third party payors attempt to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for REMOXY to operate profitably.

Competition

Our success will depend, in part, upon our ability to achieve market share at the expense of existing and established and future products in our target markets. Existing and future products, therapies, technological approaches or delivery systems will compete directly with REMOXY. Competing products may provide greater therapeutic benefits for a specific indication, or may offer comparable performance at a lower cost. Companies that currently sell generic or proprietary opioid formulations in the United States may include, but are not limited to, Purdue Pharma, Collegium, Inc., Roxane Laboratories, Mylan, Abbott Laboratories, Endo Pharmaceuticals, Teva Pharmaceuticals, Elkins-Sinn, Watson Laboratories, Hikma Pharmaceuticals, Pernix, Mallinckrodt, Eaglet Pharmaceuticals, Ortho-McNeil Pharmaceutical and Forest Pharmaceuticals, as well as several generic companies.

Alternative technologies are being developed to address the issue of abuse or misuse of opioid painkillers or increase opioid potency, as well as alternatives to opioid therapy for pain management, several of which are in clinical trials or are awaiting approval from the FDA.

We compete with fully integrated pharmaceutical companies, smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have opioid drugs already approved by the FDA or in development and operate larger research and development programs in these fields than we do. In addition, many of these competitors, either alone or together with their collaborative partners, have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing, distributing and selling drugs.

Developments by competitors may render our drug candidates or technologies obsolete or non-competitive. We also compete with these companies for qualified personnel and opportunities for product acquisitions, joint ventures or other strategic alliances.

Incorporation

We were incorporated in Delaware in May 1998.

Employees

As of December 31, 2017, we had 9 employees. We engage consultants from time to time to perform services on retainer, a per diem or hourly basis.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website at http://www.paintrials.com, by contacting our corporate offices by calling 512-501-2444 or by sending an e-mail message to IR@paintrials.com.

Item 1A. ***Risk Factors***

Investing in our common stock involves a high degree of risk.

You should carefully consider the risks described below, as well as all other information, including our financial statements, the notes thereto and the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations." If any of the following risks occur, our business, financial condition, operating results, prospects and ability to accomplish our strategic objectives could be materially harmed. As a result, the trading price of our common stock could quickly decline by a material amount, and you could lose all or part of your investment.

Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations and the market price of our common stock.

Clinical and Regulatory Risks

Our success depends in large part on receiving FDA approval for our lead product, REMOXY.

To date, we have invested substantial resources in the development of our lead product, REMOXY. Despite these investments, the REMOXY NDA received CRL from the FDA in 2008, 2011 and 2016 indicating our drug was not yet ready for approval. Collectively, these CRLs have resulted in long delays to product revenue; sudden, severe and prolonged drops in our stock price; loss of our initial competitive advantages in the market for abuse-deterrent opioid drugs; and dwindling cash balances. Accordingly, we cannot assure you that we will be able to receive FDA approval for REMOXY, or successfully commercialize this drug candidate. If we cannot do so, or are significantly delayed in doing so, our business will be materially harmed, and we may not be able to survive as a business.

The FDA may not approve product labeling for REMOXY that would permit us to market and promote this drug in the United States by describing their abuse-deterrent features.

There can be no assurance that REMOXY will receive final FDA-approved product labeling that adequately describes its abuse deterrent features. We have invested substantial time and money conducting abuse deterrence studies to ensure that REMOXY complies with the FDA's guidance regarding opioid abuse deterrence. If the FDA does not approve product labeling containing abuse deterrence claims for REMOXY, we will not be able to promote REMOXY based on its abuse deterrent features and may not be able to differentiate our drug from other opioid products containing the same active pharmaceutical ingredients. This would make REMOXY less competitive, or even un-competitive, in the market. Furthermore, the FDA's April 2015 final guidance on abuse deterrent opioids expects sponsors to compare their formulations against approved abuse deterrent versions of the same opioid based on the relevant categories of testing. If the FDA decides that REMOXY is less resistant to manipulation than an approved product, our lead drug candidate may not be approved or may lack product labeling containing abuse deterrence claims

Even if REMOXY is approved for marketing with certain abuse-deterrence claims, the April 2015 final FDA guidance on abuse-deterrent opioids is not binding law and may be superseded or modified at any time. Also, if the FDA determines that our post-marketing data do not demonstrate that REMOXY's abuse-deterrent properties do in fact result in reduction of abuse, or demonstrate a shift to routes of abuse that present a greater risk, the FDA may find that product labeling revisions are needed, and potentially may require the removal of any abuse-deterrence claims.

If we fail to obtain the necessary regulatory approvals, or if such approvals are limited, we and our collaborators will not be allowed to commercialize our drug candidates, and we will not generate product revenues.

Satisfaction of all regulatory requirements for commercialization of a drug candidate typically takes many years, is dependent upon the type, complexity and novelty of the drug candidate, and requires the expenditure of substantial resources for research and development. In December 2008, we received from the FDA a CRL for the REMOXY NDA. In this CRL, the FDA indicated that additional non-clinical data was required to support the approval of REMOXY. However, the FDA did not request or recommend additional clinical efficacy studies prior to approval. In March 2009, King Pharmaceuticals, Inc., or King, assumed sole responsibility for the regulatory approval of REMOXY. In December 2010, King resubmitted the NDA for REMOXY. In June 2011, we and Pfizer announced that King received a CRL from the FDA in response to King's

resubmission of the REMOXY NDA. The FDA's CRL raised concerns related to, among other matters, the Chemistry, Manufacturing, and Controls section of the NDA for REMOXY. Certain drug lots showed inconsistent release performance during *in vitro* testing. Pfizer completed work designed to address the June 2011 CRL. On April 21, 2015, we announced that we resumed responsibility for REMOXY under the terms of a letter agreement with Pfizer. The letter agreement was entered into within the scope of the previously disclosed provisions of the Collaboration Agreement between us and Pfizer relating to the return of REMOXY.

We believe Pfizer has now transferred to us its data, materials, capital equipment and other assets related to REMOXY. Pfizer and the FDA had discussed and agreed to a regulatory plan to refile the NDA for REMOXY. The FDA had agreed that we may follow this plan for the NDA for REMOXY.

In March 2016, we resubmitted to the FDA the NDA for REMOXY. In April 2016, the FDA determined that the NDA for REMOXY was sufficiently complete to permit a substantive review. On May 19, 2016, we announced that the FDA planned to hold an Advisory Committee meeting to review the NDA for REMOXY. On July 1, 2016, we announced that the FDA had determined that an Advisory Committee meeting for REMOXY was unnecessary and would not be held.

In September 2016, we received a CRL from the FDA on the resubmission of NDA for REMOXY. The CRL informed us that the NDA for REMOXY could not be approved in its present form and specifies additional actions and data that are needed for drug approval. The CRL focuses on the abuse-deterrent properties of REMOXY and proposed drug labeling.

On February 13, 2017, we met with the FDA regarding REMOXY. During this meeting, we reached agreement with the FDA on a roadmap to resubmit the NDA for REMOXY. Final minutes of our FDA meeting confirmed two key requirements needed for the resubmission of the REMOXY NDA: a) to conduct a clinical abuse potential study via the intranasal route of abuse; and b) to conduct a non-clinical abuse potential study using household solvents.

During 2017, we conducted these mandated studies with REMOXY. In November 2017, we concluded a regulatory meeting with the FDA. The purpose of this pre-New Drug Application (NDA) meeting was to agree on submission requirements for the REMOXY NDA under 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. We received comments and clarification from the FDA on the acceptability of the data to be included in the REMOXY NDA resubmission, including a recent intranasal study. All questions were addressed and summarized in official minutes of the meeting issued by the FDA. There are no discrepancies or requests for clarifications following receipt of final meeting minutes. As a result, we intend to resubmit the REMOXY NDA in Q1 2018 with Priority (six-month) Review.

There can be no assurance that the FDA will approve an NDA for REMOXY or that the FDA will not require submission of additional clinical or non-clinical data. Obtaining data from such studies (even if completed) that is insufficient to support approval of REMOXY, or any adverse decisions by the FDA (including any decision by the FDA to require additional clinical or non-clinical data) may significantly delay or prevent the potential approval of REMOXY.

Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for indicated uses we are studying. The FDA may require additional studies, in which case we or our collaborators would have to expend additional time and resources and would likely delay the date of potentially receiving regulatory approval. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals would:

- delay commercialization of, and product revenues from, our drug candidates; and
- diminish the competitive advantages that we may have otherwise enjoyed, which would have an adverse effect on our operating results and financial condition.

Even if we or our collaborators comply with all FDA regulatory requirements, our drug candidates may never obtain regulatory approval. If we or our collaborators fail to obtain regulatory approval for any of our drug candidates we will have fewer commercial products, if any, and corresponding lower product revenues, if any. Even if our drug candidates receive regulatory approval, such approval may involve limitations on the indications and conditions of use or marketing claims for our products. Further, later discovery of previously unknown problems or adverse events could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us or our collaborators to commit to perform lengthy Phase IV post-approval clinical efficacy or safety studies. Our expending additional resources on such trials would have an adverse effect on our operating results and financial condition.

In jurisdictions outside the United States, we must receive marketing authorizations from the appropriate regulatory authorities before commercializing our drugs. Regulatory approval processes outside the United States generally include all of the aforementioned requirements and risks associated with FDA approval.

If we are unable to design, conduct and complete preclinical and clinical trials successfully, our drug candidates will not be able to receive regulatory approval.

In order to obtain FDA approval for any of our drug candidates, we must submit to the FDA an NDA that demonstrates with substantive evidence that the drug candidate is both safe and effective in humans for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials.

Preclinical studies may not provide results we believe are sufficient to support the filing of an IND. Success in early preclinical studies does not ensure success in later preclinical or clinical studies. The FDA may disagree with the design of our preclinical studies or our interpretations of data from preclinical studies. The FDA may not accept an IND for our product candidate and may require additional preclinical studies to support the filing of an IND.

Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. Results from Phase I clinical programs may not support moving a drug candidate to Phase II or Phase III clinical trials. Phase III clinical trials may not demonstrate the safety or efficacy of our drug candidates. Results of later clinical trials may not replicate the results of prior clinical trials and preclinical studies. Even if the results of Phase III clinical trials are positive, we or our collaborators may have to commit substantial time and additional resources to conducting further preclinical studies and clinical trials before obtaining FDA approval for any of our drug candidates.

Clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous requirements. The clinical trial process also consumes a significant amount of time. Furthermore, if patients in clinical trials suffer drug-related adverse reactions during the course of such clinical trials, or if we, our collaborators or the FDA believe that participating patients are being exposed to unacceptable health risks, such clinical trials will have to be suspended or terminated. Failure can occur at any stage of the clinical trials, and we or our collaborators could encounter problems that cause abandonment or repetition of clinical trials.

Clinical trials with REMOXY and our potential future clinical trials for other drug candidates for treatment of pain measure clinical symptoms, such as pain and physical dependence, that are not biologically measurable. The success in these clinical trials depends on reaching statistically significant changes in patients' symptoms based on clinician-rated scales. Due in part to a lack of consensus on standardized processes for assessing clinical outcomes, these scores may or may not be reliable, useful or acceptable to regulatory agencies.

In addition, completion of clinical trials can be delayed by numerous factors, including:

- delays in identifying and agreeing on acceptable terms with prospective clinical trial sites;
- slower than expected rates of patient recruitment and enrollment;
- unanticipated patient dropout rates;
- increases in time required to complete monitoring of patients during or after participation in a clinical trial; and
- unexpected need for additional patient-related data.

Any of these delays could significantly impact the timing, approval and commercialization of our drug candidates and could significantly increase our overall costs of drug development.

Even if clinical trials are completed as planned, their results may not support expectations or intended marketing claims. The clinical trials process may fail to demonstrate that our drug candidates are safe and effective for indicated uses. Such failure would cause us to abandon a drug candidate and could delay development of other drug candidates.

Clinical trial designs that were discussed with regulatory authorities prior to their commencement may subsequently be considered insufficient for approval at the time of application for regulatory approval.

We discuss with and obtain guidance from regulatory authorities on certain of our clinical development activities. With the exception of our Special Protocol Assessment (SPA), these discussions are not binding obligations on the part of regulatory authorities.

Regulatory authorities may revise previous guidance or decide to ignore previous guidance at any time during the course of our clinical activities or after the completion of our clinical trials. Even with successful clinical safety and efficacy data, including such data from a clinical trial conducted pursuant to a SPA, we or our collaborators may be required to conduct additional, expensive clinical trials to obtain regulatory approval.

Developments by competitors may establish standards of care that affect our ability to conduct our clinical trials as planned.

We have conducted clinical trials of our drug candidates comparing our drug candidates to both placebo and other approved drugs. Changes in standards related to clinical trial design could affect our ability to design and conduct clinical trials as planned. For example, regulatory authorities may not allow us to compare our drug candidates to placebo in a particular clinical indication where approved products are available. In that case, both the cost and the amount of time required to conduct a clinical trial could increase.

The U.S. Drug Enforcement Agency, or DEA, limits the availability of the active ingredients in certain of our current drug candidates and, as a result, quotas for these ingredients may not be sufficient to complete clinical trials, or to meet commercial demand, or may result in clinical delays.

The DEA regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Certain active ingredients in our current drug candidates, such as oxycodone, are listed by the DEA as Schedule II under the Controlled Substances Act of 1970. Consequently, their manufacture, research, shipment, storage, sale and use are subject to a high degree of oversight and regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances that can be obtained for clinical trials and commercial distribution is limited by the DEA and quotas for these substances may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that DEA regulations may interfere with the supply of the drugs used in clinical trials for our product candidates, and, in the future, the ability to produce and distribute our products in the volume needed to meet commercial demand.

Conducting clinical trials of our drug candidates or potential commercial sales of a drug candidate may expose us to expensive product liability claims, and we may not be able to maintain product liability insurance on reasonable terms or at all.

The risk of product liability is inherent in the testing of pharmaceutical products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or terminate testing of one or more of our drug candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our drug candidates. We currently carry clinical trial insurance but do not carry product liability insurance. If we successfully commercialize one or more of our drug candidates, we may face product liability claims, regardless of FDA approval for commercial manufacturing and sale. We may not be able to obtain such insurance at a reasonable cost, if at all. Even if our agreements with any current or future corporate collaborators entitle us to indemnification against product liability losses, such indemnification may not be available or adequate should any claim arise.

If our drug candidates receive regulatory approval, we and our collaborators will be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our and our collaborators' ability to commercialize our potential drugs.

Any regulatory approvals that our drug candidates receive may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if the FDA approves any of our drug candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including but not limited to adverse events of unanticipated severity or frequency, or the discovery that adverse events previously observed in preclinical research or clinical trials that were believed to be minor actually constitute much more serious problems, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Any of these events could prevent us from marketing our drugs and our business could suffer.

We may not be able to successfully develop or commercialize FENROCK, a proprietary abuse-deterrent transdermal pain patch (fentanyl), designed to prevent common methods of abuse of fentanyl.

We have no history of developing transdermal patches. We do not know whether any of our planned development activities for FENROCK will result in approval of such drug candidate by the FDA, or, if FENROCK is approved, it will be a commercially viable product.

We may not be able to successfully develop or commercialize PTI-125, a proprietary drug candidate to treat Alzheimer's disease.

We have no history of developing treatment for AD. The biopharmaceutical industry as a whole has a poor track record in developing drugs for AD. Drug candidates aimed at AD have almost universally failed in every attempt to show late-stage efficacy in clinical studies. We do not know whether any of our planned development activities for AD will result in approval of such drug candidate by the FDA, or, if PTI-125 is approved, it will be a commercially viable product.

We may not be able to successfully develop or commercialize PTI-125DX, a blood-based test to detect Alzheimer's disease.

We have no history of developing diagnostics. The biopharmaceutical industry as a whole has a poor track record in developing blood-based diagnostics for AD. Diagnostics aimed at detecting AD have almost universally failed in large studies despite evidence of success in early testing. We do not know whether any of our planned development activities for AD will result in approval of a diagnostic by the FDA, or, if PTI-125DX is approved, it will be a commercially viable product.

Risks Relating to our Collaboration Agreements

If Pfizer did not transfer to us all data and documentation or the quality of the data and documentation transferred is insufficient, our ability to achieve approval of the NDA for REMOXY will be negatively impacted and our business will suffer.

In April 2015, we announced that we resumed responsibility for REMOXY under the terms of a letter agreement with Pfizer. The letter agreement was entered into within the scope of the previously disclosed provisions of the Collaboration Agreement between us and Pfizer relating to the return of REMOXY.

We believe Pfizer has transferred to us data, materials, capital equipment and other assets related to REMOXY. In preparing to resubmit the NDA for REMOXY, we may find that there are additional data, materials or agreements that Pfizer should have transferred to us. If Pfizer did not meet its obligations to transfer all such materials or if the quality of the data and documentation transferred is insufficient, we would be significantly delayed in our ability to achieve FDA approval of the NDA for REMOXY, and may need to conduct further development activities or clinical trials to prepare any potential resubmission. As a result, any further development, regulatory approval and product introduction for REMOXY would be delayed or prevented and our business would suffer.

If outside collaborators fail to devote sufficient time and resources to drug development programs related to our product candidates, or to the manufacture of our products, or if their performance is substandard, regulatory submissions and introductions for our products may be delayed.

We rely on Durect as the sole-source provider of certain components of REMOXY. Durect's failure for any reason to provide these components could result in delays or failures in product testing or delivery, cost overruns or other problems that could materially harm our business.

We depend on independent investigators and collaborators, such as universities and medical institutions, to conduct our clinical trials under agreements with us. These investigators and collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. They may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such activities ourselves. If these investigators or collaborators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, the approval of our regulatory submissions and our introductions of new drugs will be delayed or prevented.

Our collaborators may also have relationships with other commercial entities, some of which may compete with us. If outside collaborators assist our competitors to our detriment, the approval of our regulatory submissions will be delayed and the sales from our products, if any are commercialized, will be less than expected.

If we fail to enter into or maintain collaboration agreements and licenses for REMOXY and other drugs designed to reduce potential risks of unintended use, we may have to reduce or delay our drug candidate development.

Our plan for developing, manufacturing and commercializing REMOXY currently requires us to successfully maintain our license from Durect. If we are unable to meet the obligations necessary to maintain our license with Durect for one or more potential products we may lose the rights to utilize Durect's technology for such potential products, our potential future revenues may suffer and we may have to reduce or delay development of our other drug candidates. In addition, we expect to seek a new corporate collaborator with respect to REMOXY. If we do not enter into a new collaboration with respect to the continued development and potential commercialization of REMOXY, we will be required to undertake and fund such activities ourselves and may need to seek additional capital (which may not be available on acceptable terms, if at all), personnel or other resources. If we are not successful in such efforts, development and commercialization of REMOXY and our other drug candidates would be delayed or prevented, and our business would suffer.

We may not succeed at in-licensing drug candidates or technologies to expand our product pipeline.

We may not successfully in-license drug candidates or technologies to expand our product pipeline. The number of such candidates and technologies is limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising drug candidates and technologies is intense because such companies generally desire to expand their product pipelines through in-licensing. If we fail to carry out such in-licensing and expand our product pipeline, our potential future revenues may suffer.

Our collaborative agreements may not succeed or may give rise to disputes over intellectual property, disputes concerning the scope of collaboration activities or other issues.

Our collaborative agreements with third parties, such as our license agreement with Durect, are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property under collaborations or disputes concerning the scope of collaboration activities. Such disputes can delay or prevent the development of potential new drug products, or can lead to lengthy, expensive litigation or arbitration. Other factors relating to collaborative agreements may adversely affect our business, including:

- the development of parallel products by our collaborators or by a competitor;
- arrangements with collaborative partners that limit or preclude us from developing certain products or technologies;
- premature termination of a collaborative or license agreement; or
- failure by a collaborative partner to provide required funding, to devote sufficient resources to the development of or legal defense of our potential products or to provide data or other information to us as required by our collaborative agreements.

Risks Relating to Commercialization

We currently have no in-house capabilities to manufacture or commercialize our drug products. If we are unable to develop our own manufacturing, sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, or at all, our product revenues could be disappointing.

We currently rely on Mallinckrodt as the sole manufacturer for REMOXY and commercialization of REMOXY is dependent on continuation of such relationship. Disputes in the past have arisen with Mallinckrodt with respect to us fulfilling our obligations under the Mallinckrodt Agreement. There can be no guarantee that such disputes will not arise again in the future, which may lead to Mallinckrodt terminating the Mallinckrodt Agreement. If the Mallinckrodt Agreement is terminated, we would not be able to commercialize REMOXY until another manufacturer is identified and we have entered into a manufacturing agreement with such manufacturer. If we are required to replace Mallinckrodt as the manufacturer of REMOXY, it is likely to delay commercialization of REMOXY for an extended period of time.

We currently have no sales, marketing or distribution capabilities. We have not established commercial strategies regarding any of our product candidates, including REMOXY. In order to commercialize our products, if any are approved by the FDA, we will either have to develop such capabilities internally or collaborate with third parties who can perform these services for us.

If we decide to commercialize any of our drugs ourselves, we may not be able to

- hire and retain the necessary experienced personnel;
- build sales, marketing and distribution operations in a cost-effective manner which are capable of successfully launching new drugs;
- obtain access to adequate numbers of physicians to prescribe our products; or
- generate sufficient product revenues.

In addition, establishing such operations on our own will take time and involve significant expense. If our commercial operations lack complementary products, we may not be able to compete in a cost-effective manner with competitors with more products to sell. If we engage third-party collaborators to perform any commercial operations, our future revenues may depend significantly upon the performance of those collaborators.

If we decide to enter into new co-promotion or other licensing arrangements with third parties, we may be unable to locate acceptable collaborators because the number of potential collaborators is limited and because of competition from others for similar alliances with potential collaborators. Even if we are able to identify one or more acceptable new collaborators, we may not be able to enter into any collaborative arrangements on favorable terms, or at all.

In addition, due to the nature of the market for our drug candidates, it may be necessary for us to license all or substantially all of our drug candidates to a single collaborator, thereby eliminating our opportunity to commercialize these other products independently. If we enter into any such new collaborative arrangements, our revenues are likely to be lower than if we marketed and sold our products ourselves.

In addition, any revenues we receive would depend upon our collaborators' efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, business combinations or other factors outside of our control. Depending upon the terms of our collaboration, the remedies we have against an under-performing collaborator may be limited. If we were to terminate the relationship, it may be difficult or impossible to find a replacement collaborator on acceptable terms, or at all.

If physicians and patients do not accept and use our drugs, we will not achieve sufficient product revenues and our business will suffer.

Even if the FDA approves our drugs, physicians and patients may not accept and use them. Acceptance and use of our drugs will depend on a number of factors including:

- when the drug is launched into the market and related competition;
- approved label claims;
- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs, and, in particular, the effectiveness of REMOXY in reducing potential risks of unintended use;
- perceptions by physicians regarding the cost benefit of REMOXY in reducing potential risks of unintended use;
- published studies demonstrating the cost-effectiveness of our drugs relative to competing products;
- availability of reimbursement for our products from government or healthcare payers;
- our or our collaborators' ability to implement a risk management plan prior to the distribution of any Schedule II drug; and
- effectiveness of marketing and distribution efforts by us and other licensees and distributors.

Because we expect to rely on sales generated by our current lead drug candidates for substantially all of our revenues for the foreseeable future, the failure of any of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

The science of abuse-deterrence is relatively new.

The analytical, clinical, and statistical methods for evaluating abuse-deterrent technologies and study results are new and rapidly evolving. Although we believe the FDA will take a flexible, adaptive approach to the evaluation and labeling of potentially abuse-deterrent products, such as REMOXY, we cannot be certain that our interpretation of abuse-deterrent data for REMOXY is consistent with the views of the FDA. In our opinion, the FDA has limited data correlating the potentially abuse-deterrent properties of certain opioid drug products, such as REMOXY, with actual reduction in abuse or adverse events associated with abuse. In addition, the FDA has stated it is not able to provide specific guidance on the magnitude of effect that would be sufficient to support any particular type of label claim for abuse-deterrence.

Our ability to market and promote REMOXY and its abuse-deterrent features will be determined by FDA-approved labeling.

The commercial success of REMOXY and certain of our other product candidates will depend upon our ability to obtain FDA-approved labeling describing their abuse-deterrent features. Our failure to achieve FDA approval of product labeling containing such information will prevent us from advertising and promoting the abuse-deterrent features of our product candidates in order to differentiate them from other similar products. This would make our products less competitive in the market.

Abuse-deterrent label claims for REMOXY may not be broad enough to demonstrate a substantial benefit to health care providers and patients.

FDA approval is required in order to make claims that a product has an abuse-deterrent effect. In April 2015, the FDA published final guidance with regard to the evaluation and labeling of abuse-deterrent opioids. The guidance provides direction as to the studies and data required for obtaining abuse-deterrent claims in a product label. FDA guidance describes three categories of pre-market studies that may lead to an abuse-deterrent claim:

Category 1 – laboratory manipulation and extraction studies;

Category 2 – pharmacokinetic studies; and

Category 3 – human abuse potential studies.

According to the FDA guidance, label claims for abuse-deterrence should describe the product's specific abuse-deterrent properties as well as the specific routes of abuse that the product has been developed to deter. When data predict or show that a product's potentially abuse-deterrent properties can be expected to, or actually do, result in a significant reduction in that product's abuse potential, these data, together with an accurate characterization of what the data mean, may be included in product labeling.

If a product is approved by the FDA to include such claims in its label, the applicant may use the approved labeling information about the abuse-deterrent features of the product in its marketing efforts to physicians.

Although we intend to provide data to the FDA to support approval of abuse-deterrence label claims for REMOXY, there can be no assurance that REMOXY or any of our other product candidates will receive FDA-approved labeling that describes the abuse-deterrent features of such products. The FDA may find that our studies and data do not support abuse-deterrent labeling or that our product candidates do not provide substantial abuse-deterrence because, for example, their deterrence mechanisms do not address the way they are most likely to be abused. Further, the FDA is not required to follow its guidance and could change this guidance, which could require us to conduct additional studies or generate additional data. If the FDA does not approve abuse-deterrent labeling, we will not be able to promote such products based on their abuse-deterrent features and our business may suffer.

Even if we do receive FDA approval for abuse-deterrent claims, the claims may not be broad enough to demonstrate a substantial benefit to health care providers and patients. For instance, the claims may not encompass the more common forms of abuse for products like our product candidates. Moreover, continued investigation in Phase IV studies following product approval, if required, is expensive and may not support the continued use of abuse-deterrent claims.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our drug candidates is characterized by intense competition and rapid technological advances. If our drug candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products are unable to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We and our collaborators will compete for market share against fully integrated pharmaceutical companies or other companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have drugs already approved or drug candidates in development that will or may compete against our approved drug candidates. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- conducting preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;

- formulating and manufacturing drugs; and
- launching, marketing, distributing and selling drugs.

If we fail to obtain acceptable prices or an adequate level of reimbursement for our products from healthcare payers, our ability to generate product revenues will be diminished.

Our ability to commercialize drugs we (alone or with other collaborators) may develop will depend in part on the extent to which reimbursement can be obtained for such drugs from:

- government and health administration authorities;
- private health maintenance organizations and health insurers; and
- other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, health maintenance organizations and managed care organizations, are challenging the prices charged for medical products and services and/or are seeking pharmacoeconomic data to justify formulary acceptance and reimbursement practices. We currently have not generated pharmacoeconomic data on any of our drug candidates. Government and other healthcare payers increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs, and by refusing, in some cases, to provide coverage for uses of approved products for disease indications for which the FDA has or has not granted labeling approval. Adequate third-party insurance coverage may not be available to patients for any products we discover and develop, alone or with collaborators. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our products, market acceptance of our drug candidates could be limited.

Enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and may reduce the prices we are able to obtain for our product candidates.

Legislative and regulatory changes and future changes regarding the healthcare system could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities or affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The Medicare Modernization Act, including its cost reduction initiatives, could limit the coverage and reimbursement rate that we receive for any of our approved products. Private payors may follow Medicare coverage policies and payment limitations in setting their own reimbursement rates resulting in similar limits in payments from private payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription drug products. It also contains substantial provisions intended to, among other things, broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, and impose additional health policy reforms, any of which could have a material adverse effect on our business. A significant number of provisions are not yet, or have only recently become, effective, but the Affordable Care Act may result in downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

The Affordable Care Act, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may compromise our ability to generate revenue, attain profitability or commercialize our products.

The Affordable Care Act is a highly complex piece of legislation that continues to evolve. We do not and cannot understand or anticipate the full impact and potential implications of the Affordable Care Act on our business or on our drugs.

Even if we are able to commercialize any of our product candidates, our products may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could have a material adverse effect on our business.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be and whether it will be satisfactory. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Public concern over the abuse of opioids, including law enforcement concerns over diversion of opioid and regulatory efforts to combat abuse, could decrease the potential market for our product candidates.

Media stories regarding prescription drug abuse and the diversion of opioids and other controlled substances are commonplace. Law enforcement and regulatory agencies may apply policies that seek to limit the availability of opioids. Such efforts may inhibit our ability to commercialize our product candidates. Aggressive enforcement and unfavorable publicity regarding, for example, the use or misuse of oxycodone or other opioid drugs; the limitations of ADFs; the ability of drug abusers to discover previously unknown ways to abuse our products; public inquiries and investigations into prescription drug abuse; litigation; or regulatory activity regarding sales, marketing, distribution or storage of opioid drugs could have a material adverse effect on our reputation. Such negative publicity could reduce the potential size of the market for our product candidates and decrease the revenues we are able to generate from their sale. To the extent opioid abuse becomes less prevalent or less urgent of a public health issue, regulators and third party payers may not be willing to pay a premium for ADFs of opioids.

Efforts by the FDA and other regulatory bodies to combat abuse of opioids may negatively impact the market for our product candidates. For example, on September 10, 2013, the FDA announced its intention to effect labeling changes to all approved long-acting opioid formulations. In particular, the FDA announced its intention to update the indication for long-acting opioid formulations so that long-acting opioid formulations will be indicated only for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. On April 16, 2014, the FDA updated these indications. It is possible that such changes could reduce the number of prescriptions for opioids written by physicians and negatively impact the potential market for our product candidates.

If the FDA or other applicable regulatory authorities approve generic products with abuse-deterrent claims that compete with any of our product candidates, it could reduce our sales of those product candidates.

Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA, or ANDA. Potential competitors may create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These competitors might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredients, dosage form, strength, route of administration, and conditions of use, or labeling, as our products and that the generic product is absorbed in the body at the same rate and to the same extent as, or is bioequivalent to, our products. These generic equivalents would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to our products would substantially limit our ability to generate revenues and therefore to obtain a return on the investments we have made in our product candidates.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we may obtain marketing approval. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal, state and foreign healthcare laws and regulations may affect our ability to operate and expose us to areas of risk, including:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. 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 federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute to defraud any healthcare benefit program or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- federal laws requiring drug manufacturers to report information related to payments and other transfers of value made to physicians and other healthcare providers, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, commonly known as the Sunshine Act, as well as other state and foreign laws regulating marketing activities; and
- state and foreign equivalents of each of the above laws, including state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers; state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Nonetheless, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

Government agencies may establish and promulgate usage guidelines that could limit the use of our drug candidates.

Government agencies, professional and medical societies, and other groups may establish usage guidelines that apply to our drug candidates. These guidelines could address such matters as usage and dose, among other factors. Application of such guidelines could limit the clinical use or commercial appeal of our drug candidates.

Risks Relating to our Intellectual Property

Our ability to commercialize our drug candidates will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing the intellectual property rights of third parties, such litigation will be costly and time consuming and an unfavorable outcome would have a significant adverse effect on our business.

Our ability to commercialize our drug candidates will depend on our ability to sell such products without infringing the patents or other proprietary rights of third parties. Intellectual property rights in the areas of controlled-release technology and pharmaceutical ingredients are complicated and are continuously evolving. Holders of patent rights in these areas may allege that the commercialization of REMOXY or our other drug candidates infringes such patent rights. While we believe that we would have valid defenses to any claim of infringement, there can be no assurance that these or other third-party patents will not limit our ability to commercialize REMOXY or our other drug candidates.

In addition, because patent applications are published sometime after filing, and because applications can take several years to issue, there may be currently pending third party patent applications that are unknown to us, which may later result in issued patents. If a third party claims that we infringe on its patents or other proprietary rights, we could face a number of issues that could seriously harm our competitive position, including:

- infringement claims that, with or without merit, can be costly and time consuming to litigate, can delay the regulatory approval process and can divert management’s attention from our core business strategy;
- substantial damages for past infringement which we may have to pay if a court determines that our products or technologies infringe upon a competitor’s patent or other proprietary rights;
- a court order prohibiting us from commercializing our products or technologies unless the holder licenses the patent or other proprietary rights to us, which such holder is not required to do;
- if a license is available from a holder, we may have to pay substantial royalties or grant cross licenses to our patents or other proprietary rights; and

- redesigning our process so that it does not infringe third party intellectual property rights, which may not be possible, or which may require substantial time and expense including delays in bringing our own products to market. Such actions could harm our competitive position and our ability to generate revenue and could result in increased costs.

If we are unable to protect our intellectual property, our competitors could develop and market products with similar features that may reduce demand for our drug candidates.

Our success, competitive position and potential future revenues will depend in part on our ability to protect our intellectual property. If we or our collaborators fail to file, prosecute, obtain or maintain certain patents, our competitors could market products that contain features and clinical benefits similar to those of our products, and demand for our products could decline as a result.

We and our collaborators have filed patent applications in the United States and select international jurisdictions to protect our intellectual property. The coverage sought in a patent application can be denied or significantly reduced before or after the patent is issued. Consequently, we do not know whether any of our pending applications will result in the issuance of patents, or if any existing or future patents will provide significant protection or commercial advantage or will be circumvented by others. There can be no assurance that patents will issue from our pending or future patent applications or, if issued, that such patents will be of commercial benefit to us, afford us adequate protection from competing products, or not be challenged or declared invalid. Thus, if these patent applications do not result in issued patents or result in a patent that is challenged by others, the duration or scope of our patent rights may be limited and our future revenues could be lower as a result.

We may be involved in challenges to our intellectual property. If our competitors are able to successfully challenge the validity or scope of our patent rights, based on the existence of prior art or otherwise, they might be able to market products that contain features and clinical benefits similar to those of our drug candidates, and demand for our drug candidates could decline as a result. An adverse outcome of a challenge to our intellectual property could result in loss of claims of patents or other intellectual property rights that pertain to certain drugs we currently have under development and could have a material adverse impact on our future revenues.

We intend to file additional patent applications relating to our technology, products and processes. We may direct our collaborators to file additional patent applications relating to the licensed technology or we may do so ourselves. However, our competitors may challenge, invalidate or circumvent any of our current or future patents. These patents may also fail to provide us with meaningful competitive advantages.

We may become involved in expensive litigation or other legal proceedings related to our existing intellectual property rights, including patents.

We expect that we will rely upon patents, trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. While we use confidentiality agreements with our employees, consultants and certain of our contractors, if trade secrets or other confidential information is made public, our business may be harmed and our legal remedies may be limited or insufficient. Others may independently develop substantially equivalent proprietary information or be issued patents that may prevent the sale of our products or know-how or require us to license such information and pay significant fees or royalties in order to produce our products.

Our technology could infringe upon claims of patents owned by others. If we were found to be infringing on a patent held by another, we might have to seek a license to use the patented technology. In that case, we might not be able to obtain such a license on terms acceptable to us, or at all. If a legal action were to be brought against us or our licensors, we could incur substantial defense costs, and any such action might not be resolved in our favor. If such a dispute were to be resolved against us, we could have to pay the other party large sums of money and our use of our technology and the testing, manufacture, marketing or sale of one or more of our proposed products could be restricted or prohibited.

If we are unable to protect the confidentiality of our intellectual property, the value of our intellectual property could be materially adversely affected and our business would be harmed.

We seek to protect our intellectual property, in part, by confidentiality agreements with our employees, consultants, scientific advisors, contractors and collaborators. However, there can be no assurance that our intellectual property will not be disclosed or that competitors will not otherwise gain access to our intellectual property or independently develop

substantially equivalent intellectual property. For example, if our confidential information were disclosed in violation of our confidentiality agreements, we may not be able to obtain adequate remedies for such breaches. We also seek to protect our intellectual property by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our intellectual property were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that intellectual property to compete with us, which could harm our business.

Risks Relating to our Business and Strategy

Our business may fail without a new equity incentive plan.

We depend heavily on equity incentives to retain the services of all of our personnel, without which we are not able to retain or hire qualified personnel or board members. In particular, our independent board members receive no form of compensation for their services other than new equity incentives every year. The 2008 Equity Plan expired in December 2017. Furthermore, in 2017, shareholders rejected a proposal to renew an equity incentive plan. As a result, going-forward we are no longer able to grant new equity incentives to any of our personnel, including new potential hires and board members, until and unless shareholders approve a new equity incentive plan. The loss of personnel and board members, and our potential inability to hire replacement personnel, will materially delay or disrupt our operations and will put us out of compliance with various legal standards and regulations for listed companies, all of which may force us to curtail or cease operations.

If we are not successful in attracting and retaining qualified personnel, we could experience delays in completing necessary clinical trials, in the regulatory approval process or in formulating, manufacturing, marketing and selling our potential products.

We depend on the services of our key personnel, including Remi Barbier, our Chairman, President and Chief Executive Officer. On February 14, 2017, Peter S. Roddy resigned, effective March 9, 2017, as Vice President, Chief Financial Officer and Secretary. Remi Barbier, President and Chief Executive Officer, has assumed the role of Principal Financial Officer until such time as a new Chief Financial Officer is appointed.

The loss of key personnel, including members of executive management as well as key bioengineering, product development, and technical personnel, could disrupt our operations and have an adverse effect on our business. We will need to hire additional qualified personnel with expertise in clinical research, preclinical testing, government regulation, formulation and manufacturing and sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals is intense, and our search for such personnel may not be successful. Attracting and retaining qualified personnel is critical to our success.

We have employees whose equity ownership in the Company could result in a substantial increase in personal wealth if the fair value of our common stock increases. Over time, this increase in personal wealth may make it more challenging to retain these employees.

If third-party manufacturers of our drug candidates fail to devote sufficient time and resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed and our costs may be higher than expected.

We have no manufacturing facilities and have limited experience in drug product development and commercial manufacturing. We lack the resources and expertise to formulate, manufacture or test the technical performance of our drug candidates. We rely on and expect to continue to rely on a limited number of experienced personnel and a small number of contract manufacturers and other vendors to formulate, test, supply, store and distribute drug supplies for our preclinical studies and clinical trials. Our reliance on a limited number of vendors exposes us to the following risks, any of which could delay our clinical trials, and, consequently, FDA approval of our drug candidates and commercialization of our products, result in higher costs, or deprive us of potential product revenues:

- Contract commercial manufacturers, their sub-contractors or other third parties we rely on and expect to rely on, may encounter difficulties in achieving the volume of production needed to satisfy preclinical and clinical needs or commercial demand, may experience technical issues that impact quality or compliance with applicable and strictly enforced regulations governing the manufacture of pharmaceutical products, and may experience shortages of qualified personnel to adequately staff production operations.
- Our contract manufacturers could default on their agreements with us to provide supplies or meet our requirements for commercialization of our products.
- For certain of our drug candidates, the use of alternate manufacturers may be difficult because the number of potential manufacturers that have the necessary governmental licenses to produce narcotic products is limited. Additionally, the FDA and the DEA must approve any alternative manufacturer of our products before we may use the alternative manufacturer to produce our supplies.
- It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all. Our contract manufacturers and vendors may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our products.
- If any contract manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to such innovation.

We may not be able to successfully develop or commercialize potential drug candidates for indications other than pain.

Our research and development activities include development of potential drug candidates for indications other than pain. We have no history of developing such drug candidates. We do not know whether any of our planned development activities will result in marketable products. We do not anticipate that our drug candidates in these areas will reach the market for at least several years, if at all.

Our employees and consultants are generally subject to confidentiality or other agreements with their former employers and they may inadvertently or otherwise violate those agreements.

Many of our employees and consultants were previously employed at universities or biotechnology or pharmaceutical companies. While we require our employees and consultants to honor any agreements they may have entered into prior to working with us, we may be subject to claims that we inadvertently or otherwise used or disclosed trade secrets or other confidential information belonging to former employers. Failure to defend such claims could result in loss of valuable rights or personnel, which in turn could harm or prevent commercialization of our drug candidates. Successful defense against such claims can be expensive and might distract us from executing our strategies.

Law enforcement concerns over diversion of opioids and social issues around abuse of opioids may make the regulatory approval process and commercialization of our drug candidates very difficult.

Law enforcement agencies or regulatory agencies may apply policies that seek to limit the availability of opioids. Such efforts may adversely affect the regulatory approval and commercialization of our drug candidates.

Developments by competitors may render our products or technologies obsolete or non-competitive.

Alternative technologies and products are being developed to improve or replace the use of opioids for pain management, several of which are in clinical trials or are awaiting approval from the FDA. In addition, the active ingredients in nearly all opioid drugs are available in generic form. Drug companies that sell generic opioid drugs represent substantial competition. Many of these organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, greater experience in drug development and in obtaining regulatory approvals and greater manufacturing and marketing capabilities than we do. Our competitors may market less expensive or more effective drugs that would compete with our drug candidates or reach market with competing drugs before we are able to reach market with our drug candidates. These organizations also compete with us to attract qualified personnel and partners for acquisitions, joint ventures or other collaborations.

Business interruptions could limit our ability to operate our business.

Our operations, as well as those of our collaborators on which we depend, are vulnerable to damage or interruption from computer viruses, human error, natural disasters, electrical and telecommunication failures, international acts of terror and similar events. We have not established a formal disaster recovery plan and our back-up operations and business interruption insurance may not be adequate to compensate us for losses we may suffer. A significant business interruption could result in losses or damages incurred by us and require us to cease or curtail our operations.

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations.

We use information technology, computer systems and networks to process, transmit and store electronic information in connection with our business activities. Cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency, scope and sophistication in every industry. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data, and may cause a disruption in our operations, harm our reputation and increase our stock trading risk. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our third-party collaborators, distributors and other contractors and consultants will be successful in protecting our data that is stored on their systems. A cyberattack or destruction or loss of data could have a material adverse effect on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Unfavorable media coverage of opioid pharmaceuticals could negatively affect our business.

Opioid drug abuse receives a high degree of media coverage. Unfavorable publicity regarding, for example, the use or misuse of oxycodone or other opioid drugs, the limitations of ADFs, public inquiries and investigations into prescription drug abuse, litigation or regulatory activity could adversely affect our reputation. Such negative publicity could have an adverse effect on the potential size of the market for our drug candidates and decrease revenues and royalties, which would adversely affect our business and financial results.

Risks Relating to Manufacturing

We do not own any manufacturing facilities and we rely on third-party commercial drug manufacturers for drug supply.

We do not own any manufacturing facilities. We plan to continue to outsource formulation, manufacturing and related activities.

We rely on a limited number of third-party suppliers to formulate, manufacture, fill, label, ship or store all of our drug candidates. These suppliers must comply with current good manufacturing practices, or GMP, regulations enforced by the FDA and other government agencies and DEA regulations, and are subject to ongoing periodic unannounced inspection, including preapproval inspections by the FDA and DEA and corresponding state and foreign government agencies to ensure

strict compliance with GMP and other government regulations and corresponding foreign standards. These manufacturers may subsequently be stopped from producing, storing, shipping or testing our drug products due to their non-compliance with federal, state or local regulations. We do not have control over our suppliers' compliance with these regulations and standards.

If REMOXY is approved, our commercial suppliers may encounter difficulties in achieving high volumes of production to satisfy commercial demands.

We cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers would be expensive and time consuming.

Failure by any of our suppliers to perform as expected could delay or prevent commercialization of REMOXY or result in shortages, cost overruns, or other problems and would materially harm our business.

We will rely on Durect as the sole source of certain excipients in REMOXY. Durect has limited experience manufacturing pharmaceutical products and maintaining GMP-compliant operations. We currently do not have a long-term commercial supply agreement in place with Durect. We expect that we and Durect will negotiate a supply agreement for these excipients. We may not be able to establish a commercial supply agreement on acceptable terms, or at all.

If we receive marketing approval for and commercially launch REMOXY, Durect may need to materially expand its manufacturing capacity. Durect may not be able to increase its manufacturing capacity for REMOXY in a timely or economic manner, or at all. Moreover, significant scale up of manufacturing will require additional validation studies, which are subject to FDA review and approval. If Durect is unable to successfully increase the manufacturing capacity, at an acceptable cost or otherwise, and we are unable to establish alternative manufacturing capabilities, there may be a shortage in supply, which would harm our future revenues and cause our business to suffer.

If Durect fails to supply excipients to us, they may be in breach of their supply obligations. With or without a commercial supply agreement, Durect's failure for any reason to supply these excipients, including failure resulting from Durect relying on sole source providers, could delay or prevent commercialization of REMOXY or result in shortages, delays, unexpected costs or other problems and would materially harm our business.

We expect to rely on Noramco as the sole source of the oxycodone in REMOXY. We currently do not have a long-term commercial supply agreement in place with Noramco. Effective July 1, 2016, Noramco is owned by SK Capital Partners, a private investment firm. We expect to negotiate with Noramco a commercial supply agreement to supply us with oxycodone. We may not be able to establish a commercial supply agreement on acceptable terms, or at all. Until we have a commercial supply agreement in place with Noramco, we expect to obtain oxycodone from Noramco via purchase orders. There can be no assurance that Noramco will accept our purchase orders on acceptable terms, or at all. With or without a commercial supply agreement, Noramco's failure for any reason to supply us with oxycodone could delay or prevent commercialization of REMOXY or result in shortages, cost overruns or other problems that would materially harm our business.

We will need to identify a third-party to manufacture commercial supplies of REMOXY. Without a commercial manufacturer, we may not be able commercialize REMOXY. To date, we have not identified such third-party manufacturer and we may never find a viable source of commercial supplies of REMOXY. We expect to rely on such third party as the sole-source drug product manufacturer of REMOXY pursuant to a supply agreement. In addition to drug product manufacturing, this third-part manufacturer will need to be responsible for sourcing excipients in REMOXY other than those provided by the Durect Agreement. Failure for any reason to manufacture and supply REMOXY could delay or prevent commercialization of REMOXY or result in shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that would materially harm our business.

If we cannot formulate and scale-up additional dosage forms of REMOXY, the commercial opportunity for REMOXY might be diminished.

We plan to formulate and scale-up additional dosage forms of REMOXY. We may not be able to successfully complete our formulation or scale-up activities or we may determine that the commercial opportunity for REMOXY in certain dosage forms is too limited to warrant further investment. If we are unsuccessful in our formulation or scale-up activities with REMOXY, our future revenue may be less than expected and our operations may suffer.

We rely solely on Durect to provide us with certain components of drug candidates and will continue to rely on Durect as the sole-source provider of these components.

We rely on Durect as the sole-source provider of certain components of REMOXY and other drug candidates designed to reduce the potential risks of unintended use, and will rely solely on Durect to produce commercial supplies of these components. Durect's failure for any reason to provide these components or to achieve and maintain satisfactory manufacturing standards could result in product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could materially harm our business.

Durect may encounter manufacturing difficulties involving production yields, quality control and quality assurance. Durect is subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign agencies to ensure strict compliance with government regulations and corresponding foreign standards. We cannot control Durect's compliance with these regulations and standards.

If we receive marketing approval for and commercially launch REMOXY, Durect may need to materially expand its manufacturing capacity. Durect may not be able to increase its manufacturing capacity for REMOXY in a timely or economic manner, or at all. Moreover, significant scale up of manufacturing will require additional validation studies, which are subject to FDA review and approval. If Durect is unable to successfully increase the manufacturing capacity for such components of REMOXY, at an acceptable cost or otherwise, and we are unable to establish alternative manufacturing capabilities, commercialization of REMOXY may be delayed, prevented or impaired or there may be a shortage in supply, which would harm our future revenues and cause our business to suffer.

We expect to rely on Noramco as the sole source of the oxycodone in REMOXY.

We expect to rely on Noramco as the sole source of the oxycodone in REMOXY. We expect we and Noramco will negotiate a supply agreement to supply us with the oxycodone in REMOXY. Noramco's operation is subject to regulation by the DEA and the Controlled Substances Act. Noramco's failure for any reason to manufacture and supply us with the oxycodone in REMOXY could result in shortages, cost overruns or other problems that could materially harm our business.

Risks Relating to our Financial Position and Need for Financing

Our operating history may make it difficult for you to evaluate our business to date and to assess its future viability.

Our operations from our inception to date have been limited to organizing and staffing our company, acquiring, developing and securing our technology, undertaking preclinical studies and clinical trials of our drug candidates and forming collaborations. We have not yet demonstrated our ability to obtain regulatory approval, formulate and manufacture our drug candidates on a commercial scale or conduct sales and marketing activities. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We have a history of losses and expect to incur substantial losses and negative operating cash flows for the foreseeable future.

Although we were profitable in some years in the past based on payments received pursuant to collaboration agreements and interest income, we have yet to generate any revenues from product sales. We have an accumulated deficit of $157 million at December 31, 2017. Even if we succeed in developing and commercializing one or more of our drug candidates, we expect to continue to use significant cash resources in our operations for the foreseeable future.

We anticipate that our expenses will increase substantially in the foreseeable future as we:

- continue to conduct preclinical studies and clinical trials for our drug candidates;
- seek regulatory approvals for our drug candidates;
- develop, formulate, manufacture and commercialize our drug candidates;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies, or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional personnel.

We will need to generate significant revenues to achieve and maintain profitability. If we or our collaborators cannot successfully develop, obtain regulatory approval for and commercialize our drug candidates, we will not be able to generate such revenues or achieve profitability in the future. Our failure to achieve or maintain profitability would have a material adverse impact on the market price of our common stock.

If we cannot raise additional capital on acceptable terms, we may be unable to complete planned clinical trials of any or some of our drug candidates or to pursue attractive business opportunities.

We have funded all of our operations and capital expenditures with the proceeds from our public and private stock offerings, payments received under collaboration agreements and interest earned on our investments. We expect that our current cash, cash equivalents and marketable securities will be sufficient to meet our working capital and capital expenditure needs for at least the next twelve months. However, we may elect to raise additional funds within such twelve-month period or need to raise additional funds thereafter and additional financing may not be available on favorable terms, if at all. Even if we succeed in selling additional securities to raise funds, our existing stockholders' ownership percentage would be reduced and new investors may demand rights, preferences or privileges senior to those of existing stockholders. If we raise additional capital through debt financing, if available, such financings may involve covenants that restrict our business activities. If we raise additional capital through strategic alliance and license arrangements, we may have to trade our rights to our technology, intellectual property or drug candidates to others in such arrangements on terms that may not be favorable to us.

If we determine that we need to raise additional funds and we are not successful in doing so, we may be unable to complete the clinical development of some or all of our drug candidates or to seek or obtain FDA approval of our drug candidates. We then could be forced to discontinue product development, enter into a relationship with an additional strategic partner earlier than currently intended, relinquish or license on unfavorable terms our rights to technologies or drug candidates that we would seek to develop ourselves or significantly delay, scale-back or curtail our operations.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Risks Relating to an Investment in our Common Stock

Our stock price has been volatile and could experience a sudden decline in value.

Our common stock has experienced significant price and volume fluctuations and may continue to experience volatility in the future. You may not be able to sell your shares quickly or at the latest market price if trading in our stock is not active or the volume is low.

The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- results of or delays in efforts to seek regulatory approval for REMOXY, and in preclinical studies and clinical trials for our other drug candidates;
- publicity regarding products under development by us or others, including with respect to actual or potential medical results relating to such matters;
- announcements of technological innovations or new commercial products by us or others;
- developments in patent or other proprietary rights by us or others;
- comments or opinions by securities analysts or major stockholders;
- adverse media coverage related to opioid pharmaceuticals;
- future sales of our common stock by existing stockholders;
- developments with respect to potential merger and acquisition activity of companies with whom we have strategic alliances or other agreements;
- regulatory developments or changes in regulatory guidance enacted by applicable governmental or other authorities;
- litigation or threats of litigation;
- economic and other external factors or other disaster or crises;
- the departure of any of our officers, directors or key employees;
- period-to-period fluctuations in financial results;
- announcement or expectations of additional financing efforts;
- changes in accounting practices;
- changes in the structure of the healthcare payment system;
- market conditions in the biopharmaceutical industry;
- publication of research reports about us, our competitor or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts; and
- limited daily trading volume.

We are a smaller reporting company and we cannot be certain if the reduced disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors.

We are currently a “smaller reporting company” as defined in the Securities Exchange Act of 1934, and are thus allowed to provide simplified executive compensation disclosures in our filings, are exempt from the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that an independent registered public accounting firm provide an attestation report on the effectiveness of internal control over financial reporting and have certain other reduced disclosure obligations with respect to our SEC filings. We will remain a “smaller reporting company” until the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our recently completed second fiscal quarter is $75 million or more. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We have in the past and may in the future fail to meet all applicable listing requirements, our common stock may be delisted from The Nasdaq Global Market, which could have an adverse impact on the liquidity and market price of our common stock.

Our common stock is currently listed on The Nasdaq Global Market, which has qualitative and quantitative listing criteria. If we are unable to meet any of the Nasdaq listing requirements in the future, such as the corporate governance requirements, the minimum closing bid price requirement, the minimum market value of listed securities requirement, total assets and total revenues, net income from continuing operations, the number of publicly held shares or any other Nasdaq requirements. Nasdaq could determine to delist our common stock. A delisting of our common stock could adversely affect the market

liquidity of our common stock, decrease the market price of our common stock, adversely affect our ability to obtain financing for the continuation of our operations and result in the loss of confidence in our company. On November 16, 2016, we received notice from the Listing Qualifications Department of the Nasdaq Stock Market (the "Staff") indicating that, for the previous 30 consecutive business days, the bid price for our common stock closed below the minimum $1.00 per share required for continued inclusion on The Nasdaq Global Market. The notification letter stated that we would be afforded 180 calendar days, or until May 15, 2017, to regain compliance with the minimum bid price requirement. In order to regain compliance, on May 4, 2017, our board of directors and stockholders approved the Charter Amendment to effect the Reverse Stock Split. On May 10, 2017, our common stock began trading on The Nasdaq Global Market on a split-adjusted basis at a ratio of 7-for-1. On May 24, 2017, we received a letter from the Staff indicating that we had regained compliance with the $1.00 minimum closing bid price requirement. Despite effecting the Reverse Stock Split, there can be no assurance that the market price per share of our common stock will remain in excess of the $1.00 minimum closing bid price requirement in the future. The continuing effect of the Reverse Stock Split on the market price of our common stock cannot be predicted with any certainty, and the history of similar stock split combinations for companies in like circumstances is varied.

Anti-takeover provisions in our charter documents and Delaware law may prevent or delay removal of incumbent management or a change of control.

Anti-takeover provisions of our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law may have the effect of deterring or delaying attempts by our stockholders to remove or replace management, engage in proxy contests and effect changes in control. The provisions of our charter documents include:

- a classified board so that only one of the three classes of directors on our board of directors is elected each year;
- elimination of cumulative voting in the election of directors;
- procedures for advance notification of stockholder nominations and proposals;
- the ability of our board of directors to amend our bylaws without stockholder approval; and
- the ability of our board of directors to issue up to 10,000,000 shares of preferred stock without stockholder approval upon the terms and conditions and with the rights, privileges and preferences as our board of directors may determine.

In addition, as a Delaware corporation, we are subject to Delaware law, including Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless certain specific requirements are met as set forth in Section 203.

These provisions, alone or together, could have the effect of deterring or delaying changes in incumbent management, proxy contests or changes in control.

Our share ownership is concentrated, and our officers, directors and principal stockholders can exert significant control over matters requiring stockholder approval.

Due to their combined stock holdings, our officers, directors and principal stockholders (stockholders holding greater than 5% of our common stock) acting collectively may have the ability to exercise significant influence over matters requiring stockholder approval including the election of directors and approval of significant corporate transactions. In particular, Remi Barbier, our founder, Chairman of the Board of Directors, President and Chief Executive Officer, owns or controls a significant amount of the voting power of our outstanding capital stock. This concentration of ownership may delay or prevent a change in control of the Company and may make some transactions, including but not limited to any merger, consolidation, or sale of substantially all of our assets, more difficult or impossible to complete without the support of key stockholders.

Publicly available information regarding stockholders' ownership may not be comprehensive because the SEC does not require certain large stockholders to publicly disclose their stock ownership positions.

If the fair value of our stock increases and outstanding Performance Awards vest, we expect to use substantial amounts of cash to fund employee tax liabilities.

We have Performance Awards outstanding. If these Performance Awards vest, we expect to issue our employees shares of our common stock net of statutory employment taxes. This net issuance results in fewer shares issued and uses our cash to

fund these taxes. The use of cash could be substantially higher, depending on the fair value of our common stock on the date the Performance Awards vest. If our use of cash to fund these taxes is substantial, our cash balance could substantially decline and our stock price could also decline.

We may in the future seek to fund the cash used for Performance Awards through the sale of our common stock. However, we may not be successful in selling shares of our common stock to fund the cash used for Performance Awards. If the number of shares we sell to fund the cash used for Performance awards is significant, our stock price could decline.

Volatility in the stock prices of other companies may contribute to volatility in our stock price.

The stock market in general, Nasdaq and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of management's attention and resources.

Our operating results may fluctuate from quarter to quarter and this fluctuation may cause our stock price to decline.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. Factors contributing to these fluctuations include, among other items, the timing and enrollment rates of clinical trials for our drug candidates, our need for clinical supplies and the valuation of stock-based compensation. Thus, quarter-to-quarter comparisons of our operating results may not be not indicative of what we might expect in the future. As a result, in some future quarters our clinical, financial or operating results may not meet the expectations of securities analysts and investors and could result in a decline in the price of our stock.

If securities or industry analysts publish inaccurate or unfavorable research about our business or product candidates, our stock price could decline.

Securities or industry analysts publish research and reports about our business or product candidates. An analyst's conclusions regarding prospects for product candidates in the biopharmaceutical industry can include judgments based on the limited publicly-available data. If one or more analysts issues unfavorable research about our business or our product candidates, including a downgrade of our common stock, the price of our stock may decline.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in prior offerings, and investors purchasing our shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our common stock or securities convertible into or exchangeable for our common Stock in future transactions may be higher or lower than the price per share in prior offerings.

There may not be an active, liquid trading market for our common stock.

There is no guarantee that an active trading market for our common stock will be maintained on Nasdaq. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

We lease approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires in December 2020. We believe that our facilities are adequate and suitable for our current needs.

Item 3. ***Legal Proceedings***

None.

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***

Our common stock is quoted on Nasdaq, under the symbol "PTIE." The following table sets forth the high and low sales prices per share of our common stock as reported on Nasdaq for the periods indicated.

	Sales Prices	
	High	Low
Fiscal 2016:		
First Quarter	$ 2.40	$ 1.55
Second Quarter	$ 2.63	$ 1.95
Third Quarter	$ 3.00	$ 0.96
Fourth Quarter	$ 1.04	$ 0.51
Fiscal 2017:		
First Quarter	$ 9.31	$ 3.71
Second Quarter	$ 7.42	$ 3.38
Third Quarter	$ 4.30	$ 3.10
Fourth Quarter	$ 6.49	$ 3.10

We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and, notwithstanding our special nondividend distributions in December 2012 (of $0.75 per share of common stock totaling $34.0 million) and December 2010 (of $2.00 per share of common stock totaling $85.7 million), we have not paid and do not anticipate paying any cash dividends in the foreseeable future. As of January 12, 2018, there were approximately 48 holders of record of our common stock.

Item 6. ***Selected Financial Data***

Not applicable.

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

This discussion and analysis should be read in conjunction with our financial statements and accompanying notes included elsewhere in this report. Operating results are not necessarily indicative of results that may occur in future periods.

Overview

Pain Therapeutics, Inc. develops proprietary drugs that offer significant improvements to patients and healthcare professionals. We generally focus our drug development efforts on disorders of the nervous system.

Our expertise consists of developing new drug candidates and guiding these through various regulatory and development pathways in preparation for their eventual commercialization. By necessity, the conduct of drug development is complex, lengthy, expensive and risky. The FDA has not yet established the safety or efficacy of our drug candidates.

The following is a summary of our pipeline of drug assets:

REMOXY ER (extended-release oxycodone capsules CII) – REMOXY, our lead drug candidate, is a proprietary abuse-deterrent, twice-daily, oral oxycodone to treat severe chronic pain. We plan to resubmit the REMOXY NDA to the FDA, with Priority Review in Q1 2018. We own exclusive rights to develop and commercialize REMOXY worldwide, with a sales royalty obligation to one of our technology partners.

FENROCK™ (transdermal fentanyl patch CII) – FENROCK is a proprietary, abuse-deterrent fentanyl skin patch to treat severe pain. This is an early-stage program that is substantially funded by a competitive research grant award from the National Institute on Drug Abuse (NIDA), the primary agency of the U.S. government for research on drug abuse. We own exclusive, worldwide rights to FENROCK, with no royalty obligations to any third party.

PTI-125 – PTI-125 is a proprietary small molecule drug for the treatment of Alzheimer's disease (AD). In 2017, we completed a first-in-human Phase I study with PTI-125. This program is substantially funded by competitive research grant awards from the National Institutes of Health (NIH), the primary agency of the U.S. government for biomedical research. We own exclusive, worldwide rights to PTI-125, with no royalty obligations to any third party.

PTI-125DX – PTI-125 is a proprietary, blood-based diagnostic/biomarker to detect Alzheimer's disease (AD). This clinical-stage program is substantially funded by competitive research grant awards from the NIH. We own exclusive, worldwide rights to PTI-125DX, with no royalty obligations to any third party.

Financial Overview

We have yet to generate any revenues from product sales. We have an accumulated deficit of $157 million at December 31, 2017. These losses have resulted principally from costs incurred in connection with research and development activities, salaries and other personnel-related costs and general corporate expenses. Research and development activities include costs of preclinical and clinical trials as well as clinical supplies associated with our drug candidates. Salaries and other personnel-related costs include non-cash stock-based compensation associated with options and other equity awards granted to employees and non-employees. Our operating results may fluctuate substantially from period to period as a result of the timing of preclinical activities, enrollment rates of clinical trials for our drug candidates and our need for clinical supplies.

We believe that our cash and cash equivalents at December 31, 2017, will enable us to fund our operating expenses for at least the next 12 months. In addition, we will seek in the future to fund our operations through additional public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we are unable to obtain financing or increase profitability, the related lack of liquidity will have a material adverse effect on our operations and future prospects.

We expect to continue to use significant cash resources in our operations for the next several years. Our cash requirements for operating activities and capital expenditures may increase substantially in the future as we:

- conduct preclinical and clinical trials for our drug candidates;
- seek regulatory approvals for our drug candidates;
- develop, formulate, manufacture and commercialize our drug candidates;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies, or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional personnel.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our drug candidates. If our development efforts result in regulatory approval and successful commercialization of our drug candidates, we will generate revenue from direct sales of our drugs and/or, if we license our drugs to future collaborators, from the receipt of license fees and royalties from sales of licensed products. We conduct our research and development programs through a combination of internal and collaborative programs. We rely on arrangements with universities, our collaborators, contract research organizations and clinical research sites for a significant portion of our product development efforts.

We focus substantially all our research and development efforts on research and development in the areas of neurology. The following table summarizes expenses by category for research and development efforts (in thousands):

	Years ended December 31,	
	2017	2016
Compensation	$ 2,913	$ 3,561
Contractor fees and supplies	3,989	4,842
Other common costs	713	773
	$ 7,615	$ 9,176

Contractor fees and supplies generally include expenses for preclinical studies and clinical trials and costs for formulation and manufacturing activities. Other common costs include the allocation of common costs such as facilities.

Our technology has been applied across certain of our portfolio of drug candidates. Data, know-how, personnel, clinical results, research results and other matters related to the research and development of any one of our drug candidates also relate to, and further the development of, our other drug candidates. As a result, costs allocated to a specific drug candidate may not necessarily reflect the actual costs surrounding research and development of that drug candidate due to cross application of the foregoing.

Estimating the dates of completion of clinical development, and the costs to complete development, of our drug candidates would be highly speculative, subjective and potentially misleading. Pharmaceutical products take a significant amount of time to research, develop and commercialize. The clinical trial portion of the development of a new drug alone usually spans several years. We expect to reassess our future research and development plans based on our review of data we receive from our current research and development activities. The cost and pace of our future research and development activities are linked and subject to change.

Critical Accounting Policies

The preparation of our financial statements in accordance with United States generally accepted accounting principles requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and interest income in our financial statements and accompanying notes. We evaluate our estimates on an ongoing basis, including those estimates related to agreements, research collaborations and investments. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual

results may differ from these estimates under different assumptions or conditions. The following items in our financial statements require significant estimates and judgments:

- *Stock-based compensation*. We recognize non-cash expense for the fair value of all stock options and other share-based awards. We use the Black-Scholes option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. For options granted to employees and directors, we recognize the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally four years. For options granted to non-employees, we remeasure the fair value expense using Black-Scholes each reporting period.

  We have granted share-based awards that vest upon achievement of certain performance criteria, or Performance Awards. We multiply the number of Performance Awards by the fair market value of our common stock on the date of grant to calculate the fair value of each award. We estimate an implicit service period for achieving performance criteria for each award. We recognize the resulting fair value as expense over the implicit service period when we conclude that achieving the performance criteria is probable. We periodically review and update as appropriate our estimates of implicit service periods and determinations on achievement of the performance criteria. Performance Awards vest and common stock is issued upon achievement of the performance criteria.

- *Income Taxes.* We make estimates and judgments in determining the need for a provision for income taxes, including the estimation of our taxable income or loss for each full fiscal year. We have accumulated significant deferred tax assets that reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of deferred tax assets is dependent upon future earnings, if any. We are uncertain as to the timing and amount of any future earnings. Accordingly, we offset these deferred tax assets with a valuation allowance. We may in the future determine that our deferred tax assets will likely be realized, in which case we will reduce our valuation allowance in the quarter in which such determination is made. If the valuation allowance is reduced, we may recognize a benefit from income taxes in our statement of operations in that period. We classify interest recognized in connection with our tax positions as interest expense, when appropriate.

Recent Accounting Pronouncements

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*. This ASU provides guidance on statement of cash flows presentation for eight specific cash flow issues where diversity in practice exists. This ASU is effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company expects that the adoption will not have a material impact on its financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The core principle of Topic 842 is that a lessee should recognize the assets and liabilities that arise from leases. For operating leases, a lessee is required to recognize a right-of-use asset and a lease liability, initially measured at the present value of the lease payments, in the statement of financial position. This ASU is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is evaluating the effect that the adoption of this ASU will have on its financial statements. The Company currently expects that its operating lease commitment will be subject to the new standard and recognized as right-of-use asset and operating lease liability upon adoption of ASU 2016-02, which will increase the total assets and total liabilities that it reports relative to such amounts prior to adoption.

Results of Operations

Research and Development Expense

Research and development expense consists primarily of costs of drug development work associated with our drug candidates, including:

- preclinical testing,
- clinical trials,
- clinical supplies and related formulation and design costs, and

- compensation and other personnel-related expenses.

Research and development expenses decreased to $7.6 million in 2017 from $9.2 million in 2016, primarily due to decreases in REMOXY related expenses and non-cash Performance Award related expenses in the year ended 2017 as compared to the same period in 2016. We received a $1.4 million research grant in 2017 from the NIH that we recorded as a reduction to our research and development expense compared to a $1.5 million research grant in 2016.

Research and development expenses included non-cash stock-related compensation expenses of $1.2 million in 2017 compared to $1.8 million in 2016.

We expect research and development expense to fluctuate over the next several years as we continue our development efforts. We expect our development efforts to result in our drug candidates progressing through various stages of clinical trials. Our research and development expenses may fluctuate from period to period due to the timing and scope of our development activities and the results of clinical trials and preclinical studies.

General and Administrative Expense

General and administrative expense consists primarily of compensation and other general corporate expenses. General and administrative expense decreased to $4.3 million in 2017 from $5.8 million in 2016 primarily due to decreases in non-cash Performance Award related expenses and the departure of our CFO in 2017 as compared in 2016.

General and administrative expenses included non-cash stock-related compensation expenses of $1.8 million in 2017 compared to $2.6 million in 2016.

We expect other general and administrative expense for 2018 will be consistent with 2017.

Interest Income

Interest and other income, net, was $38,000 in 2017 compared to $107,000 in 2016. We expect our interest income to decrease in the future as we use cash to fund our operations.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through public and private stock offerings, payments received under collaborative agreements and interest earned on our investments. We intend to continue to use our capital resources to fund research and development activities, capital expenditures, working capital requirements and other general corporate purposes. As of December 31, 2017, cash, cash equivalents and marketable securities were $10.5 million.

Net cash used in operating activities was $8.2 million for 2017 compared to $12.2 million for in 2016. The decrease was primarily due to lower research and development expenses during 2017 as compared in 2016.

Net cash provided by investing activities was $2.1 million in 2017 compared to net cash used in investing activities of $2.2 million in 2016. Investing activities for both years consisted primarily of the purchase and maturities of marketable securities.

Net cash used by financing activities was $0.3 million in 2016 resulting primarily from issuing shares of our common stock to employees for vested Performance Awards net of statutory employment taxes.

Realization of our deferred tax assets is dependent on future earnings, if any. We are uncertain about the timing and amount of any future earnings. Accordingly, we offset these net deferred tax assets with a valuation allowance.

We lease approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires in 2020. Future minimum lease payments are $0.3 million at December 31, 2017.

We have license agreements that require us to make milestone payments upon the successful achievement of milestones, including clinical milestones. Our license agreements also require us to pay certain royalties to our licensors if we succeed in

fully commercializing products under these license agreements. All of these potential future payments are cancelable as of December 31, 2017. Our formulation agreement with Durect Corporation obligates us to make certain milestone payments upon achieving clinical milestones and regulatory milestones.

We have an accumulated deficit of $157 million at December 31, 2017. We expect our cash requirements to be significant in the future. The amount and timing of our future cash requirements will depend on regulatory and market acceptance of our drug candidates and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We believe that our current resources should be sufficient to fund our operations for at least the next 12 months. We may seek additional future funding through public or private financing within this timeframe, if such funding is available and on terms acceptable to us.

Off-balance Sheet Arrangements

As of December 31, 2017, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. In addition, we do not engage in trading activities involving non-exchange traded contracts. Therefore, we are not materially exposed to financing, liquidity, market or credit risk that could arise if we had engaged in these relationships. We do not have relationships or transactions with persons or entities that derive benefits from their non-independent relationship with us or our related parties.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

The primary objective of our cash investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. For example, if we hold a security that was issued with a fixed interest rate at the then-prevailing rate and the interest rate later rises, the principal amount of our investment will probably decline. A hypothetical 50 basis point increase in interest rates reduces the fair value of our available-for-sale securities at December 31, 2017 by approximately $2,000. To minimize this risk in the future, we intend to maintain our portfolio of cash equivalents and marketable securities in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities. We have no holdings of derivative financial or commodity instruments. As of December 31, 2017, our investments consisted of investments in commercial paper, corporate notes and obligations or in money market accounts and checking funds with variable market rates of interest. We believe our credit risk is immaterial.

Item 8. ***Financial Statements and Supplementary Data***

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Pain Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Pain Therapeutics, Inc. (the Company) as of December 31, 2017 and 2016, the related statements of operations, comprehensive income (loss), stockholders' equity and cash flows for each of the two years in the period ended December 31, 2017, 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, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

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/ Ernst & Young LLP

We have served as the Company’s auditor since 2002.

Austin, Texas
February 6, 2018

PAIN THERAPEUTICS, INC.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
ASSETS		
Current assets:		
Cash and cash equivalents	$ 10,479	$ 16,615
Marketable securities	—	2,099
Other current assets	184	356
Total current assets	10,663	19,070
Property and equipment, net	156	232
Other assets	12	—
Total assets	$ 10,831	$ 19,302
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 424	$ 303
Accrued development expense	399	27
Accrued compensation and benefits	309	335
Total current liabilities	1,132	665
Noncurrent liabilities	—	—
Total liabilities	1,132	665
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $.001 par value; 10,000,000 shares authorized, none issued and outstanding	—	—
Common stock, $.001 par value; 120,000,000 shares authorized; 6,595,509 and 6,591,705 shares issued and outstanding at December 31, 2017 and 2016, respectively	7	7
Additional paid-in capital	167,091	164,118
Accumulated other comprehensive income	—	—
Accumulated deficit	(157,399)	(145,488)
Total stockholders' equity	9,699	18,637
Total liabilities and stockholders' equity	$ 10,831	$ 19,302

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Years ended December 31,	
	2017	**2016**
Operating expenses:		
Research and development	$ 7,615	$ 9,176
General and administrative	4,334	5,781
Total operating expenses	11,949	14,957
Operating loss	(11,949)	(14,957)
Interest income	38	107
Net loss	$ (11,911)	$ (14,850)
Net loss per share, basic and diluted	$ (1.82)	$ (2.28)
Shares used in computing net loss per share, basic and diluted	6,537	6,520

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.

STATEMENTS OF COMPREHENSIVE INCOME (LOSS)

(in thousands)

	Years ended December 31,	
	2017	**2016**
Net loss	$ (11,911)	$ (14,850)
Other comprehensive income (loss):		
Net unrealized gains (losses) on marketable securities	—	—
Comprehensive loss	$ (11,911)	$ (14,850)

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands)

	Common stock		Additional paid-in capital	Accumulated other comprehensive income	Accumulated deficit	Total stockholders' equity
	Shares	Par value				
Balance at December 31, 2015	6,536,588	7	159,998	—	(130,638)	29,367
Non-cash stock-related compensation for:						
Stock options for employees	—	—	3,467	—	—	3,467
Stock options for non-employees	—	—	25	—	—	25
Performance Awards and related non-cash stock-related compensation	69,286	—	842	—	—	842
Performance Awards related to statutory taxes	(14,169)	—	(214)	—	—	(214)
Other comprehensive loss	—	—	—	—	—	—
Net loss	—	—	—	—	(14,850)	(14,850)
Balance at December 31, 2016	6,591,705	7	164,118	—	(145,488)	18,637
Non-cash stock-related compensation for:						
Stock options for employees	—	—	2,954	—	—	2,954
Stock options for non-employees	—	—	19	—	—	19
Issuance of common stock pursuant to 7 to 1 Reverse stock split round up	3,804	—	—	—	—	—
Net loss	—	—	—	—	(11,911)	(11,911)
Balance at December 31, 2017	6,595,509	$ 7	$ 167,091	$ —	$(157,399)	$ 9,699

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Years ended December 31,	
	2017	**2016**
Cash flows from operating activities:		
Net loss	$ (11,911)	$ (14,850)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash stock-based compensation	2,973	4,334
Depreciation and amortization	68	58
Non-cash net interest income	(2)	(8)
Changes in operating assets and liabilities:		
Other current assets	172	86
Other non-current assets	(12)	12
Accounts payable	129	(711)
Accrued development expense	372	(867)
Accrued compensation and benefits	(26)	(288)
Net cash used in operating activities	(8,237)	(12,234)
Cash flows from investing activities:		
Purchases of property and equipment	—	(75)
Purchases of marketable securities	(399)	(4,141)
Sales of marketable securities	400	—
Maturities of marketable securities	2,100	2,050
Net cash provided (used in) investing activities	2,101	(2,166)
Cash flows from financing activities:		
Cash used for statutory taxes for net exercise of Performance Awards	—	(214)
Deferred financing costs	—	(70)
Net cash used in financing activities	—	(284)
Net decrease in cash and cash equivalents	(6,136)	(14,684)
Cash and cash equivalents at beginning of period	16,615	31,299
Cash and cash equivalents at end of period	$ 10,479	$ 16,615

See accompanying notes to financial statements.

1. General and Liquidity

Pain Therapeutics, Inc. develops proprietary drugs that offer significant improvements to patients and healthcare professionals. We generally focus our drug development efforts on disorders of the nervous system, such as chronic pain.

On November 16, 2016, we received a letter from the Listing Qualifications staff of Nasdaq (the "Staff") notifying us that, for the previous 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement (the "Minimum Price Requirement") under Nasdaq's Listing Rule 5450(a)(1) for continued listing on The Nasdaq Global Market. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), if during the 180 calendar days following the date of the notification, or prior to May 15, 2017, the closing bid price of our common stock is at or above $1.00 for a minimum of 10 consecutive business days, the Staff will provide us with written confirmation of compliance. On May 24, 2017, we received a letter from the Staff indicating that we had regained compliance with the $1.00 minimum closing bid requirement following completion of the reverse stock split described below.

On May 4, 2017, following stockholder approval, our board of directors approved a reverse stock split at a ratio of 7-for-1. On May 4, 2017, we filed with the Secretary of State of the State of Delaware a Certificate of Amendment to the Company's Amended and Restated Certificate of Incorporation to effect the 7-for-1 reverse stock split of our outstanding shares of common stock. The number of outstanding shares of common stock on the date of the reverse split was reduced from 46.1 million to 6.6 million shares. Our common stock began trading on the Nasdaq Global Market on a split-adjusted basis when the market opened for trading on May 10, 2017. As a result, all common stock share amounts included in these consolidated financial statements have been retroactively reduced by a factor of seven, and all common stock per share amounts have been increased by a factor of seven, with the exception of our common stock par value.

Liquidity

The Company has incurred significant net losses and negative cash flows since inception, and as a result has an accumulated deficit of $157 million at December 31, 2017. We expect our cash requirements to be significant in the future. The amount and timing of our future cash requirements will depend on regulatory and market acceptance of our drug candidates and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We may seek additional future funding through public or private financing within this timeframe, if such funding is available and on terms acceptable to us.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires that management make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenue earned and expenses incurred during the reporting period. Actual results could differ from those estimates.

Proceeds from Grants

In 2017, we received $1.4 million in research grants from the NIH and NIDA and $1.5 million in 2016. We record the proceeds from the grant as a reduction to our research and development expenses.

Cash Equivalents, Marketable Securities and Concentration of Credit Risk

We invest in cash equivalents and marketable securities. We consider highly-liquid financial instruments with original maturities of three months or less to be cash equivalents. Our marketable securities include interest-bearing financial instruments, generally consisting of corporate or government securities.

Our investment policy allows for investments in marketable securities with active secondary or resale markets, establishes diversification and credit quality requirements and limits investments by maturity and issuer. We maintain our investments at one financial institution.

A change in prevailing interest rates may cause the fair value of the investment to fluctuate. We do not recognize an impairment charge related to this type of fluctuation because the fluctuation is temporary and eliminated by the time an investment matures. We would recognize an impairment charge if and when we determine that a decline in the fair value below the amortized cost of an investment is other-than-temporary. We consider various factors in determining whether to recognize an impairment charge, including any adverse changes in the investees' financial condition, how long the fair value has been below the amortized cost and whether it is more likely than not that we would elect to or be required to sell the marketable security before its anticipated recovery.

We may elect to sell marketable securities before they mature. We hold these investments as "available for sale" and include these investments in our Balance Sheets as current assets, even though the contractual maturity of a particular investment may be beyond one year.

Fair Value Measurements

We report our cash equivalents and marketable securities at fair value as Level 1, Level 2 or Level 3 using the following inputs:

- Level 1 includes quoted prices in active markets. We base the fair value of money market funds and U.S. treasury securities on Level 1 inputs.
- Level 2 includes significant observable inputs, such as quoted prices for identical or similar investments, or other inputs that are observable and can be corroborated by observable market data for similar securities. We use market pricing and other observable market inputs obtained from third-party providers. We use the bid price to establish fair value where a bid price is available. We base the fair value of our marketable securities on Level 2 inputs.
- Level 3 includes unobservable inputs that are supported by little or no market activity. We do not have any investments where the fair value is based on Level 3 inputs.

We include unrealized gains or losses on our investments as Accumulated other comprehensive income (loss) in the Stockholders' equity section of our Balance Sheets. We include changes in net unrealized gains or losses in our Statements of Comprehensive Income (Loss). We would recognize significant realized gains and losses on a specific identification basis as other income in our Statements of Operations.

Business Segments

We report segment information based on how we internally evaluate the operating performance of our business units, or segments. Our operations are confined to one business segment: the development of novel drugs.

Stock-based Compensation

We recognize non-cash expense for the fair value of all stock options and other share-based awards. We use the Black-Scholes option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. For options granted to employees and directors, we recognize the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally four years. For options granted to non-employees, we remeasure the fair value expense using Black-Scholes each reporting period.

We have granted share-based awards that vest upon achievement of certain performance criteria, or Performance Awards. We multiply the number of Performance Awards by the fair market value of our common stock on the date of grant to calculate the fair value of each award. We estimate an implicit service period for achieving performance criteria for each award. We recognize the resulting fair value as expense over the implicit service period when we conclude that achieving the performance criteria is probable. We periodically review and update as appropriate our estimates of implicit

service periods and conclusions on achieving the performance criteria. Performance Awards vest and common stock is issued upon achievement of the performance criteria.

Net Loss per Share

Basic net loss per share is computed on the basis of the weighted-average number of common shares outstanding for the reporting period. Diluted net loss per share is computed on the basis of the weighted-average number of common shares outstanding plus dilutive potential common shares outstanding using the treasury-stock method. Potential dilutive common shares consist of outstanding equity awards and warrants. The numerators and denominators in the calculation of basic and diluted net loss per share were as follows (in thousands):

	Years ended December 31,	
	2017	2016
Numerator:		
Net loss	$ (11,911)	$ (14,850)
Denominator:		
Shares used in computing net loss per share, basic and diluted	6,537	6,520
Net loss per share, basic and diluted	$ (1.82)	$ (2.28)
Dilutive common shares excluded from net loss per share, diluted	2,497	2,535

We excluded weighted equity awards outstanding to purchase common stock from the calculation of diluted net loss per share because the effect of including these shares in this calculation would be anti-dilutive.

Income Taxes

We make estimates and judgments in determining the need for a provision for income taxes, including the estimation of our taxable income or loss for each full fiscal year.

We have accumulated significant deferred tax assets that reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of certain deferred tax assets is dependent upon future earnings. We are uncertain about the timing and amount of any future earnings. Accordingly, we offset these deferred tax assets with a valuation allowance.

We may in the future determine that certain deferred tax assets will likely be realized, in which case we will reduce our valuation allowance in the period in which such determination is made. If the valuation allowance is reduced, we may recognize a benefit from income taxes in our Statement of Operations in that period.

We classify interest recognized pursuant to our deferred tax assets as interest expense, when appropriate.

Recent Accounting Pronouncements

We reviewed recently issued accounting pronouncements and plan to adopt those that are applicable to us. We do not expect the adoption of these pronouncements to have a material impact on our financial position, results of operations or cash flows.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*. This ASU provides guidance on statement of cash flows presentation for eight specific cash flow issues where diversity in practice exists. This ASU is effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company expects that the adoption will not have a material impact on its financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The core principle of Topic 842 is that a lessee should recognize the assets and liabilities that arise from leases. For operating leases, a lessee is required to recognize a right-of-use asset and a lease liability, initially measured at the present value of the lease payments, in the statement of financial position. This ASU is effective for fiscal years beginning after December 15, 2018, including

interim periods within those fiscal years. The Company is evaluating the effect that the adoption of this ASU will have on its financial statements. The Company currently expects that its operating lease commitment will be subject to the new standard and recognized as right-of-use asset and operating lease liability upon adoption of ASU 2016-02, which will increase the total assets and total liabilities that it reports relative to such amounts prior to adoption.

3. Collaboration Agreements

Durect Corporation

We have an exclusive, worldwide Development and License Agreement, or the Durect Agreement, with Durect to use a patented controlled-release technology that forms the basis for REMOXY. Under the terms of the Durect Agreement, we are solely responsible for clinical development, Durect is responsible for furnishing suitable laboratory facilities, equipment and personnel during pre-clinical phases of development and we and Durect are jointly responsible for certain pre-clinical activities. We reimburse Durect's expenses and have made milestone payments based on the achievement of certain clinical or regulatory milestones.

4. Cash and Cash Equivalents and Marketable Securities

Cash, cash equivalents and marketable securities held as available-for-sale consisted of the following (in thousands):

	Cash, Cash Equivalents and Marketable Securities					
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value	Accrued Interest	Total Value
December 31, 2017						
Cash	$ 158	$ —	$ —	$ 158	$ —	$ 158
Cash equivalents	10,321	—	—	10,321	—	10,321
Total cash and cash equivalents	$ 10,479	$ —	$ —	$ 10,479	$ —	$ 10,479
Reported as:						
Cash and cash equivalents	$ 10,479	—	—	$ 10,479	$ —	$ 10,479
Marketable securities	—	—	—	—	—	—
	$ 10,479	$ —	$ —	$ 10,479	$ —	$ 10,479
Maturities:						
Matures in one year or less	$ 10,479	$ —	$ —	$ 10,479	$ —	$ 10,479
Matures one to three years	—	—	—	—	—	—
	$ 10,479	$ —	$ —	$ 10,479	$ —	$ 10,479
December 31, 2016						
Cash	$ 1,434	$ —	$ —	$ 1,434	$ —	$ 1,434
Cash equivalents	12,783	—	—	12,783	—	12,783
Commercial paper	4,497	—	—	4,497	—	4,497
Total cash and cash equivalents	$ 18,714	$ —	$ —	$ 18,714	$ —	$ 18,714
Reported as:						
Cash and cash equivalents	$ 16,615	—	—	$ 16,615	$ —	$ 16,615
Marketable securities	2,099	—	—	2,099	—	2,099
	$ 18,714	$ —	$ —	$ 18,714	$ —	$ 18,714
Maturities:						
Matures in one year or less	$ 18,714	$ —	$ —	$ 18,714	$ —	$ 18,714
Matures one to three years	—	—	—	—	—	—
	$ 18,714	$ —	$ —	$ 18,714	$ —	$ 18,714

To date we have not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

Our assets measured at fair value were (in thousands):

	Level 1	Level 2	Level 3	Total
December 31, 2017				
Cash and cash equivalents	$ 10,479	$ —	$ —	$ 10,479
Commercial paper	—	—	—	—
	$ 10,479	$ —	$ —	$ 10,479
December 31, 2016				
Cash and cash equivalents	$ 14,217	$ —	$ —	$ 14,217
Commercial paper	—	4,497	—	4,497
	$ 14,217	$ 4,497	$ —	$ 18,714

5. Property and Equipment

Property and equipment includes furniture and equipment with a purchase value of $1.0 million at December 31, 2017 and 2016. Depreciation is recognized using the straight-line method over the expected life of the property and equipment. Accumulated depreciation was $0.8 million at December 31, 2017 and $0.7 million at December 31, 2016.

6. Stockholders' Equity and Stock-Based Compensation

Preferred Stock

Our Board of Directors has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges, restrictions and the number of shares constituting any series or the designation of the series.

2008 Equity Incentive Plan

Under our 2008 Equity Incentive Plan, or 2008 Equity Plan, our employees, directors and consultants received share-based awards, including grants of stock options and Performance Awards. Our Board of Directors or a designated Committee of the Board is responsible for administration of the 2008 Equity Plan and determined the terms and conditions of each option granted, consistent with the terms of the plan. The 2008 Equity Plan expired in December 2017. Share-based awards generally expire ten years from the date of grant.

When stock options or Performance Awards are exercised net of the exercise price and taxes, the number of shares of stock issued is reduced by the number of shares equal to the amount of taxes owed by the award recipient and that number of shares are cancelled. We then use our cash to pay tax authorities the amount of statutory taxes owed by and on behalf of the award recipient.

Stock Options

The following summarizes information about stock option activity during 2017:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			In years	In millions
Outstanding as of December 31, 2016	2,435,249	$ 25.19	4.8	$ —
Options granted	1,026,410	$ 3.68		
Options exercised	—	$ —		
Options forfeited/canceled	(479,504)	31.73		
Outstanding as of December 31, 2017	2,982,155	$ 16.74	6.2	$ 0.4
Vested and expected to vest at December 31, 2017	2,982,155	$ 16.74	6.2	$ 0.4
Exercisable at December 31, 2017	1,757,688	$ 24.02	4.1	$ —

The following summarizes information about stock options at December 31, 2017 by a range of exercise prices:

		Options outstanding			Options exercisable	
Range of exercise prices		Number of outstanding options	Weighted average remaining contractual life (in years)	Weighted average exercise price	Number of vested options	Weighted average exercise price
From	To					
$ 3.24	$ 4.09	933,200	9.8	$ 3.59	46,458	$ 3.25
$ 4.10	$ 15.61	620,243	7.5	$ 11.63	345,168	$ 12.51
$ 16.31	$ 23.38	628,411	3.9	$ 19.05	597,399	$ 19.16
$ 23.59	$ 35.00	656,841	2.9	$ 30.41	626,841	$ 30.24
$ 36.40	$ 53.55	143,460	3.4	$ 51.66	141,822	$ 51.82
		2,982,155	6.2	$ 16.74	1,757,688	$ 24.02

We use Black-Scholes to estimate the fair value of options granted. Black-Scholes considers a number of factors, including the market price of our common stock. For options granted to employees and directors, we used certain factors to value each stock option granted, which resulted in a weighted average fair value of options granted during 2017 and 2016, as follows:

	2017	2016
Volatility	79% to 83%	72%
Risk-free interest rates	2% to 2.4%	1% to 2%
Expected life of option	7 years	7 years
Dividend yield	zero	zero
Forfeiture rate	zero	zero
Weighted average fair value of stock options granted	$2.74	$1.60

Volatility is based on reviews of the historical volatility of our common stock. Risk-free interest rates are based on yields of U.S. treasury notes in effect at the date of grant. Expected life of option is based on actual historical option exercises. Dividend yield is zero because we do not anticipate paying cash dividends in the foreseeable future. We estimate forfeitures and adjust this estimate periodically based in part on the extent to which actual forfeitures differ from our estimates.

For options granted to non-employees, we estimate the fair value of stock options granted using factors similar to those used for stock options granted to employees and directors and appropriate for the terms underlying the stock options granted to non-employees. We re-measure the compensation expense for options granted to non-employees each reporting period.

As of December 31, 2017, we expect to recognize compensation expense of $5.3 million related to non-vested options held by employees and directors over the weighted average remaining recognition period of 3.2 years.

Performance Awards

The following summarizes information about Performance Award activity during 2017:

	Number of Performance Awards
Outstanding as of December 31, 2016	222,060
Granted	—
Vested Performance Awards	—
Forfeited/Canceled	(69,720)
Outstanding as of December 31, 2017	152,340

If and when outstanding Performance Awards vest, we would recognize $2.5 million in non-cash stock-based compensation expense. These Performance Awards expire between 2022 and 2026.

Stock-Based Compensation Expense

The following summarizes information about non-cash stock-based compensation expense, in thousands:

	Years ended December 31,	
	2017	2016
Research and development		
Vesting of stock options	$ 1,205	$ 1,313
Vesting of Performance Awards	—	438
	1,205	1,751
General and administrative		
Vesting of stock options	1,768	2,179
Vesting of Performance Awards	—	404
	1,768	2,583
Total non-cash stock-based compensation expenses		
Vesting of stock options	2,973	3,492
Vesting of Performance Awards	—	842
	$ 2,973	$ 4,334

Non-cash stock-related compensation expense related to vesting of Performance Awards was associated with the resubmission of the NDA for REMOXY.

7. Employee 401(k) Benefit Plan

We have a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all employees. Employees are eligible to participate in the plan the first day of the month after hire and may contribute up to the current statutory limits under Internal Revenue Service regulations. The 401(k) plan permits us to make additional matching contributions on behalf of all employees. Through December 31, 2017, we have not made any matching contributions to the 401(k) plan.

8. Income Taxes

U.S. Tax Reform

On December 22, 2017, legislation commonly known as the Tax Cuts and Jobs Act, or the Act, was signed in to law. The Tax Act, among other changes, reduces the U.S. federal corporate tax rate from 35% to 21%, requires taxpayers 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 sourced earnings. On December 31, 2017, the Company did not have any foreign subsidiaries and the international aspects of the Tax Act are not applicable.

In connection with the initial analysis of the impact of the Tax Act, the Company remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The remeasurement of the Company's deferred tax balance was primarily offset by application of its valuation allowance. The Company is still in the process of analyzing the impact to the Company of the Tax Act. Where the Company has been able to make reasonable estimates of the effects for which its analysis is not yet complete, the Company has recorded provisional amounts. Where the Company has not yet been able to make reasonable estimates of the impact of certain elements, the Company has not recorded any amounts related to those elements and has continued accounting for them in accordance with ASC 740 on the basis of the tax laws in effect immediately prior to the enactment of the Tax Act.

We did not provide for income taxes in 2017 and 2016 because we had a net operating loss for tax purposes in those years and the tax benefit that would have resulted from the statutory rate was fully offset by the valuation allowance.

Deferred tax assets and valuation allowance

Deferred tax assets reflect the tax effects of net operating loss and tax credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. We reduced our deferred taxes assets at December 31, 2017 for the reduced corporate tax rate to 21% in recently enacted tax legislations. We offset our deferred tax assets by a valuation allowance because we are uncertain about the timing and amount of any future profits. Significant components of our deferred tax assets are as follows (in thousands):

	December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 15,600	$ 22,300
Stock-related compensation	5,300	9,100
Research & development credit carryforwards	6,400	6,200
Other	200	200
	27,500	37,800
Valuation allowance	(27,500)	(37,800)
	$ —	$ —

As of the beginning of 2017, we increased both our net operating loss carryforwards and our valuation allowance by $0.9 million when we adopted ASU 2016-09 for certain tax deductions associated with stock option transactions greater than the stock-related compensation expense in our financial statements. The valuation allowance decreased by $10.3 million in 2017 and increased by $3.6 million in 2016.

Our pre-tax net operating loss carryforwards of $74 million are federal and expire between 2029 and 2036. As of December 31, 2017, we had federal research and development tax credits of approximately $10.7 million, which expire in the years 2023 through 2036.

Unrecognized tax benefits

We have unrecognized tax benefits related to tax credits. We added to our unrecognized tax benefits in 2017 and 2016 as follows (in thousands):

	2017	2016
Beginning balance	$ 4,200	$ 4,000
Additions based on tax positions related to the current year	100	200
Ending balance	$ 4,300	$ 4,200

9. Leases and Commitments

We lease approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires in December 2020. Future minimum lease payments are (in thousands).

	2018	2019	2020	Total
Minimum lease payments	$ 91	$ 95	$ 99	$ 285

We believe that our facilities are adequate and suitable for our current needs. Rent expense was $0.1 million both in 2017 and 2016.

We conduct our product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. We have contractual arrangements with these organizations, however these contracts are cancelable on thirty days' notice and our obligations under these contracts are largely based on services performed.

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

None.

Item 9A. *Controls and Procedures*

Evaluation of disclosure controls and procedures.

Our management, with the participation of our Chief Executive Officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer (as Principle Executive Officer and Principal Financial Officer) has concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission, or SEC, rules and forms and that such information is accumulated and communicated to management as appropriate to allow timely decisions regarding required disclosures.

Management's annual report on internal control over financial reporting. We are responsible for establishing and maintaining adequate internal control over our financial reporting. We have assessed the effectiveness of internal control over financial reporting as of December 31, 2017. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control-Integrated Framework (2013 Framework).

Our internal control over financial reporting is a process designed 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. Our internal control over financial reporting includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our 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 authorizations of our management and board of directors; and
(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Based on the COSO criteria, we believe our internal control over financial reporting as of December 31, 2017 was effective.

Changes in internal control over financial reporting.

As previously announced, on February 14, 2017, Peter S. Roddy resigned, effective March 9, 2017, as Vice President, Chief Financial Officer and Secretary. Remi Barbier, President and Chief Executive Officer, has assumed the role of Principal Financial Officer until such time as a new Chief Financial Officer is appointed.

Item 9B. *Other Information*

None**.**

PART III

Item 10. *Directors and Executive Officers and Corporate Governance*

The information regarding our directors, executive officers, director nomination process and the audit committee of our board of directors is incorporated by reference from "Directors and Executive Officers" in our Proxy Statement for our 2018 Annual Meeting of Stockholders.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Securities Exchange Act of 1934, as amended requires our executive officers and directors and persons who own more than ten percent (10%) of a registered class of our equity securities to file reports of ownership and changes in ownership with the SEC. Executive officers, directors and greater than ten percent (10%) stockholders are required to furnish us with copies of all Section 16(a) forms they file. We believe all of our executive officers and directors complied with all applicable filing requirements during 2017.

Code of Ethics

We have adopted a Code of Ethics that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. We publicize the Code of Ethics through posting the policy on our website, http://www.paintrials.com. We will disclose on our website any waivers of, or amendments to, our Code of Ethics.

Item 11. *Executive Compensation*

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Executive Compensation and Other Matters."

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

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Security Ownership of Certain Beneficial Owners and Management."

The following table summarizes the securities authorized for issuance under our equity compensation plans as of December 31, 2017:

	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans
Equity compensation plans approved by stockholders	3,134,495	$ 15.92	58,017
Equity compensation plans not approved by stockholders	—	—	—
	3,134,495	$ 15.92	58,017

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

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Certain Relationships and Related Transactions."

Item 14. ***Principal Accountant Fees and Services***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading **"**Principal Accountant Fees and Services."

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of this Form 10-K:

(1) *Financial Statements (included in Part II of this report):*
Report of Independent Registered Public Accounting Firm
Balance Sheets
Statements of Operations
Statements of Comprehensive Income
Statements of Stockholders' Equity
Statements of Cash Flows
Notes to Financial Statements

(2) *Financial Statement Schedules:*
All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

(3) *Management Contracts, Compensatory Plans and Arrangements.*
Management contracts, compensatory plans and arrangements are indicated by the symbol "*" in the applicable exhibits listed in Item 15(b), below.

(b) *Exhibits*

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished.

			Incorporated by Reference			
Exhibit No.		Description	Form	Filing Date	Exhibit No.	Filed Herewith
3.1		Amended and Restated Certificate of Incorporation.	10-Q	7/29/2005	3.1	
3.2		Amended and Restated Bylaws.	10-Q	4/24/2013	3.2	
3.3		Amended and Restated Certificate of Incorporation	8-K	5/8/2017	3.1	
4.1		Specimen Common Stock Certificate.	10-Q	7/29/2005	4.1	
10.1	*	Form of Indemnification Agreement between Pain Therapeutics and each of its directors and officers.	S-1	3/14/2000	10.1	
10.3	*	Employment Agreement dated October 23, 2001, between Registrant and Nadav Friedmann, PhD. M.D.	10-K	3/22/2002	10.5	
10.4	+	Development and License Agreement dated December 19, 2002 between Registrant and DURECT Corporation and Southern Biosystems, Inc.	10-K	2/24/2006	10.10	
10.5	+	Amendment dated December 15, 2005 to Development and License Agreement dated December 19, 2002 between Registrant and DURECT Corporation and Southern Biosystems, Inc.	10-K	2/24/2006	10.11	
10.11	*	Employment Agreement dated July 1, 1998 and amended December 17, 2008 between Registrant and Remi Barbier.	10-K	2/13/2009	10.12	
10.12	*	2000 Employee Stock Purchase Plan, as amended and restated.	10-Q	7/29/2010	10.1	
10.13		Lease agreement, dated as of February 14, 2011 between Registrant and StoneCliff Office, L.P.	10-Q	4/27/2011	10.1	
10.14	*	Amendment Number 1 to the 2008 Equity Incentive Plan.	10-Q	8/1/2013	10.1	
10.15	*	Amendment No. 2 to Employment Agreement between Registrant and Remi Barbier.	10-Q	8/1/2013	10.2	
10.16		Second Amendment to Lease Agreement, dated as of April 8, 2014 between Registrant and StoneCliff Office, L.P.	10-Q	8/6/2014	10.1	
10.17		Third Amendment to Lease Agreement, dated as of November 3, 2017 between Registrant US REIF Eurus Austin, LLC dba StoneCliff Building as successor in interest to StoneCliff Office, L.P.				X
23.1		Consent of Independent Registered Public Accounting Firm.				X

24.1	Power of Attorney (included in the signature page to this report).	X
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1	Certifications of the Chief Executive Officer and the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	XBRL Instance Document.	X
101.SCH	XBRL Taxonomy Extension Schema Document.	X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.	X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.	X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.	X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	X

* Management contract, compensatory plan or arrangement.
+ Portions of this Exhibit are subject to a confidential treatment order.

(c) *Financial Statement Schedules*

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

Item 16. ***Form 10-K Summary***

The Company has elected not to included summary information.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Pain Therapeutics, Inc.
(Registrant)

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

Dated: February 6, 2018

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Remi Barbier his true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ REMI BARBIER Remi Barbier	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer and Principal Financial Officer)	February 6, 2018
/s/ NADAV FRIEDMANN, PH.D., M.D. Nadav Friedmann, Ph.D., M.D.	Chief Operating and Medical Officer and Director	February 6, 2018
/s/ ROBERT Z. GUSSIN, PH.D. Robert Z. Gussin, Ph.D.	Director	February 6, 2018
/s/ MICHAEL J. O'DONNELL, ESQ. Michael J. O'Donnell, Esq.	Director	February 6, 2018
/s/ SAIRA RAMASASTRY Saira Ramasastry	Director	February 6, 2018
/s/ SANFORD R. ROBERTSON Sanford R. Robertson	Director	February 6, 2018
/s/ PATRICK SCANNON, M.D, PH.D. Patrick Scannon, M.D., Ph.D.	Director	February 6, 2018

Exhibit 10.17

October 3, 2017

THIRD AMENDMENT TO LEASE AGREEMENT

Re: Lease Agreement dated December 28, 2010, by and between US REIF Eurus Austin, LLC dba StoneCliff Building as successor in interest to StoneCliff Office, L.P., as Lessor, and Pain Therapeutics, Inc., as Lessee, as amended in that First Amendment to Lease Agreement dated September 21, 2011, as amended in that Second Amendment dated April 3, 2014 (collectively referred to as the "Lease Agreement"), demising 5,679 rentable square feet of space locally known as Suite 260 in the StoneCliff building, located at 7801 Capital of Texas Highway, Austin, Travis County, Texas, 78731.

This Third Amendment shall amend and modify the Lease Agreement as follows:

1. Lease Term. Lessor and Lessee acknowledge and agree that Lessee's lease term shall be extended thirty-six (36) months from the current expiration of December 31, 2017 to December 31, 2020.

2. Base Rent. Effective January 1, 2018, Lessee shall pay to Lessor Base Rent as set forth in the rent schedule below:

Term	Monthly Base Rent	Term Base Rent	Annual Base Rent PSF
01/01/2018 - 12/31/2018	$7,572.00	$90,864.00	$16.00
01/01/2019 - 12/31/2019	$7,926.94	$95,123.25	$16.75
01/01/2020 - 12/31/2020	$8,281.88	$99,382.50	$17.50

3. Tenant Finish Out. None. Lessee accepts premises on an "as is" basis.

4. Additional Rents. Effective January 1, 2018, Lessee's expense stop shall adjust to a $0.00 Base Year, and Lessee shall thereafter reimburse Lessor for its pro rata share of Building Operating Expenses (currently estimated to be $13.22 per square foot per year or $6,256.37 per month), as defined in Exhibit C of the Lease Agreement.

5. Reserved Parking: Lessee shall have Three (3) covered reserved parking spaces free of charge.

Except as provided to the contrary herein, all the remaining terms, covenants, and provisions of the Lease Agreement shall remain in full force and effect and unmodified hereby. Each party hereby acknowledges that the other is not in default under the Lease Agreement in any respect. Each signatory hereto represents and warrants that he or she is authorized to execute this document and that upon said execution by both parties, this document will constitute the binding obligation of the party on behalf of whom such person has signed, without the necessity of joinder of any other person or entity.

EXECUTED on the dates set forth below our respective signatures.

LESSOR:		LESSEE:	
US REIF EURUS AUSTIN, LLC dba STONECLIFF BUILDING		PAIN THERAPEUTICS, INC.	
By:	/s/ Paul J. Nasser	By:	/s/ Remi Barbier
Name:	Paul J. Nasser	Name:	Remi Barbier
Title:	CFO/COO	Title:	President & CEO
Date:	November 7, 2017	Date:	November 3, 2017

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements (Forms S-3 No. 333-217319) of Pain Therapeutics, Inc. and in the related Prospectus, and in the Registration Statements (Form S-8 No. 333-168390) 2000 Employee Stock Purchase Plan of Pain Therapeutics, Inc. of our report dated February 6, 2018, with respect to the financial statements of Pain Therapeutics, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/Ernst &Young LLP

Austin, Texas
February 6, 2018

EXHIBIT 31.1

PRINCIPAL EXECUTIVE OFFICER CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Remi Barbier, certify that:

1. I have reviewed this Report on Form 10-K of Pain Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 6, 2018

CERTIFICATIONS OF THE CHIEF EXECUTIVE OFFICER AND THE
CHIEF FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Remi Barbier, Chairman of the Board of Directors, President and Chief Executive Officer (as Principal Executive Officer and Principal Financial Officer) of Pain Therapeutics, Inc. (the "Company"), hereby certify that to the best of our knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and to which this certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13 (a) or 15 (d) of the Securities Exchange Act of 1934, and

2. The information contained in this Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 6, 2018

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)