Recro Pharma, Inc.
Form 10-K
March 09, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission File Number: 001-36329

Recro Pharma, Inc.

(Exact name of registrant as specified in its charter)

Pennsylvania	26-1523233
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
490 Lapp Road, Malvern, Pennsylvania	19355
(Address of principal executive offices)	(Zip Code)

(484) 395-2470

(Registrant’s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Exchange on Which Registered
Common Stock, par value $0.01	Nasdaq Capital Market

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 (§229.405) 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, or a smaller reporting company. See the definitions of “large accelerated filer,” “accelerated filer,” and “smaller reporting company” in Rule 12b-2 of the Exchange Act.

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

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

On the last business day of the most recently completed second fiscal quarter, the aggregate market value (based on the closing sale price of its common stock on that date) of the voting stock held by non-affiliates of the registrant was $36.1 million.

As of March 8, 2017, there were 19,050,966 shares of common stock outstanding, par value $0.01 per share.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates certain information by reference from the registrant's proxy statement for the 2017 annual meeting of shareholders to be filed no later than 120 days after the end of the registrant's fiscal year ended December 31, 2016.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K and the documents incorporated by reference herein contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this Annual Report on Form 10-K or the documents incorporated by reference herein regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “pla “predict,” “project,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward- looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K and the documents incorporated herein by reference include, among other things, statements about:

- our estimates regarding expenses, future revenue, capital requirements and timing and availability of and the need for additional financing;
- the results, timing and outcome of our clinical trials of injectable meloxicam or our other product candidates, and any future clinical and preclinical studies;
- the ability to obtain and maintain regulatory approval of injectable meloxicam and our product candidates, and the labeling under any approval that we may obtain;
- our ability to successfully commercialize injectable meloxicam or our other product candidates, upon regulatory approval;
- our ability to comply with the regulatory schemes applicable to our business and other regulatory developments in the United States and foreign countries;
- our ability to raise future financing and attain profitability for continued development of our business and our product candidates and to meet required debt payments, and any milestone payments owing to Alkermes plc, or Alkermes, or our other licensing and collaboration partners;
- our ability to operate under increased leverage and associated lending covenants;
- the performance of third-parties upon which we depend, including third-party contract research organizations, or CRO’s, and third-party suppliers and manufacturers;
- our ability to obtain patent protection and defend our intellectual property rights against third-parties;
- our ability to maintain our relationships and contracts with our key commercial partners;
- our ability to recruit or retain key scientific, technical, commercial, and management personnel or to retain our executive officers; and
- our ability to comply with stringent U.S. and foreign government regulation in the manufacture of pharmaceutical products, including Good Manufacturing Practice, or cGMP, compliance and U.S. Drug Enforcement Agency, or DEA, compliance.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly under “Risk Factors,” that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we incorporate by reference herein completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

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PART I

Item 1. Business

Overview

We are a specialty pharmaceutical company that operates through two business divisions: an Acute Care division and a revenue-generating contract development and manufacturing, or CDMO division, through which we operate a manufacturing facility in Gainesville, Georgia. We believe that we can bring valuable therapeutic options for patients, prescribers and payors, such as our lead product candidate, injectable meloxicam, and other products, to the hospital and related markets. We believe we can create value for our shareholders through the development, approval and commercialization of our pipeline assets as well as through the ongoing contributions of our cash-flow positive CDMO division. In addition to our pipeline, we are always evaluating acquisition and in-licensing opportunities that can contribute additional revenue and cash flow.

Acute Care

Our Acute Care division is primarily focused on developing innovative products for hospital and related settings. Our lead product candidate is a proprietary injectable form of meloxicam, a long-acting preferential COX-2 inhibitor. Intravenous, or IV, meloxicam has successfully completed two pivotal Phase III clinical trials in prescription of post-operative pain, one evaluating pain relief over a 48-hour period in a hard tissue, post-operative pain model (bunionectomy) and the other evaluating pain relief over a 24-hour period in a soft tissue, post-operative pain model (abdominoplasty). We believe that IV meloxicam compares favorably to competitive therapies in onset of pain relief, duration of pain relief, extent of pain relief and time to peak analgesic effect and that it has been well tolerated. Overall we expect to enroll a total of approximately 1,100 patients in our Phase III program. To complete this program, we await final visits for more than 700 patients enrolled following a variety of surgical procedures in our additional safety study of IV meloxicam. Assuming we continue to observe a favorable safety profile in the safety study, we anticipate filing a new drug application, or NDA, for IV meloxicam with the U.S. Food and Drug Administration, or FDA, in the summer of 2017. We believe injectable meloxicam, as a non-opioid product, will overcome many of the issues associated with commonly prescribed opioid therapeutics, including respiratory depression and constipation, along with excessive nausea and vomiting, as well having no addiction potential while maintaining analgesic, or pain relieving, effects. We are pursuing a Section 505(b)(2) regulatory strategy for injectable meloxicam.

Our pipeline also includes other early-stage product candidates. Dex-IN, a proprietary intranasal formulation of dexmedetomidine, or Dex, is in a class of drugs called alpha-2 adrenergic agonists. We have studied Dex-IN for the treatment of post-operative pain and, based on clinical trial results and feedback from the FDA, we are exploring Dex-IN for use in treatment of peri-procedural pain. In addition to Dex-IN, we have another selective alpha-2 agonist product candidate in our pipeline, Fadolmidine, or Fado, which we believe also shows promise in neuropathic pain based on preclinical data.

Pipeline

CDMO

Our CDMO division leverages our formulation expertise to develop and manufacture pharmaceutical products using our proprietary delivery technologies for commercial partners who commercialize or plan to commercialize these products. These collaborations result in revenue streams including royalties, profit sharing, research and development and manufacturing, which support continued operations for our CDMO division and have contributed funds to be used in our research and development in our Acute Care division. We operate a 97,000 square foot, DEA-licensed manufacturing facility in Gainesville, Georgia and we currently develop and/or manufacture the following key products with our commercial partners: Ritalin LA®, Focalin XR®, Verelan PM®, generic Verapamil and Zohydro ER®, as well as development stage products.

Our Strategy

We believe that we can bring valuable therapeutic options for patients, prescribers and payors, such as injectable meloxicam and other projects to the hospital and related markets. We believe we can create value for our shareholders through the development, approval and commercialization of our pipeline assets as well as through the ongoing contributions of our cash-flow positive CDMO division. In addition to our pipeline, we are always evaluating acquisition and in-licensing opportunities that can contribute additional revenue and cash flow. Near term goals for our Acute Care division include:

Complete clinical development and regulatory approval of injectable meloxicam for moderate to severe pain. Our key 2017 goal is to file an NDA, and ultimately receive FDA approval of injectable meloxicam for the management of moderate to severe pain. IV meloxicam has recently successfully completed two pivotal Phase III clinical trials in pain management. To complete our Phase III program, we await final visits for more than 700 patients enrolled following a variety of surgical procedures in our additional safety study of IV meloxicam. Assuming we continue to observe a favorable safety profile in the safety study, we anticipate filing the NDA for IV meloxicam with the FDA in the summer of 2017.

Commercialize injectable meloxicam in the United States independently or with third-parties. We believe injectable meloxicam targets a group of specialist prescribers which would allow for successful marketing and commercialization by a company of our size. We are currently preparing for a potential U.S. commercial launch of IV meloxicam, if approved, and we plan to establish sales, marketing and reimbursement functions to commercialize IV meloxicam in the United States.

Enter into strategic partnerships to maximize the potential of our product candidates outside of the United States. We intend to pursue strategic collaborations with other pharmaceutical companies to develop and commercialize our product candidates outside of

the United States. We believe that our management expertise and unique product candidates make us an attractive partner to potential strategic companies.

Leverage our management and development experience to explore other indications for injectable meloxicam and to develop our other pipeline product candidates. If we have sufficient additional resources, we plan to evaluate injectable meloxicam for potential additional indications. In addition, our early-stage product pipeline includes proprietary drug solutions for peri-procedural pain, chronic pain, post-operative pain and peripheral neuropathy, utilizing multiple delivery systems, including intrathecal/epidural, transdermal, intranasal and sublingual platforms. Our goal is to leverage our drug development expertise along with innovative delivery systems to develop these product candidates to improve quality of life for the millions of people suffering from moderate-to-severe pain annually.

Acquire additional products and product candidates. We may identify and license, co-promote or acquire commercial products or product candidates for use in hospital or related settings.

Near term goals for our CDMO division include:

Expand our contract development and manufacturing business. We are focused on the growth of our development, formulation and manufacturing services. We intend to seek additional manufacturing and development partnerships with partners through ongoing business development efforts, as well as possibly through expansion of our proprietary drug delivery technologies, and service offerings.

Acute Care

Our Acute Care division is primarily focused on developing innovative products for hospital and related settings.

Our Lead Product Candidate – Injectable Meloxicam

Meloxicam is a long-acting, preferential COX-2 inhibitor that possesses analgesic, anti-inflammatory, and antipyretic activities, which are believed to be related to the inhibition of cyclooxygenase, or COX, and subsequent reduction in prostaglandin biosynthesis.

Our proprietary injectable form of the drug, which utilizes NanoCrystal™ technology, provides a faster onset of action of meloxicam and provides a rapid treatment of acute pain which lasts for approximately 24 hours.

Post-Operative Pain Market

Based upon statistics from the National Center for Health Statistics, it is estimated that there are over 100 million surgeries performed in the United States each year. Of these surgeries, we believe at least 50 million procedures require post-operative pain medication. Additionally, despite efforts to improve the provision of perioperative analgesia, the proportion of patients reporting moderate to severe pain after surgery has remained constant over the past decade.

While opioids provide effective analgesia for post-operative pain, their use should be limited due to the know side effects of constipation, nausea, vomiting, respiratory depression, the development of tolerance and the potential for addiction and abuse. Due to the potential for abuse, opioids are regulated as controlled substances and are listed on Schedule II and III by the DEA. According to a January 2016 article in the New England Journal of Medicine, overdose deaths from prescription painkillers (defined to mean opioid or narcotic pain relievers) have increased significantly over the past 14 years and emergency department visits involved with misusing or abusing prescription

opioid painkillers increased 153% between 2004 and 2011. In the acute care setting, and according to the Joint Commission Sentinel Event Alert on the Safe Use of Opioids in Hospitals, opioid analgesics rank among the drugs most frequently associated with adverse drug events. As a result of the addictive potential and side effects, pain sufferers tend to limit their use of opioids, resulting in as many as 40% of post-operative patients reporting inadequate pain relief. This reduces the quality of life for individuals and creates an economic burden estimated to be at least $560 to $635 billion a year in medical costs and lost productivity.

Efforts to improve pain control with multimodal analgesia are being mandated by many medical societies as a way to decrease opioid-related morbidity and mortality. Multimodal analgesia, or MMA, refers to the use of two or more drugs or nonpharmacologic interventions with differing mechanisms. Its use has been demonstrated to limit the amount of opioids consumed and provide more effective pain control than opioids alone. Effective MMA may further lessen the cost burden and personal toll of opioid-centric regimens. Opioid-related adverse events negatively impact patients and the healthcare system and cause a 55% longer length of hospital stay, 47% higher cost of care, 36% higher 30-day readmission rates and a 3.4% higher risk of inpatient mortality.

We believe that injectable meloxicam offers an attractive alternative for relief of moderate to severe pain without the risks associated with opioids. We also believe it can be an important part of an MMA approach for patients in the post-operative setting. Accordingly, we believe that physicians, hospitals and third-party payors, including Medicare and Medicaid, are highly interested in new non-opioid pain therapies that provide effective post-operative pain relief without the adverse issues associated with opioids.

Injectable Meloxicam Advantages

We believe injectable meloxicam has a number of advantages over existing, FDA approved analgesics, including the following:

Does not cause respiratory depression. Meloxicam does not cause respiratory depression. Besides the addictive nature of opioids, we believe that medical practitioners are highly concerned with respiratory depression, which is a well-documented side effect of opioid use (all opioids, including fentanyl and oxycodone). Respiratory depression, which is defined by inadequate ventilation leading to increased carbon dioxide levels and respiratory acidosis, is an established outcome of opioid use. One of the more concerning adverse effects of chronic opioid use, for which tolerance does not develop, is respiratory depression during sleep, which can be life threatening. Meloxicam has demonstrated through multiple clinical trials and patient use that it does not cause respiratory depression.

Not considered a controlled substance. Meloxicam is not an opioid and not a controlled substance. Opioid therapeutics are currently controlled by the DEA under the Controlled Substances Act. Under this act, opioids have been scheduled based on their potential for abuse and/or addiction. For those opioids placed in Schedule II, federal law prohibits the refilling of prescriptions, thus requiring patients to request, and physicians to write, additional prescriptions for each refill. Examples of Schedule II opioids include morphine, fentanyl, sufentanil, hydrocodone and oxycodone.

Onset of pain relief. IV NanoCrystal™ results in a rapid onset of pain relief in approximately 10 minutes (Study-04). IV Ketorolac, for example, can take up to 30 minutes for the onset of pain relief.

Duration of pain relief. IV meloxicam utilizing NanoCrystal™ technology has demonstrated the potential to be an effective analgesic for up to 24 hours after a single dose in clinical trials. IV forms of ketorolac, ibuprofen and acetaminophen provide effective pain relief up to four to six hours, resulting in the need for four to six doses for every 24 hours.

Time to peak analgesic effect. Clinical data has demonstrated that IV meloxicam reaches peak analgesic effect within approximately 40 minutes of administration, reaching its peak faster than competing non-opioid therapeutics. Ketorolac can take between 1 to 2 hours to reach its peak analgesic effect.

Administration. We believe that IV meloxicam has an administration advantage in terms of bolus injection, whereas ibuprofen and acetaminophen can take up to 15 to 30 minutes to infuse. In addition, there is an Intramuscular, or IM, formulation of meloxicam, while neither ibuprofen nor acetaminophen currently have IM formulations.

GI Tolerability. Unlike opioids, the mechanism of action of meloxicam provides analgesic activity with limited adverse activity on gastrointestinal motility thus limiting or avoiding the common unwanted side effects of opioids, referred to as Opioid Induce Bowel Dysfunction, or OIBD. OIBD comprises several symptoms including constipation, anorexia, nausea and vomiting, gastroesophageal reflux, delayed digestion, abdominal pain, flatulence, bloating, hard stool, straining during bowel movement and incomplete evacuation.

Clinical Development

Multiple clinical trials have been conducted to evaluate the safety, pharmacokinetics and analgesic potential of IV meloxicam. Based on the results of these trials, we believe IV meloxicam has the potential to be a potent analgesic in the management of moderate to severe pain. In early 2016, based on feedback from the FDA, we commenced our Phase III clinical trial program for IV meloxicam. The program includes two pivotal Phase III clinical trials, in both hard and soft tissue post-op patients; both of which have been successfully completed. Overall we expect to enroll a total of approximately 1,100 patients in our Phase III program. To complete this program, we await final visits for more than 700 patients enrolled following a variety of surgical procedures in our additional safety study of IV meloxicam. The population selected for inclusion in the safety study is intended to replicate real world use of injectable meloxicam. Assuming we continue to observe a favorable safety profile in the safety study, we anticipate filing an NDA for IV meloxicam with the FDA in the summer of 2017. In addition, we plan to conduct Phase IIIB clinical trials for IV meloxicam.

Additional studies with IV meloxicam evaluated the pharmacokinetics of IV meloxicam in subjects with mild renal impairment as well as IV meloxicam’s potential to impact electrocardiogram, or ECG, parameters. These studies demonstrated that there is not a meaningful clinical difference in meloxicam plasma exposure in subjects older than 65 years with mild renal impairment compared to

a younger, healthy group of subjects and that therapeutic and supratherapeutic doses of IV meloxicam did not affect cardiac repolarization in the form of prolonged QTcF interval, or in other measures including QTcB, HR, PR and QRS. Per the Pediatric Study Plan Agreement with FDA, two clinical trials will be conducted in the pediatric population. These trials will be initiated following an NDA approval of IV meloxicam.

Phase III Clinical Trials

Study REC-15-016

In July 2016, we announced positive results from one pivotal clinical trial, evaluating pain relief over a 48-hour period in a hard tissue, post-operative pain model (bunionectomy). In the trial, IV meloxicam achieved the primary endpoint of a statistically significant difference in Summed Pain Intensity Difference, or SPID, over the first 48 hours, or SPID48, compared to placebo. This was a Phase III, randomized, multicenter, multi-dose, double-blind, placebo-controlled study evaluating IV meloxicam in the management of post-operative pain following bunionectomy surgery. Two hundred and one patients who met the eligibility criteria were randomized to receive either IV meloxicam (30 mg) or placebo once daily for three days. Following the beginning of treatment, patients remained under observation for 48 hours at study centers. Patients were followed for seven days after the initial dose of study medication. There was an oral opioid rescue treatment available to all patients, if required. The primary objective of the trial was to evaluate pain relief over a 48-hour period of IV meloxicam when administered as a bolus injection (over 15-30 seconds).

The primary efficacy endpoint of the trial was SPID48, utilizing a windowed 2-hour last observation carried forward, or W2LOCF, analysis method. Secondary efficacy endpoints included use of opioid rescue medication, SPIDs over various time intervals, and patient global assessment, or PGA, of pain control. The IV meloxicam treatment arm demonstrated a statistically significant reduction in SPID48 (p=0.0034) compared to the placebo arm (Figure 1).

Figure 1: SPID48

The study also achieved 15 secondary endpoints, including statistically significant differences in SPID6 (p=0.0153), SPID12 (p=0.0053), SPID24 (p=0.0084), SPID24-48 (p=0.0050), time to first use of rescue medication (p=0.0076), and several other rescue use and pain relief metrics during the first 48 hours, compared to placebo (Table 1).

Table 1: Summary of Secondary Endpoints

Parameter	p-value
SPID6	0.0153
SPID12	0.0053
SPID24	0.0084
SPID24-48	0.0050
Time to First Rescue Analgesia	0.0076
Number of Subjects Rescued 0-24 Hours	0.0002
Number of Subjects Rescued 24-48 Hours	0.0009
Number of Subjects Rescued 0-48 Hours	0.0002
Number of Times Rescued 0-24 Hours	0.0025
Number of Times Rescued 24-48 Hours	0.0108
Number of Times Rescued 0-48 Hours	0.0014
% Subjects with >30% Improvement – 6 Hours	0.0451
% Subjects with >30% Improvement – 24 Hours	0.0107
% Subjects with >50% Improvement – 24 Hours	0.0430
PGA of Pain Control at 48 hours	0.0046

Times to Perceptible and Meaningful Pain Relief, % Subjects with >50% Improvement within 6 Hours, and PGA of Pain Control at 24 hours were not significantly different between treatment groups.

The safety results demonstrated that IV meloxicam was well tolerated with no serious adverse events, or SAEs, or bleeding events in the IV meloxicam-treated patients. The most common adverse events, or AEs, occurring in at least 3% of IV meloxicam-treated treated patients, were nausea, headache, pruritus, constipation vomiting, dizziness, flushing and somnolence, and were comparable to the placebo group (Table 2). The IV meloxicam-treated patients experienced injection site pain and injection site erythema at a rate comparable to placebo. The majority of treatment emergent AEs, or TEAEs, were mild in nature and there were no discontinuations due to AEs. There were no meaningful differences between treatment groups in vital signs, ECGs, or clinical lab assessments.

Table 2: Adverse Events reported by ≥3% of subjects from any treatment group

	n (%) of Subjects	
Preferred Term	IV meloxicam 30 mg (N=100)	Placebo (N=101)
Subjects with ≥1 TEAE	44 (44.0)	54 (53.5)
Nausea	20 (20.0)	26 (25.7)
Headache	8 (8.0)	12 (11.9)
Vomiting	3 (3.0)	9 (8.9)

Pruritus	8 (8.0)3 (3.0)
Decreased appetite	2 (2.0)7 (6.9)
Constipation	4 (4.0)5 (5.0)
Abdominal pain	— 6 (5.9)
Dizziness	3 (3.0)4 (4.0)
Flushing	3 (3.0)1 (1.0)
Somnolence	3 (3.0)2 (2.0)
ALT increased	— 3 (3.0)

**Two (2) subjects experienced Serious Adverse Events during this study. Both subjects were randomized to placebo.
Study REC-15-015

In November 2016, we announced positive results from the second of our two pivotal clinical trials, evaluating pain relief over a 24-hour period in a soft tissue, post-operative pain model (abdominoplasty). In the trial, IV meloxicam achieved the primary endpoint of a statistically significant difference in SPID over the first 24 hours, or SPID24, compared to placebo. This was a Phase III, randomized, multicenter, multi-dose, double-blind, placebo-controlled study evaluating IV meloxicam in the management of post-operative pain following abdominoplasty surgery. Two hundred nineteen patients who met the eligibility criteria were randomized to

receive either IV meloxicam (30 mg) or placebo once daily for three days. Following the beginning of treatment, patients remained under observation for48 hours at study centers. Patients were followed for seven days after the initial dose of study medication. There was an oral opioid rescue treatment available to all patients, if required. The primary objective of the trial was to evaluate pain relief over a 24-hour period of IV meloxicam when administered as a bolus injection (over 15-30 seconds).

The primary efficacy endpoint of the trial was SPID24 (0-24), utilizing a W2LOCF analysis method. Secondary efficacy endpoints included use of opioid rescue medication, SPIDs over various time intervals, time to pain relief and PGA of pain control. The IV meloxicam treatment arm demonstrated a statistically significant reduction in SPID24 (p=0.0145) compared to the placebo arm (Figure 2).

Figure 2: SPID24

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The study also achieved statistical significance for 10 of the secondary endpoints, including statistically significant differences in SPID12 (p=0.0434), time to perceptible pain relief (p=0.0050), subjects with ≥30% improvement at 24 hours (p=0.0178), number of times patients required rescue in the first 24 hours after randomization (p=0.0275), as well as number of times rescued from 24 to 48 hours (p=0.0009), and several other pain relief metrics, compared to placebo (Table 3).

Table 3: Summary of Secondary Endpoints

Parameter	p-value
SPID12	0.0434
SPID48	0.0040
SPID24-48	0.0028
Number of Subjects Rescued 24-48 Hours	0.0014
Number of Times Rescued 0-24 Hours	0.0275
Number of Times Rescued 24-48 Hours	0.0009
Number of Times Rescued 0-48 Hours	0.0027
Time to Perceptible Pain Relief	0.0050
% Subjects with ≥30% Improvement – 24 Hours	0.0178
PGA of Pain Control at 48 hours	0.0027

SPID6, Times to Meaningful Pain Relief and First Rescue, Number of Subjects rescued 0-24 and 0-48 hours, % Subjects with ≥30 and ≥50% Improvement within 6 Hours and ≥50% within 24 hours, and PGA of Pain Control at 24 hours were not significantly different between treatment groups.

The safety results demonstrated that IV meloxicam was well tolerated with no difference in SAEs related to bleeding for IV meloxicam treated patients versus placebo (1 each). There were two additional SAEs observed in the placebo group. The most common (≥2% in the IV meloxicam group) AEs were nausea, headache, vomiting, and dizziness (Table 4). The incidence of these events was lower than those observed in the placebo group. The majority of AEs were mild in nature and one patient in the placebo group discontinued treatment due to an adverse event of post-procedural bleeding. There were no meaningful differences between treatment groups in vital signs, ECGs or clinical lab assessments.

Table 4: Adverse Events reported by ≥2% of subjects from any treatment group

	n (%) of Subjects	
	IV meloxicam 30 mg	Placebo
Preferred Term	(N=110)	(N=109)
Subjects with >=1 TEAE	58 (52.7)	80 (73.4)
Nausea	30 (27.3)	41 (37.6)
Headache	13 (11.8)	18 (16.5)
Vomiting	5 (4.5)	10 (9.2)
Dizziness	4 (3.6)	10 (9.2)

** Four (4) subjects experienced Serious Adverse Events during this study. Three subjects were randomized to placebo and one to IV meloxicam.

Phase II Clinical Trials

IV meloxicam has also been studied in several Phase II clinical trials, including Study IV Meloxicam-04, a Phase II, multicenter, randomized, double-blind, placebo-and active-controlled study in 486 female subjects who underwent open abdominal hysterectomy. Following surgery on post-operative day 1, or Post Op Day 1, subjects received a single dose of either IV placebo, morphine or meloxicam 5 mg, 7.5 mg, 15 mg, 30 mg or 60 mg. Starting at the time of study drug administration and continuing for 24 hours thereafter, subjects had access to rescue medication. During the 24-hour double-blind evaluation period, efficacy measurements of pain intensity and pain relief were made using the 100-mm visual analogue scale to assess pain intensity and a 5-point categorical scale (ranging from none to complete) to assess pain relief

Overall, all active treatment doses produced statistically significant reductions in SPID24 (a co-primary endpoint) compared to placebo ($p < 0.001$), utilizing the LOCF analysis method. In addition, all active treatment doses also produced statistically significant improvement in total pain relief from hour 0 to 24 (a co-primary efficacy endpoint) compared to placebo ($p < 0.001$). Statistically significant decreases in pain intensity from baseline were detected as early as 10 minutes post-dose and continued throughout the 24-hour post-dose period. In general, the greatest decreases were seen in the 30 mg and 60 mg dose groups followed by the 15 mg group (Figure 3).

Figure 3: Pain Intensity Differences at Various Time Points

Rescue medication use during the 24-hour double-blind period was reduced by approximately 90% in the meloxicam 30 mg and 60 mg dose groups, and by 86%, 77%, 81%, and 71% in the 15 mg, 7.5 mg, 5 mg, and morphine groups, respectively, compared to placebo. Statistically significant differences were seen between each active group and placebo ($p < 0.001$). The percentage of subjects using rescue medication is presented in Figure 4. The median time to rescue (based on the lower bound of the 95% confidence interval for the 50th percentile) was greatest for meloxicam 30 mg (21.9 hours), followed by 60 mg (20.6 hours), 15 mg (18.3 hours), 5 mg (12.2 hours), 7.5 mg (8.3 hours), morphine (6.6 hours), and placebo (1.1 hours).

Figure 4: Percentage of Subjects Using Rescue Medication

Study medication was well tolerated. A total of five SAEs were reported in the study, and none were assessed as related to treatment. There were no clinically meaningful trends in vital signs, ECGs or laboratory assessments. AE rates were generally low and consistent with this surgical population under study (Table 5).

Table 5: Adverse Events reported by ≥3% of subjects from any treatment group

					IV Meloxicam 5 mg		7.5 mg		15 mg		30 mg		60 mg	
	Placebo		Morphine		N = 60		N = 91		N = 60		N = 60		N = 89	
	N = 64		N = 62											
	n (%)		n (%)		n (%)		n (%)		n (%)		n (%)		n (%)	
Anemia	2	(3.1)	3	(4.8)	2	(3.3)	12	(13.2)	2	(3.3)	1	(1.7)	9	(10.1)
Leukocytosis	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	2	(3.3)	0	(0.0)
Sinus tachycardia	0	(0.0)	0	(0.0)	2	(3.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Abdominal distension	2	(3.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Constipation	0	(0.0)	3	(4.8)	3	(5.0)	1	(1.1)	1	(1.7)	0	(0.0)	0	(0.0)
Flatulence	0	(0.0)	3	(4.8)	1	(1.7)	1	(1.1)	2	(3.3)	0	(0.0)	0	(0.0)
Nausea	2	(3.1)	1	(1.6)	1	(1.7)	1	(1.1)	1	(1.7)	1	(1.7)	2	(2.2)
Pyrexia	1	(1.6)	2	(3.2)	2	(3.3)	2	(2.2)	0	(0.0)	0	(0.0)	0	(0.0)
Anemia post-operative	0	(0.0)	1	(1.6)	0	(0.0)	0	(0.0)	0	(0.0)	2	(3.3)	0	(0.0)
Hypokalemia	0	(0.0)	2	(3.2)	1	(1.7)	1	(1.1)	0	(0.0)	1	(1.7)	0	(0.0)
Insomnia	3	(4.7)	5	(8.1)	6	(10.0)	4	(4.4)	3	(5.0)	3	(5.0)	4	(4.5)
Ketonuria	5	(7.8)	6	(9.7)	4	(6.7)	9	(9.9)	9	(15.0)	6	(10.0)	9	(10.1)

Our Other Pipeline Candidates

Dex

Dex is a selective alpha-2 adrenergic agonist that has demonstrated sedative, analgesic and anxiolytic properties. Dex has an extensive history of safe IV use. We have formulated Dex-IN, a proprietary intranasal formulation of Dex, at a significantly lower dose (perhaps as low as 1/10th) than the currently recommended IV dosage levels. Based upon our lower dose, we have seen minimal sedation to date in our clinical trials while still demonstrating an analgesic effect.

We initially studied Dex-IN for the treatment of post-operative pain. Based on clinical trial results and feedback from the FDA, we are exploring Dex-IN in peri-procedural pain. If approved, Dex-IN would also be the first and only approved peri-procedural pain drug in its class of drugs.

Fado

We also have another selective alpha-2 agonist product candidate in our pipeline, Fado. Fado is similar to Dex and different from clonidine in that it is a full agonist of all subtypes of alpha-2 adrenoreceptor. Unlike Dex, Fado does not cross the blood/brain barrier, and this accounts for the targeting of Fado use for either intrathecal administration for pain or anesthesia, or potentially for topical use to treat pain associated with regional nerve pain from underlying nerve damage, also called “neuropathies.” Various preclinical models of pain have been employed and have demonstrated Fado’s potential as an analgesic, including its potential for use in neuropathies and post-operative pain. In Orion sponsored studies, Fado appeared to delay the onset of pain while doses of Fado greater than 120 mcg also appeared to suppress pain. In addition, Fado was well tolerated by subjects.

CDMO Division

Through our CDMO division, we leverage our formulation and development expertise to develop and manufacture pharmaceutical products using our proprietary delivery technologies for commercial partners who commercialize or plan to commercialize these products. Our manufacturing and development capabilities include formulation and progressing product development through commercial manufacturing and specialized capabilities for solid oral dosage forms as wells as extended release and controlled substance manufacturing. In a typical collaboration, we license certain intellectual property to our commercial partners and work with our commercial partners to develop product candidates, or new formulations of existing product candidates. We also typically exclusively manufacture and supply clinical and commercial supplies of these product candidates. These collaborations result in revenue streams including from royalties, profit sharing, research and development and manufacturing, which support continued operations for our CDMO division as well as our research and development of proprietary product candidates in our Acute Care division.

The table below details the key products developed and/or manufactured with our key commercial partners:

Product	Indication	Technology	Territory	Revenue Source	Commercial Partner
Ritalin LA®	Attention Deficit Hyperactivity Disorder	OCR (SODAS)	Worldwide	Royalty Manufacturing	Novartis Pharma AG
Focalin XR®	Attention Deficit Hyperactivity Disorder	OCR (SODAS)	Worldwide, except Canada	Royalty Manufacturing	Novartis Pharma AG
Verelan PM®	Hypertension	OCR (SODAS)	United States	Royalty Manufacturing	Lannett Company, Inc.
Verapamil (generic)	Hypertension	OCR (SODAS)	United States	Profit Sharing Manufacturing	Teva Pharmaceutical Industries Ltd.
Zohydro ER®	Severe Pain	OCR (SODAS)	United States	Royalty Manufacturing	Pernix Therapeutics, Inc.

Canada	Royalty	Paladin Labs, Inc.
	Manufacturing	

In addition to these key products, we also develop and manufacture other development stage products. The manufacture of these products for clinical trials and commercial use is subject to cGMPs and other regulatory agency regulations. We own and operate a 97,000 square foot, DEA-licensed manufacturing facility in Gainesville, Georgia, which has been inspected by U.S., EU, Turkish and Brazilian regulatory authorities for compliance with required cGMP standards for continued commercial manufacturing.

With each product, we either purchase active drug substance from third parties or receive it from our commercial partners to formulate product using our technologies. Although some materials for our products are currently available from a single source or a limited number of qualified sources, we attempt to acquire an adequate inventory of such materials, establish alternative sources and/or negotiate long-term supply arrangements. We do not currently have any significant issues finding suppliers. However, there is no certainty that we will be able to obtain long-term supplies of our manufacturing materials in the future.

Permits and Regulatory Approvals

We hold various licenses for our CDMO division manufacturing activities. The primary licenses held are FDA Registrations of Drug Establishments and DEA Controlled Substance Registration. Due to certain U.S. state law requirements, we also hold certain state licenses for distribution activities throughout certain states. We also hold cGMP certifications for EU importation of products made in Gainesville for sale in the EU.

We do not generally act as the product authorization holder for products that have been developed on behalf of a commercial partner. In such cases, our commercial partner typically holds the relevant authorization from the FDA or other national regulator, and we support this authorization by furnishing a letter of reference to the Drug Master File, or the chemistry, and manufacturing and related data to the relevant regulator or sponsor to provide adequate manufacturing support in respect of the product. We generally update this information annually with the relevant regulator.

We also hold the approved NDAs for Verelan and Verapamil, which we license to Lanett Company, Inc. and Teva Pharmaceutical Industries, Inc., respectively.

Customer Agreements

We are party to agreements with each of our commercial partners governing the development, formulation and/or supply services we provide, as well as any applicable intellectual property licenses. Each commercial partner generally remains responsible for distributing, marketing and promoting their respective products. These collaborations result in revenue streams including royalties, profit sharing, etc., which support continued operations for our CDMO division and have contributed funds to be used in our research and development and pre-commercialization activities in our Acute Care division. We are dependent on a small number of commercial partners, with our four largest customers (Novartis Pharma AG, Teva Pharmaceutical Industries, Inc., Pernix Therapeutics, Inc. and Lannett Company, Inc.) having generated 97% of our revenues for the twelve months ended December 31, 2016, of which one customer, Novartis Pharma AG, generated 45% of our revenue under two separate customer agreements, and another customer, Teva Pharmaceutical Industries, Inc., generated 36% of our revenue under one customer agreement.

Intellectual Property

Acute Care

We own patents and patent applications for injectable meloxicam, that cover compositions, including compositions produced using NanoCrystal® technology, method of making and method of treating. These issued patents expire in 2022 in the United States. We also in-license from Alkermes, on a perpetual, royalty-free basis, composition and methods of making patent and patent applications (specifically directed to the prevention of flake like substances) which expire in 2030.

We hold patent applications directed to the analgesia indication, formulations and intranasal and transmucosal methods of use of Dex, and we are progressing through the patent application process globally, including the United States. Several patent applications have issued as patents outside the United States for transmucosal methods, and the resulting patent protection will last into 2030, subject to any disclaimers or extensions. If the intranasal patent applications are issued as patents, the resulting patent protection will last into 2032, subject to any disclaimers or extensions. For Fado, we have a pro-drug patent that expires in 2025.

We are party to an exclusive license with Orion for the development and commercialization of Dex for use in the treatment of pain in humans in any dosage form for transdermal, transmucosal (including sublingual and intranasal), topical, enteral or pulmonary (inhalational) delivery, but specifically excluding delivery vehicles for administration by injection or infusion, worldwide, except for Europe, Turkey, and the CIS (currently includes Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine and Uzbekistan), referred to herein as the Territory. We have the right to sublicense the rights under such license at any time. We are required to pay Orion lump sum payments on the achievement of certain developmental milestones and upon the achievement of certain commercial milestones, as well as a royalty on net sales during the term, which varies from 10% to 20% depending on annual sales levels. We will pay milestone payments to Orion of up to €20.5 million ($21.6 million as of December 31, 2016) after regulatory approval of Dex dosage forms and upon achieving certain sales milestones. Through December 31, 2016, no such milestones have been achieved. The initial term of this license is 15 years from the first commercial sale in the Territory, with automatic two year extensions, unless either party provides written notice of termination.

We are also party to an exclusive license agreement with Orion for the development and commercialization of Fado for use as a human therapeutic, in any dosage form in the Territory. We have the right to sublicense the rights under such license at any time. In consideration for this license, we paid Orion an upfront payment and are required to pay certain lump-sum amounts on completion of certain development milestones, as well as on achievement of certain commercial milestones. We will pay milestone payments to Orion of up to €12.2 million ($12.9 million as of December 31, 2016), based on regulatory filings and approval and on

commercialized net sales levels. We will also pay Orion royalty payments on net sales of Fado ranging from 10% to 15%. Through December 31, 2016, no such milestones have been achieved. The initial term of this license is 15 years from the first commercial sale in the Territory, with automatic three year extensions, unless either party provides written notice of termination at least six months prior to expiration or unless otherwise terminated pursuant to the terms of the license agreement.

Our intellectual property rights related to injectable meloxicam and Dex are held by our Irish subsidiary, Recro Ireland Limited.

CDMO Division

We also own various controlled release formulation patents, including patents in the United States, Canada, and Europe, related to our proprietary delivery technologies that we utilize in our drug development, formulation and manufacturing business through our CDMO division. These patents are scheduled to expire between 2019 and 2026. We own patents and patent applications in the United States and Canada directed to the composition of, manufacturing of, and formulating of Zohydro ER®. We license our U.S. patents and patent applications to our commercial partner, Pernix Therapeutics Holdings, Inc., or Pernix, in the United States. We also own Canadian patents and patent applications relating to the same technology, which we license to our commercial partner, Paladin Labs Inc., in Canada. The patent protection for Zohydro ER® provides for protection of Zohydro ER® through 2034, subject to any extensions or disclaimers.

Intellectual Property Protection Strategy

We intend to rely on a combination of patents and trade secrets, as well as confidentiality agreements and license agreements, to protect our product candidates. Our patent strategy is designed to facilitate commercialization of our current product candidates and future product candidates, as well as create barriers to entry for third parties. One focus of our claim strategy is on formulation claims and method of treatment claims.

We are seeking patent protection in the United States and internationally for our product candidates. Our policy is to pursue, maintain and defend patent rights and to protect the technology, inventions and improvements that are commercially important to the development of our business. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology. We also intend to rely on trade secrets to protect our product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for our product candidates;
- defend our patents;
- develop trade secrets as needed and preserve the confidentiality of our trade secrets; and
- operate our business without infringing the patents and proprietary rights of third parties.

We have taken steps to build and will continue to build proprietary positions for our product candidates and related technology in the United States and abroad. We note that the patent laws of foreign countries differ from those in the United States, and the degree of protection afforded by foreign patents may be different from the protection offered by United States patents.

Sales and Marketing

Our current intent is to develop and commercialize our product candidates in the United States and Canada while out-licensing development and commercialization rights for other territories outside the United States and Canada for which we own the territorial rights. We believe the initial target audience for our product candidates will be specialty physicians, including surgeons, anesthesiologists and pain specialists. Our management team has experience building and launching therapeutics to specialty physicians. As this target audience is smaller than general practitioners, we believe we have the capabilities to build a sales and marketing infrastructure and effectively market our product candidates upon commercial approval. While our stated intention is to develop and commercialize our product candidates, we will evaluate potential strategic collaborations that could accelerate or enhance our development and, upon approval, commercial success of our product candidates.

We are currently preparing for a potential U.S. commercial launch of IV meloxicam, if approved, and we plan to establish sales, marketing and reimbursement functions to commercialize IV meloxicam in the United States.

Manufacturing and Supply of our Product Candidates

We currently rely on contract manufacturers to produce drug product for our clinical studies under cGMPs, with oversight by our internal managers. We plan to continue to rely on contract manufacturers to manufacture development quantities of our product candidates, as well as commercial quantities of our product candidates, if and when approved for marketing by the FDA. We currently rely on a single manufacturer for the clinical supplies of our drug product for each of our product candidates and do not currently have agreements in place for redundant supply or a second source for any of our product candidates. We have identified other drug product manufacturers that could satisfy our clinical study requirements, but this would require significant expense and could produce a significant delay in setting up the facility and moving equipment. Additionally, should a supplier or a manufacturer on whom we rely to produce a product candidate provide us with a faulty product or a product that is later recalled, we would likely experience significant delays and additional costs.

Injectable Meloxicam

Alkermes is currently our exclusive supplier of injectable meloxicam. Pursuant to a Development, Manufacturing and Supply Agreement, or Supply Agreement, Alkermes (through a subsidiary), will provide (i) clinical and commercial bulk supplies of injectable meloxicam formulation and (ii) development services with respect to the Chemistry, Manufacturing and Controls section of the NDA for injectable meloxicam. Pursuant to the Supply Agreement, Alkermes will supply us with such quantities of bulk injectable meloxicam formulation as shall be reasonably required for the completion of clinical trials of injectable meloxicam, subject to a maximum of eight clinical batches in any twelve-month period, unless otherwise agreed by the parties. During the term of the Supply Agreement, we will purchase our clinical and commercial supplies of bulk injectable meloxicam formulation exclusively from Alkermes. Sterile fill-finish of injectable meloxicam will be completed by a third-party fill-finish facility. If the first commercial sale of injectable meloxicam occurs on or prior to December 31, 2020, the Supply Agreement will have an initial term expiring ten years following the date of such first commercial sale. The Supply Agreement will then automatically renew for successive one-year terms unless terminated by either party upon written notice at least 180 days prior to the expiration of the applicable term. If the first commercial sale of injectable meloxicam has not occurred by December 31, 2020, the Supply Agreement will expire on that date.

The Supply Agreement may be terminated earlier (i) by us upon 180 days' written notice following the date of first generic entry; (ii) by either party upon twelve months' written notice following the first anniversary of the approval of the NDA for meloxicam; (iii) by either party upon written notice to the other party in the event of uncured material breach of the other party; and (iv) by Alkermes upon written notice in certain events of uncured non-payment.

Dex

We are party to an API supply agreement with Orion, whereby Orion provides us with API for the development and commercialization of our Dex product candidates. Prior to obtaining regulatory approval, subject to advance notice to Orion, Orion will provide API without charge for agreed upon amounts. Any amounts ordered by us that are greater than the planned supply will be charged at 50% of the supply price for commercial product. The initial term of the agreement is the later of 15 years from the first commercial sale and 15 years after the effective date of the agreement, and in each case, will be automatically extended for one or more periods of two years unless terminated. After the initial term, the agreement may be terminated upon six months' notice to the other party.

The single unit dose intranasal sprayer for Dex-IN is manufactured by a supplier of proprietary components and devices, and equipment is leased from the device supplier for filling at a contract manufacturer. It is possible that we will continue with this arrangement through clinical development, evaluate the option of entering a manufacturing agreement with the device originator or evaluate alternative devices prior to commercialization. Suppliers of

components, subassemblies and other materials are located in Europe, Asia and the United States.

Competition

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological change. Our current and future competitors include pharmaceutical, biotechnology and specialty pharmaceutical companies. Many of our competitors have greater financial and other resources than we have, such as more commercial resources, larger research and development staffs and more extensive marketing and manufacturing organizations. As a result, these companies may obtain marketing approval more rapidly than we are able to obtain and may be more effective in selling and marketing their products. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than our product candidates or any other products that we may develop which could render our products obsolete and noncompetitive. We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price and the availability of reimbursement from government and other third-party payors. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize our product candidates in our target commercial markets.

In the post-operative pain relief setting, we believe patients are prescribed injectable acetaminophen, nonsteroidal anti-inflammatory drugs, or NSAIDs, sodium channel blockers and opioids, depending on the severity of pain. Specifically, acetaminophen, NSAIDs and sodium channel blockers, we believe, are prescribed for mild to moderate pain relief, whereas we believe opioids are prescribed for moderate to severe pain relief. While we will compete with all of these compounds in the post-operative pain setting, we believe injectable meloxicam will be prescribed for moderate to severe pain, competing with opioids and other non-opioid pain treatments. There are a number of pharmaceutical companies that currently market therapeutics in the pain relief area, including Johnson & Johnson, Purdue Pharma, L.P., Mallinckrodt plc, Teva Pharmaceutical Industries, Inc., Depomed, Inc. and Pacira Pharmaceuticals, Inc. Purdue is the primary competitor in the manufacture, marketing and commercialization of opioid therapeutics. Mallinckrodt commercializes an injectable formulation of acetaminophen. Pacira commercializes an intraoperative formulation of bupivacaine, a sodium channel blocker. Additionally, companies such as Adynxx, Inc., AcelRx Pharmaceuticals, Inc., Durect Corporation, Heron Therapeutics, Inc., Trevena, Inc. and Cara Therapeutics, Inc. are currently developing post-operative pain therapeutics that could compete with us in the future.

With our CDMO division, we compete with contract pharmaceutical formulation and manufacturing companies such as Catalent, Inc., Patheon Holdings Coôperatief U.A., Adare Pharmaceuticals, Inc., Metrics, Inc., a subsidiary of Mayne Pharma Group Limited, and other formulation, development and manufacture-related service providers.

Research and Development

Research activities represent a significant part of our businesses. In the years ended December 31, 2016 and 2015, respectively, we incurred research and development expenses of $33.3 million and $12.3 million, respectively.

Government Regulation

Governmental authorities in the United States at the federal, state and local level, and the equivalent regulatory authorities in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our product candidates, including our formulations of injectable meloxicam, Dex and Fado, must be approved by the FDA before they may legally be marketed in the United States. In addition, to the extent we choose to clinically evaluate or market any products in other countries or develop these products for future licensing to third parties, we are subject to a variety of regulatory requirements and to the authority of the competent regulatory authorities of those other countries.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and ensuring compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval p