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, 2018

OR

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

For the transition period from _____ to _____

Commission File Number: 001-35902

Insys Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**51-0327886**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*
1333 S. Spectrum Blvd, Suite 100, Chandler, Arizona	**85286**
(Address of Principal Executive Offices)	**(Zip Code)**

(480) 500-3127

(Registrant's Telephone Number, Including Area Code)

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

Title Of Each Class	**Name Of Each Exchange On Which Registered**
Common Stock, $0.01 Par Value Per Share	**The NASDAQ Global Market LLC**

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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit 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 of this Form 10-K. ☐

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	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 of the registrant was approximately $196 million as of June 30, 2018 based on the closing sales price of the common stock on the NASDAQ Global Market.

There were 74,428,260 shares of the registrant's common stock issued and outstanding as of March 4, 2019.

Documents Incorporated by Reference

Portions of the registrant's Proxy Statement relating to its 2019 Annual Meeting of Stockholders, to be filed with the Securities and Exchange Commission ("SEC") pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference in Part III of this Form 10-K.

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2018 FORM 10-K ANNUAL REPORT
GLOSSARY OF TERMS

The following glossary provides definitions for certain acronyms and terms used in this Annual Report on Form 10-K. These acronyms and terms are specific to our Company, commonly used in our industry, or are otherwise frequently used throughout our document.

Abbreviated Term	Defined Term
AIDS	Acquired Immune Deficiency Syndrome
ANDA	Abbreviated New Drug Application
API	Active pharmaceutical ingredient
Aptar	AptarGroup, Inc.
ASC	Accounting Standards Codification
ASU	Accounting Standards Update
ATRA	American Taxpayer Relief Act of 2012
AUC	Area under the curve
AVC	Assurance of Voluntary Compliance
BTCP	Breakthrough cancer pain
CBD	Synthetic cannabidiol
cGMP	Current Good Manufacturing Practices
CID	Civil Investigative Demand
CINV	Chemotherapy-induced nausea and vomiting
CMS	Centers for Medicare & Medicaid Services
CODM	Chief Operating Decision Maker
CRO	Contract Research Organization
CSA	Federal Controlled Substances Act of 1970
DEA	U.S. Drug Enforcement Administration
DOJ	U.S. Department of Justice
DOJ Investigations	HHS and HIPAA investigations, collectively
ESI	Express Scripts, Inc.
FASB	Financial Accounting Standards Board
FDA	U.S. Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act
FSS	Federal Supply Schedule
GAO	Government Accountability Office
GCP	Good Clinical Practices
GI	Gastrointestinal
GLP	Good Laboratory Practices
HHS	U.S. Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act of 1996
HITECH	Health Information Technology for Economic and Clinical Health Act of 2009
IND	Investigational New Drug Application
Insys Pharma	Insys Pharma, Inc.
Insys Therapeutics	Insys Therapeutics, Inc.
IPO	Initial public offering
IQVIA	IQVIA Holdings Inc. (formerly IMS Health, or “IMS”)
IRB	Institutional Review Board
MMA	Medicare Prescription Drug, Improvement, and Modernization Act of 2003
NDA	New Drug Application
NOL	Net operating loss
NRV	Net Realizable Value

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Abbreviated Term	Defined Term
NSAID	Non-steroidal anti-inflammatory drug
OIG	HHS Office of Inspector General
ODOJ	Oregon Department of Justice
Orange Book	FDA's Approved Drug Products with Therapeutic Equivalence Evaluations
PBM	Pharmacy Benefit Managers
PDEs	Prescription Drug Events
PDMA	Prescription Drug Marketing Act
PDUFA	Prescription Drug User Fee Act
PK	Pharmacokinetics
PPACA	Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010
QSR	FDA's Quality System Regulation
REMS	Risk Evaluation and Mitigation Strategy
Renaissance	Renaissance Acquisition Holdings, LLC (formerly DPT Lakewood, LLC, or “DPT”)
RLD	Reference listed drug
SEC	U.S. Securities and Exchange Commission
THC	Delta-9-tetrahydrocannabinol
TIRF	Transmucosal immediate-release fentanyl
TIRF REMS	Transmucosal immediate release fentanyl risk evaluation and mitigation strategy
USAO	United States Attorney Office
U.S. GAAP	Accounting Principles Generally Accepted in the United States of America
USPTO	United States Patent and Trademark Office
VC	Vomiting center

PART I

ITEM 1. BUSINESS

Overview

As used in this Form 10-K, "we," "us," "our," and "the Company" refer to Insys Therapeutics, Inc. and our subsidiaries.

We are a specialty pharmaceutical company that develops and commercializes innovative drugs and novel drug delivery systems of therapeutic molecules that improve patients' quality of life. We have two marketed products: SUBSYS®, a proprietary sublingual fentanyl spray indicated for the management of BTCP patients 18 years of age and older who are already receiving and are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain; and SYNDROS®, a proprietary, orally administered liquid formulation of dronabinol for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments and anorexia associated with weight loss in patients with AIDS. As discussed below, on November 5, 2018, we announced a process to review strategic alternatives for our opioid-related assets including SUBSYS®. The Company has also engaged Lazard Freres & Co. LLC to advise the Company on capital planning and the evaluation of strategic alternatives. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic licensing and partnerships, joint ventures, restructurings, divestitures, business combinations and investments.

Insys Therapeutics, Inc. was incorporated in Delaware in June 1990, and maintains headquarters in Chandler, Arizona.

For further detail concerning our Company and communities, see the "Available Information" section included in this Item 1.

SUBSYS®

SUBSYS® is a proprietary, single-use product that delivers fentanyl, an opioid analgesic, for transmucosal absorption underneath the tongue. We filed our NDA in March 2011 and received marketing approval for SUBSYS® from the FDA in January 2012 for the treatment of BTCP. BTCP is characterized by sudden, often unpredictable, episodes of pain that can peak in severity at less than one minute to 10 minutes despite background pain controlled by around-the-clock medication. We believe SUBSYS® is an important, differentiated treatment option for patients and physicians relative to other TIRF products due to its rapid onset of action, improved bioavailability, most complete range of dosage strengths and ease of administration. Our product label includes data from our pivotal clinical trial demonstrating that SUBSYS® may provide pain relief in as little as five minutes, which represents the most rapid onset of action in the TIRF class of products. Also, in a head-to-head study, SUBSYS® demonstrated 76% bioavailability versus 51% for Teva Pharmaceutical Industries Ltd.'s ACTIQ®. Further, SUBSYS® offers the most complete range of dosage strengths in the TIRF class of products, consisting of 100 to 1,600 microgram, or mcg, doses. Patients can administer SUBSYS® in less than one minute while Teva Pharmaceutical Industries Ltd.'s ACTIQ® and FENTORA®, the leading branded TIRF products, can require 15 to 30 minutes to administer.

We launched SUBSYS® as a commercial product in March 2012. Upon launch, SUBSYS® was the fourth new branded product in the TIRF market over the prior five years. Within the first four weeks of product launch, SUBSYS® realized greater market share than the previous three branded products combined at their respective peak market penetration levels according to Source Healthcare Analytics. In December 2018, SUBSYS® was the most prescribed branded TIRF product, with approximately 24% market share on a prescription basis according to IQVIA. Approximately 900 physicians were responsible for 90% of all TIRF prescriptions dispensed in 2018, according to IQVIA. As a result, our commercial organization has been able to promote SUBSYS® using a highly targeted approach designed to maximize impact with physicians who are TIRF REMS enrolled. In addition, our commercial organization continues to specifically target oncology healthcare providers and practices.

SUBSYS® utilizes our proprietary sublingual spray technology consisting of a small, single-unit device that delivers our proprietary formulation of drug particles via a fine mist disbursed across a broad surface area of the highly permeable membrane underneath the tongue. This delivery platform is suitable for other molecules for which

there may be a benefit to a greater rate and extent of absorption, which could lead to a more rapid onset of action and enhanced bioavailability versus other oral preparations and routes of administration. We are developing our proprietary sublingual spray technology in other product applications in order to expand our portfolio of product candidates.

SYNDROS®

SYNDROS®, a proprietary, orally administered liquid formulation of dronabinol, has demonstrated rapidly detectable blood levels and a reliable absorption profile in our clinical studies. In 2012, we completed a pre-NDA meeting with the FDA and a pivotal bioequivalence study. Our pivotal bioequivalence study measured the PK of SYNDROS® versus Marinol®. This PK study demonstrated that 100% of subjects receiving SYNDROS® achieved detectable plasma levels at 15 minutes compared to less than 25% of subjects receiving Marinol®. In this study, SYNDROS® also demonstrated a 44% decrease in the patient coefficient of variation for area under the curve, or AUC, which is indicative of greater patient exposure to drug after administration. We received FDA approval for SYNDROS® in July 2016. In March 2017, the DEA issued an interim final ruling that resulted in SYNDROS® being placed in Schedule II of the CSA. The final labeling reflecting the scheduling was approved by the FDA in May 2017 and we commercially launched SYNDROS® in July 2017.

Other Products

We are leveraging our capabilities in cannabinoid formulation and manufacturing, as well as our sublingual and nasal spray drug delivery technology, to develop a portfolio of differentiated, wholly-owned product candidates. Our most advanced product candidate is a naloxone nasal spray. This product candidate possesses unique pharmacological properties that may make it effective in treating overdose due to illicitly manufactured fentanyl and other long-lasting opioid drug products. We plan to file an NDA for this product candidate with the FDA in the second quarter of 2019. We are also leveraging our spray technology to develop an epinephrine nasal spray for the treatment of anaphylaxis. This novel formulation and dosage form the potential to replace intramuscular injections. Additionally, we continue to progress with our Cannabidiol Oral Solution, a CBD, and currently have three clinical development programs underway, including two Phase 2 and one Phase 3 clinical trials.

Strategy

Strategic alternatives. On November 5, 2018, we announced that we commenced a process to review strategic alternatives for our portfolio of opioid-related assets, including SUBSYS®, as well as formulations of buprenorphine and the combination of buprenorphine/naloxone. Our decision to pursue this process is consistent with our ongoing negotiations in connection with the agreement in principle related to the DOJ Investigation, wherein we expect the OIG to require us to exit the opioid business within 12 months of executing the final settlement agreements. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of these legal matters. Furthermore, this dovetails with our strategy to become a leader in pharmaceutical cannabinoids and novel drug delivery systems and to continue shifting our focus away from opioids in our product pipeline. We anticipate that our Company has a number of clinical and regulatory milestones to achieve over the next few quarters, including the completion of the CBD and epinephrine studies and filing the naloxone NDA, that are consistent with our objectives. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic licensing and partnerships, joint ventures, restructurings, divestitures, business combinations and investments.

Advance our synthetic cannabinoid product pipeline. Clinical trials with CBD in epilepsy and Prader-Willi Syndrome continue to progress with the results from two trials expected in 2019. We have conducted a pharmacokinetic trial with a proprietary inhaled formulation of dronabinol and are planning our next steps in the product candidate's development.

SUBSYS® market share and revenues. We launched SUBSYS® as a commercial product in March 2012. As of December 31, 2018, there were approximately 4,500 physicians enrolled in the TIRF REMS program. Enrollment in this class-wide REMS program is required by the FDA in order to prescribe TIRF products. Approximately 900 physicians comprise 90% of TIRF prescriptions dispensed in 2018, according to IQVIA. Our sales and marketing

efforts have primarily targeted approximately 48% of these top 900 prescribing physicians with a focus on those prescribers with the highest number of BTCP patients.

Continue to optimize our commercial organization to market SUBSYS®, SYNDROS®, and potential pipeline products . We commercialize SUBSYS® through our commercial sales organization. We also market SYNDROS® and will market other proprietary supportive care products, if approved, using this same commercial sales organization. We may also utilize our commercial organization or third parties to market our pipeline products, once approved.

Research and develop additional sublingual and nasal spray product candidates . We believe that the delivery of certain pharmaceutical products using our sublingual or nasal spray platform technologies could have significant advantages over other methods of delivery. Our sublingual and nasal spray technologies deliver drug product directly to the sublingual or nasal mucosa, respectively, for rapid and efficient absorption into the bloodstream. This process is accomplished by delivering a ready-to-be absorbed formulation across either the sublingual or nasal mucosa. The sublingual mucosa is an efficient medium for the delivery of certain drugs because this membrane is highly permeable with a high density of blood vessels, which allows for the portion of the drug absorbed to bypass first-pass metabolism in the liver. Similarly, nasal administration of select drug products can result in the same benefits as sublingual administration. Certain drug products delivered utilizing our sublingual and nasal spray technologies can be absorbed quickly and take effect more rapidly than many other forms of administration. We are developing several product candidates, including buprenorphine, buprenorphine with naloxone, naloxone, epinephrine and rizatriptan, where we believe our proprietary sublingual and nasal spray technologies have the potential to provide a clinically meaningful therapeutic advantage over existing delivery methods.

Use our core competencies and expertise to expand our dronabinol and cannabidiol manufacturing capabilities . Because dronabinol is difficult to import, procure and produce, we have a U.S.-based, state-of-the-art dronabinol manufacturing facility, which was able to supply the API for initial launch quantities of SYNDROS®. Further, we have the ability to manufacture pure, synthetic cannabidiol at this DEA-approved and FDA-inspected manufacturing facility located in Round Rock, TX. In 2014, we completed construction of a second manufacturing facility that enables us to supply sufficient commercial quantities of dronabinol API for the commercialization of our proprietary synthetic cannabinoid product candidates.

Our Products and Product Candidates

The following table summarizes certain information regarding our marketed products and most advanced product candidates:

Product	Indication	Pathway	Status
SUBSYS® (fentanyl sublingual spray)	1. BTCP in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.	505(b)(2)	Marketed
SYNDROS® (dronabinol oral solution)	1. Nausea and vomiting associated with cancer chemotherapy in patients who have failed to adequately respond to conventional antiemetic treatments. 2. Anorexia associated weight loss in AIDS patients	505(b)(2)	Marketed
Cannabidiol Oral Solution	1.West Syndrome (Infantile Spasms) 2.Prader Willi 3.Childhood Absence Epilepsy (CAE)	505(b)(1)[1]	•Infantile Spasms Phase 3 in progress •Prader Willi Phase 2 in progress •FDA granted 'Fast Track' designation for treatment of Prader Willi •CAE Phase 2 in progress
Buprenorphine Sublingual Spray	Acute pain	505(b)(2) [2]	Phase 3 completed; NDA filed September 29, 2017; NDA accepted December 6, 2017; Complete Response Letter received July 27, 2018
Epinephrine Nasal Spray	Allergic reactions (Type 1) including anaphylaxis	505(b)(2) [2]	Proof of concept study completed; Dose-finding study is underway, to be completed in Q1 2019
Naloxone Nasal Spray	Opioid antagonist	505(b)(2) [2]	Proof of concept study completed; Preparing to file NDA in Q2 2019 upon completion of juvenile nonclinical studies

1 Application is a complete NDA that contains all the studies conducted by the applicant necessary to demonstrate a drug's safe and effective use.

2 Anticipated regulatory pathway. A 505(b)(2) NDA relies for its approval upon studies that were not conducted by or for the applicant, and for which the applicant has not obtained a right of reference. The applicant may rely on the FDA's findings of safety and/or effectiveness for a previously approved drug (the "reference drug"). However, the applicant must still provide any additional preclinical or clinical data necessary to ensure that differences from the reference drug do not compromise safety and effectiveness.

We have also engaged in the development of other earlier stage product candidates. Specifically, we are engaged in preclinical work on the following products that utilize our nasal spray technology platform with the goal of expanding our supportive care franchise:

- Rizatriptan Spray (for migraine headaches)
- Sildenafil Spray (for erectile dysfunction)

Further, we have received orphan drug designations from the FDA for the following:

Indication	Drug	Approval Date
Gastric Cancer	Liposomal Encapsulated Paclitaxel	12/3/2014
Ovarian Cancer	Liposomal Encapsulated Paclitaxel	1/21/2015
Malignant Glioma	IL-13	11/2/2001
Interstitial Pulmonary Fibrosis (IPF)	IL-13	4/30/2010
Lennox-Gastaut Syndrome (rare pediatric epilepsy)	Cannabidiol	6/23/2014
Dravet Syndrome (rare pediatric epilepsy)	Cannabidiol	7/1/2014
West Syndrome – Infantile Spasms (rare pediatric epilepsy)	Cannabidiol	7/23/2015
Glioblastoma multiforme	Cannabidiol	8/20/2014
Pontine glioma	Cannabidiol	9/24/2014
Pediatric Schizophrenia	Cannabidiol	11/17/2014

SUBSYS® -Sublingual Fentanyl Spray

SUBSYS® is a proprietary, single-use product developed for the management of BTCP patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain through the delivery of a liquid fentanyl formulation in 100, 200, 400, 600, 800, 1,200 and 1,600 mcg dosages. The 1,200 and 1,600 mcg doses of SUBSYS® are achieved by administering two 600 and 800 mcg doses, respectively. The mechanism by which the liquid is delivered is a highly consistent, one-step process in which a plume of fentanyl is generated by the actuation of the device. The plume disperses a small volume of liquid across the surface area of the sublingual mucosa and facilitates rapid absorption by the body.

Cancer Pain Market Overview

Cancer pain can occur as a result of tumors pressing on nerves, damage caused by cancer cells in bone and treatments for cancer such as chemotherapy, radiation therapy or surgery. Many cancer patients experiencing pain suffer from two types of pain: (1) persistent or continuous pain, which is typically managed by long-acting or sustained-release drugs taken by patients on a regular schedule, and (2) breakthrough pain, which can be severe and sudden, and may require a stronger, fast-acting medication. Opioids are the most widely-prescribed treatment for cancer pain followed by medications commonly used to treat inflammatory pain, such as corticosteroids, anesthetics, NSAIDs, anticonvulsants and antidepressants.

Following rapid onset that peaks at less than one minute to 10 minutes, BTCP episodes can last several minutes to an hour, and usually occur several times per day. Pain is a widely prevalent condition of cancer patients, approximately 60% of cancer patients with persistent pain may experience BTCP, which is particularly difficult to treat due to its severity, rapid onset and the often-unpredictable nature of its occurrence. Physicians typically treat BTCP with a variety of short-acting opioid medications, including morphine, morphine and codeine derivatives and fentanyl.

Morphine and codeine derivatives have been available for decades in immediate-release forms of tablets, capsules or liquids that are ingested by the patient. More recently-approved short-acting opioid-based fentanyl formulations utilize transmucosal delivery in an attempt to improve upon existing fentanyl therapies. Teva Pharmaceutical Industries Ltd.'s ACTIQ®, approved by the FDA in 1998 and currently available in several generic options, is an oral transmucosal lozenge, and FENTORA®, the second leading branded TIRF product, approved by the FDA in 2006, is a fentanyl buccal tablet. Three other companies have received approval for branded TIRF products since 2009 including BioDelivery Sciences International, Inc.'s Onsolis®, a soluble film placed on the buccal area after wetting the inside of the cheek with saliva or water, Sentynl Therapeutics' Abstral®, an immediate-release transmucosal sublingual tablet, and West Therapeutic Development, LLC's Lazanda®, a nasal spray. Although these existing therapies provide improvements over oral opioids, we believe that the market adoption of SUBSYS® to date demonstrates that the current treatment options have limitations and that there remains a significant unmet need for therapies that provide faster pain relief, more convenient dose administration and a better PK profile. According to IQVIA, SUBSYS® prescriptions were approximately 24% and 29% of the TIRF market for the years ended December 31, 2018 and 2017, respectively.

Limitations of Competing TIRF Therapies

We continue to believe that there are unmet needs in the BTCP market, which include:

- *Time until significant pain relief*: Patients suffering from BTCP require rapid pain relief as peak intensity of episodic breakthrough pain can occur at less than one minute to 10 minutes from the onset of pain symptoms. The peak effect of ACTIQ® and FENTORA® may be delayed as it may take up to 15 to 30 minutes for the lozenge or tablet to fully dissolve and be absorbed. In addition, oral immediate-release opioids are metabolized in the liver and consequently, may take up to 30 to 45 minutes to become effective.
- *PK profile*: ACTIQ® and its generic equivalents achieve bioavailability of approximately 51% and require 15 to 30 minutes for absorption. Up to half of the delivered dose of competing TIRF treatments is swallowed and is absorbed slowly through the GI tract which we believe may delay the onset of pain relief and contribute to side effects.
- *Inconvenient delivery*: We believe competing commercially available therapies do not adequately address patient ease of use and convenience needs. Competing TIRF therapies can require an administration period of several minutes, disrupt daily activities and cause patient discomfort. For example, ACTIQ® requires patients to place a lozenge between their cheeks and lower gums and rub the lozenge from side to side over a 15-minute period. In addition, patients with dry mouth and oral mucositis may experience difficulty in using ACTIQ® and other commercially available therapies.

Our Solution

We believe SUBSYS'® proprietary formulation and sublingual delivery mechanism offer several advantages over other FDA-approved TIRF products, and these advantages may lead to improved patient compliance and expanded medical use of fentanyl for BTCP. Such advantages include:

- *Pain relief in five minutes:* SUBSYS® is the only product to show pain relief when measuring the sum of pain intensity difference at five minutes in a Phase 3 BTCP clinical trial using fentanyl. We believe that SUBSYS® is able to achieve this rapid delivery of fentanyl through sublingual delivery because there is a high density of blood vessels beneath the tongue and the thin layer in the mucosa enables higher absorption. The product sprays in a manner that is designed to maximize the area covered by the product.
- *One-step administration:* SUBSYS® is administered in one step using a small handheld delivery system that sprays fentanyl beneath the patient's tongue. This delivery mechanism allows for administration in less than one minute, rather than the 15 to 30 minutes required for ACTIQ® and FENTORA®. Further, SUBSYS® can be administered without moistening the tongue or cheek, allowing for administration in cancer patients suffering from dry mouth and oral mucositis.
- *PK profile*: As compared to ACTIQ's® PK profile, SUBSYS'® PK profile is characterized by higher peak blood concentrations, which are achieved at a more rapid rate. This profile is, in part, due to greater than 85% absorption occurring transmucosally, resulting in higher bioavailability. Because a small volume of liquid is sprayed on to the sublingual mucosa, we believe this method of administration reduces the amount of liquid swallowed and subsequently absorbed via the digestive system. As a result, we believe that less fentanyl is exposed to first-pass metabolism in the liver.
- *Broad spectrum of dosage strengths allows for proper titration and better pain relief* : SUBSYS® is available in the most complete range of dosage strengths in the TIRF market, at 100, 200, 400, 600, 800, 1,200 and 1,600 mcg. We believe it is important to offer a product in all dose ranges for the treatment of BTCP, as all branded products without generic equivalents, and, to our knowledge, all product candidates currently in development, are not, or will not be, available in the 1,600 mcg dosage strength.

SUBSYS® Market Experience to Date

Prescription Trends: Monthly prescription data through December 2018 shows that approximately 184,000 prescriptions of SUBSYS® have been dispensed since launch in March 2012. In December 2018, SUBSYS® was the most prescribed branded TIRF product with approximately 24% market share on a prescription basis according to IQVIA.

The ongoing and heightened publicity surrounding the perceived national opioid epidemic continues to result in heightened sensitivity by many healthcare professionals to prescribe opioids, pharmacies to dispense opioids, patients to fill opioid prescriptions, distributors to distribute opioids and third-party payers to cover opioid prescriptions. Third-party payers, such as insurance companies and regulatory and government agencies, continue to scrutinize the prescription of opioids by healthcare professionals. In addition, we believe other high-profile initiatives, such as (i) President Trump's declaration of the opioid crisis as a public health emergency, (ii) Congressional efforts to examine the causes of the opioid epidemic in public, and (iii) states, cities and counties initiating multi-district litigation against manufacturers and distributors of opioids have likely added to this sensitivity around opioid prescribing. Consequently, these current and potential future trends have affected, and will likely continue to affect, the manner in which, and the situations when, opioids, including SUBSYS®, are being prescribed, dispensed and approved for coverage.

Physician Prescriber Base: Approximately 900 physicians were responsible for 90% of all TIRF prescriptions dispensed in 2018, according to IQVIA. We have targeted our commercialization efforts towards approximately 48% of these top 900 prescribing physicians with a focus on those prescribers with the highest number of BTCP patients. During the year ended December 31, 2018, there were approximately 800 unique physician prescribers of SUBSYS®.

Patient Use: Existing patient data generated by available databases demonstrates that the number of SUBSYS®-experienced patients has increased steadily, albeit at a much slower rate in recent years, since launch with over 24,000 unique patients as of December 2018. Importantly, the proportion of SUBSYS® prescriptions written for repeat SUBSYS® patients is approximately 91% of prescriptions as of December 2018. Generally, repeat SUBSYS® patients receive higher doses of SUBSYS® on average than first-time patients, as patients are titrated from a starter dose of SUBSYS® to their effective dose in accordance with the REMS protocol.

Patient Access: SUBSYS® is a covered medication available under most major commercial health insurance plans formularies. Some third-party payers require usage and failure on cheaper generic versions of ACTIQ® prior to providing reimbursement for SUBSYS® and other branded TIRF products. We concentrate on assisting physicians and payers with developing greater familiarity with both the differentiated features of SUBSYS® and the process to achieve patient access to the product from continued and broader usage of SUBSYS® by their patients. We offer commercially-insured patients a free trial of SUBSYS® to allow for titration to their effective dose and bridge the prior authorization process. Once third-party payer reimbursement is in place, we may offer patients coupons to reduce out of pocket costs.

Cannabinoid Product Family

SYNDROS® (dronabinol oral solution)

Our lead proprietary dronabinol product is SYNDROS®, an orally administered liquid formulation of dronabinol. The DEA issued an interim final ruling that resulted in SYNDROS® being placed in Schedule II of the CSA and the FDA approved the final labeling reflecting the scheduling in May 2017. We commercially launched SYNDROS® in July 2017. Dronabinol, the active ingredient in Marinol®, is a synthetic form of THC. THC is an orally active cannabinoid that, like other cannabinoids, has complex effects on the central nervous system. Approved by the FDA in 1985, Marinol® is indicated for the treatment of CINV in patients who have failed to respond adequately to conventional treatments, as well as for the treatment of anorexia associated with weight loss in patients with AIDS. Marinol® is formulated in sesame oil and encapsulated in soft gelatin capsules and must be stored in cool storage conditions or in a refrigerator.

We believe an unmet medical need exists for formulations of dronabinol that act more rapidly and are subject to less variable patient absorption. We completed a pivotal bioequivalence study that was a 52-patient crossover bioavailability and PK clinical trial comparing SYNDROS® with Marinol®. In the study, 100% of subjects receiving SYNDROS® achieved detectable plasma levels at 15 minutes compared to less than 25% of the subjects receiving Marinol®. Additionally, SYNDROS® demonstrated lower intra-subject variability relative to Marinol®. We believe these attributes may be a consideration for the providers in selecting the appropriate formulation of dronabinol for patients, which we also believe will allow us to further penetrate and potentially expand the market for the medical use of dronabinol.

Market Overview

CINV is a commonly known side effect of chemotherapy that can have a significant negative impact on quality of patient life. CINV is classified into five categories:

- Acute: Occurs within 24 hours of chemotherapy administration.
- Delayed: Occurs more than 24 hours after chemotherapy administration, with peak intensity two to three days post-administration and duration of up to one week.
- Anticipatory: Occurs prior to treatment.
- Breakthrough: Occurs after use of antiemetic agents.
- Refractory: Occurs after failed use of breakthrough therapy.

The majority of chemotherapy patients experience at least one type of CINV. The National Comprehensive Cancer Network estimates that 70% to 80% of patients undergoing chemotherapy experience vomiting, with 10% to 44% experiencing anticipatory vomiting. Predictive factors for developing CINV can include: age of less than 50 years, female gender, vomiting during previous chemotherapy, pregnancy-induced nausea/vomiting, history of motion sickness and anxiety. In addition to generally affecting patient quality of life, CINV can result in weakness, weight loss, electrolyte imbalance, dehydration or anorexia. According to a study published by Ballatori, et al in 2007, 90% of patients who experienced CINV reported an impact on daily activities.

Although the pathophysiology of CINV is not clearly understood, it is thought that chemotherapeutic agents cause vomiting by activating neurotransmitter receptors located in the chemoreceptor trigger zone, GI tract, and VC. Activation of the VC directly or through the chemoreceptor trigger zone results in stimulation of the salivation and respiratory centers as well as control of the pharyngeal, GI and abdominal muscles. This stimulation can trigger the body to retch and vomit.

Treatment of CINV is highly patient-specific and is based on the emetogenic potential of the chemotherapy regimen. According to IQVIA, U.S. sales for drugs treating CINV were $1.3 billion in 2013, though published reports suggest that current therapies are not entirely effective. A report published in *Cancer* estimated that approximately 35% of patients treated with CINV therapies continue to experience acute nausea, with 13% of CINV patients experiencing acute vomiting after first-line treatment.

Limitations of Existing Therapies

We believe that there are unmet needs for our cannabinoid products due to the limitations of existing therapies, which include:

- *Delayed absorption*: Marinol® is only available in a capsule formulation, which must be dissolved and digested before it is metabolized in the patient's liver, where the drug is broken down by enzymes. We believe that this capsule formulation and digestion process delays onset of action and relief of nausea and vomiting. After oral administration, Marinol® has an onset of action of approximately 30 minutes to one hour and peak effect at two to four hours.
- *Variable patient absorption*: The uptake of Marinol® into systemic circulation varies widely from dose-to-dose and patient-to-patient. In general, this level of variability is atypical relative to approved pharmaceutical products. As such, physicians are unable to predict the level of efficacy or side effects that an individual patient might experience relative to other patients or even to a patient's own last dose of dronabinol.
- *Limited second-line therapy options*: Currently, there are a limited number of different classes of medications approved for CINV that are unresponsive to initial therapy. The availability of dronabinol offers a different class of medication than more traditional first-line antiemetics.

Our Solutions

We believe our SYNDROS® product has the potential to address some of the unmet needs that exist in synthetic cannabinoid products by providing a number of key advantages, including:

- *Fast absorption*: SYNDROS® is a liquid solution and is absorbed faster than a capsule formulation that has to dissolve in the GI tract. We believe that quicker absorption may be an important consideration in the selection of a dronabinol product by physicians.
- *Reduced dose-to-dose variability*: Based on our PK study, we believe SYNDROS® has low variability of absorption between patients.

Cannabidiol Oral Solution

Cannabidiol has been shown pre-clinically to protect from seizures in various rodent models of seizures, to alleviate neuropathic pain caused by chemotherapy-induced peripheral neuropathy mouse models treated with paclitaxel, and reduce tumor burden in xenograft mouse model of human glioblastoma tumors. We have developed a Cannabidiol Oral Solution, a CBD, for the potential treatment of rare childhood epilepsy syndromes that includes West Syndrome (Infantile Spasms) and Childhood Absence Epilepsy, for which we have received or applied for Orphan Drug Designation.

In addition to the above epilepsy indications, we have also received Orphan Drug Designations for CBD in the treatment of glioblastoma multiforme, pontine glioma, and pediatric schizophrenia.

Early studies in animal models demonstrate that CBD has anticonvulsant properties and the effectiveness of CBD-enriched cannabinoids in the treatment of epilepsy has been reported. A survey of children using a CBD-enriched plant product reported an 84% reduction in their child's seizures, and 11% reported complete seizure freedom. In an open access program using a CBD-enriched plant deprived product, which included 214 patients who received drug, the median reduction in monthly motor seizures was 36.5% and the drug was generally well-tolerated. However, parental report can be subject to significant bias, especially where expectations are high.

Currently, we have two ongoing and three completed studies in epilepsy. One ongoing study is a Phase 2 study in refractory Child Absence Epilepsy, evaluating three different doses: 20 mg/kg/day, 30 mg/kg/day, and 40 mg/kg/day. The second ongoing study is for Infantile Spasms patients involving adjunctive therapy with vigabatrin using the 40 mg/kg/day dose of CBD.

The first completed study was a Phase 1b pharmacokinetic study that evaluated three different doses of CBD in pediatric patients with refractory epilepsy: 10mg/kg/day, 20mg/kg/day and 40mg/kg/day. The second completed study was a long-term safety study of the children who completed the Phase 1b pharmacokinetic study and elected to continue treatment with CBD for an additional 48 weeks.

The third completed study, a Phase 2 study to assess the efficacy and safety of Cannabidiol Oral Solution for the treatment of refractory Infantile Spasms, studied the effect of Cannabidiol Oral Solution in patients who have failed all approved treatments. This study has been completed and we are evaluating the development in Infantile Spasms in a less refractory population.

Prader-Willi Syndrome, first described in 1956, is a multifaceted developmental disorder and the most common genetic syndrome associated with obesity. It is caused by the absent expression of paternally-inherited genes in the chromosome region on 15q11-q13. While it presents with generalized hypotonia and developmental delay in infancy, Prader-Willi Syndrome then manifests with uncontrollable appetite, hyperphagia, and excessive weight gain leading to severe obesity, and it is the appetite behavior classified as hyperphagia in Prader-Willi Syndrome that is the most life threatening. Until recently, no patient lived over the age of 50 due to morbid obesity and its related complications. The mortality rate in patients with Prader-Willi Syndrome is six times higher than patients with other intellectual disabilities.

Hyperphagic behaviors can also be dangerous in persons who are not obese, with increased risks of death due to choking while sneaking food, and gastric perforations after consuming more food than usual. Approximately 8% of deaths in individuals with Prader-Willi Syndrome are reported due to the choking, especially on hot dogs. Prader-Willi Syndrome patients also are known to eat discarded (contaminated) food and items that are not for human consumption such as pet food, or even non-food items such as paint or paper.

Currently, there are no FDA-approved therapies for the treatment of hyperphagia or obesity in patients with Prader-Willi Syndrome. In addition, drugs that have demonstrated efficacy in the past have been withdrawn or have significant safety concerns (e.g., rimonabant, beloranib). Recent studies investigating modulation of the endocannabinoid system have shown promise.

The endocannabinoid system appears to be critically involved in the regulation of appetite, body weight, metabolism , hypothalamic-pituitary-adrenal axis, and reward brain circuitry. In clinical studies, compounds with endocannabinoid effects (fenfluramine, rimonabant) have shown significant effects on weight and appetite suppression. These effects on appetite also occurred in 19% of epilepsy patients treated with Epidiolex© (i.e., cannabidiol extracted from the cannabis plant) during an open-access program for patients with pediatric seizure disorder.

We are currently conducting a clinical trial of the 40 mg/kg of CBD in pediatric patients who have Prader-Willi Syndrome to evaluate its effect on hyperphagia.

We also provide Cannabidiol Oral Solution and some financial support for Investigator-Initiated Trials of Cannabidiol Oral Solution in various clinical settings such as cocaine dependence, autism, and early psychosis. These trials are currently ongoing or starting in 2019.

Other Product Candidates

Our other product candidates include other Cannabinoid line extensions and sublingual and nasal spray product candidates.

Future Cannabinoid Line Extensions . As described above, we plan to develop additional dronabinol delivery systems, including a proprietary inhalation dronabinol formulation. We also have the capability to manufacture synthetic cannabidiol and intend to work with medical researchers to determine its viability.

Sublingual Spray Product Candidates . As described above, we are conducting clinical and preclinical development for multiple well-known, approved molecules for delivery through our sublingual drug delivery technology. We intend to evaluate these and other products that we believe could have a differentiated efficacy and/or safety profile if formulated by us and delivered via a sublingual spray.

Buprenorphine Sublingual Spray. On September 29, 2017, we filed an NDA with the FDA for this product candidate, and on December 6, 2017, the FDA accepted the filing. On July 27, 2018, we received a Complete Response Letter from the FDA, indicating that, although the clinical development program demonstrated all three proposed doses of the product candidate were statistically significantly different than placebo in providing pain relief, some of the data suggested potential safety concerns. Given the attributes of our proprietary buprenorphine formulation for sublingual delivery, we continue to believe that this drug-device combination could bring value to the management of pain and will assess the next steps for this product.

Nasal Spray Product Candidates. Two drug products are currently undergoing development for use as nasal spray devices, naloxone and epinephrine. We have completed proof of concept studies for a naloxone nasal spray and are currently in the process of completing the non-clinical toxicology studies, including juvenile animal toxicity studies as part of the Pediatric Research Equity Act (“PREA”). We intend to file an NDA in the second quarter of 2019. In addition, we received fast track designation from the FDA and completed proof-of-concept and dose-finding PK studies for an epinephrine nasal spray to be used for the treatment of allergic reactions (Type 1) including anaphylaxis.

Sales and Marketing

We currently market SUBSYS® and SYNDROS® in the United States through our commercial sales organization. Our product detailing efforts focus primarily on oncologists, pain specialists and centers that cater to supportive care.

We do not currently have internal sales and marketing capabilities outside of the United States. We are evaluating opportunities to sell our products internationally, and have entered into arrangements with third parties to pursue requisite regulatory approvals in the Middle East.

We believe some of the key factors in generating growth in SUBSYS® usage include : (i) taking market share from other competing TIRF products and increasing access of the product to appropriate cancer patients suffering from BTCP, and (ii) increasing awareness of the prevalence of BTCP among oncologists and highlight the efficient benefits of SUBSYS®, which include rapid onset of analgesia, improved bioavailability, patient satisfaction and ease of administration relative to other TIRF products.

As of December 31, 2018, there were approximately 4,500 physicians enrolled in the TIRF REMS program. Enrollment in this class-wide REMS program is required by the FDA as of March 2012 in order to prescribe TIRF products. Approximately 900 physicians comprise 90% of TIRF prescriptions dispensed in 2018, according to IQVIA. Our sales and marketing efforts have primarily targeted approximately 48% of these top 900 prescribing physicians with a focus on those prescribers with the highest number of BTCP patients.

We believe some of the key factors in generating growth in SYNDROS® usage include: (i) continuing to drive product awareness of the benefits of SYNDROS® as the first FDA approved liquid cannabinoid with the appropriate healthcare professionals, (ii) increasing the education on the different mechanism of action between SYNDROS® and other antiemetics, and (iii) converting branded and generic dronabinol usage by reducing financial and payer barriers for the patient.

The majority of our sales of SUBSYS® and SYNDROS® are to wholesale pharmaceutical distributors and specialty retail pharmacies. Wholesale pharmaceutical distributors, in turn, sell the products to pharmacies, hospitals and other customers, whereas specialty retail pharmacies sell the products directly to patients. For the year ended December 31, 2018, three wholesale pharmaceutical distributors, AmerisourceBergen Corporation, McKesson Corporation, and Cardinal Health, Inc., individually comprised approximately 33%, 15%, and 10%, respectively, and two specialty retail pharmacies individually comprised 18% and 21%, of our total gross sales of SUBSYS® and SYNDROS®. For additional information, see “Risk Factors—Risks Related to Our Business and History—We depend on wholesale distributors and specialty retail pharmacies for retail distribution of SUBSYS® and SYNDROS®; if we lose any of our significant wholesale distributors or specialty retail pharmacies, our business could be harmed” in Part I, Item 1A of this report.

Manufacturing and Supply

We produce dronabinol, the API in our dronabinol product family, including our proprietary dronabinol product candidates, internally at our U.S.-based, state-of-the-art manufacturing facility located in Round Rock, TX. We believe that this facility has the capacity to supply sufficient commercial quantities of dronabinol API for SYNDROS®, as well as to support the continued development of our other cannabinoid product candidates in the near-term. We believe this facility gives us a significant competitive advantage since dronabinol API is a Schedule I material and, consequently, is subject to annual production limits set by DEA quotas for each individual facility, cannot be readily procured, is difficult to import into the United States and has a limited number of suppliers domestically. For additional information, see “Risk Factors—Risks Related to Our Business and History—We may encounter manufacturing failures that could impede or delay commercial production of SYNDROS®, or the preclinical and clinical development or regulatory approval of our dronabinol product candidates” in Part I, Item 1A of this report.

In 2014, we completed construction of a second domestic dronabinol manufacturing facility, which will enable us to supply additional commercial quantities of dronabinol API for our continued commercialization of SYNDROS® and any of our proprietary dronabinol product candidates, if approved. For additional information, see “Risk Factors—Risks Related to Our Business and History—We have expanded our SYNDROS® capacity by constructing a second facility. We may encounter a number of challenges relating to the management and operation of such a facility, and we may never realize a return on our investment” in Part I, Item 1A of this report.

The chemical materials for dronabinol API are sourced from independent suppliers and are manufactured utilizing well-established chemical techniques. Our manufacturing facility utilizes these chemical materials to produce dronabinol through a series of synthetic reactions and purification cycles. We believe that our suppliers are equipped to meet our current and future chemical material needs for the commercialization of SYNDROS®, and the development and commercialization of our dronabinol-based product candidates.

We purchase the fentanyl API utilized in connection with SUBSYS® from one vendor as our sole supplier of the API in this product. In addition, SUBSYS® is manufactured by contract manufacturers and sub-component fabricators. Aptar and Renaissance have been selected for their specific competencies in manufacturing, product design and materials. FDA regulations require that materials be produced under cGMPs or quality system regulations, as required for the respective unit operation within the manufacturing process. We believe both key suppliers have sufficient capacity to meet our projected product requirements.

Aptar

Aptar, a dispensing system company based in Illinois, developed the sublingual spray device we use for SUBSYS®. We entered into a supply agreement, effective as of March 7, 2011, with Aptar pursuant to which Aptar supplies us with the delivery system to administer SUBSYS®. We are required to provide Aptar with rolling quarterly forecasts of our requirement for SUBSYS® drug delivery systems. Under certain circumstances, such forecasts are non-binding; however, some portions of such forecasts may constitute a firm commitment to purchase delivery systems. The agreement has a term of five years from the effective date, subject to early termination clauses. On October 30, 2015, we entered into an amended and restated supply, development & exclusive licensing agreement with Aptar, which, among other things, extended our exclusive supply rights to the current sublingual device, currently utilized by SUBSYS®, as well as any new device(s) jointly developed by the two companies for a period of seven years. In addition to extending the term, this amendment added certain minimum purchase commitments and requires certain tiered royalties as a percentage of net revenue to be paid by us ranging from less than one percent to the low single digits, commencing in March 2016 through the term of the agreement, from our sales of SUBSYS® and future products that use the Aptar spray device technology.

In January 2016, we assigned our rights, title, duties and obligations of our supply, development & exclusive licensing agreement with Aptar from our parent to our manufacturing subsidiary as part of a corporate restructuring.

In April 2017, we, through our manufacturing subsidiary, entered into a further amendment to our Aptar supply, development and exclusive licensing agreement. This amendment effectively eliminated any prior minimum purchase obligations that had been set forth in the amendment, dated October 30, 2015, and beginning in 2019, replaces them with a new annual flat fee of up to $500,000 if the quantity of devices purchased in a calendar year is less than one million devices. As a result, the cumulative effect related to this amendment reduces our aggregated purchase commitment with Aptar from $20,790,000 to $9,000,000 through December 21, 2022.

Renaissance

We entered into a manufacturing agreement effective as of May 24, 2011 with Renaissance pursuant to which we engaged Renaissance on an exclusive basis to provide processing and packaging services with respect to SUBSYS®. The contract requires us to provide rolling quarterly forecasts, a portion of which constitute firm purchase commitments. In April 2015, we entered into an amendment to our manufacturing and supply agreement with Renaissance, which extends our existing manufacturing and supply agreement to produce SUBSYS® until the end of 2020. In addition to extending the term, this amendment added certain minimum purchase commitments.

In January 2016, we assigned our rights, title, duties and obligations of our manufacturing and supply agreement with Renaissance from our parent to our manufacturing subsidiary as part of a corporate restructuring.

In April 2018, we, through our manufacturing subsidiary, entered into a further amendment to our Renaissance manufacturing and supply agreement. This amendment effectively eliminated any prior minimum purchase (and batch) obligations that had been set forth in the amendment dated July 2016 and replaces them with a new annual purchase commitment of $3,000,000 for the calendar year ended December 31, 2018, and $2,000,000 for the calendar years ending December 31, 2019 and 2020. As a result, the cumulative effect related to this amendment reduces our aggregated purchase commitment with Renaissance from $12,000,000 to $7,000,000 through December 31, 2020.

In February 2019, we, through our manufacturing subsidiary, entered into a further amendment to our Renaissance manufacturing and supply agreement. This amendment effectively eliminates any prior and future minimum purchase (and batch) obligations that had been set forth in the amendment dated April 2018. In addition, we entered into an Asset Purchase Agreement in which we agreed to sell, and Renaissance agreed to purchase, certain of our manufacturing equipment.

During the years ended December 31, 2018 and 2017, we recorded a loss of $359,000 and $1,035,000, respectively, in cost of revenue in our Consolidated Statements of Comprehensive Income (Loss) for a portion of this commitment to Renaissance which represented firm, non-cancellable and unconditional purchase commitments for quantities in excess of our current forecasts for future demand.

For additional information, see “Risk Factors—Risks Related to Our Business and History—We are dependent on numerous third parties in our supply chain for the commercial supply of SUBSYS® and SYNDROS®, and if we fail to maintain our supply and manufacturing relationships with these third parties or fail to develop new relationships with other third parties, we may be unable to continue to commercialize SUBSYS® and SYNDROS®, or to develop other product candidates” in Part I, Item 1A of this report.

Competition

Our industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face competition from many different sources, such as pharmaceutical companies, including generic drug companies, biotechnology companies, drug delivery companies and academic and research institutions. We believe the key competitive factors that will affect the commercial success of our products and the development of our product candidates include, but are not limited to, onset of action, bioavailability, efficacy, cost, convenience of dosing, safety, tolerability profile, DEA scheduling and intellectual property rights. Many of our potential competitors have substantially greater financial, scientific, technical, intellectual property, regulatory and human resources than we do, and greater experience than we do commercializing products and developing product candidates, including obtaining FDA and other regulatory approvals for product candidates. Consequently, our competitors may develop products for the treatment of BTCP, CINV and anorexia associated with weight loss in patients with AIDS, or other indications we pursue that are more effective, better tolerated, more widely-prescribed or accepted, more useful and less costly, and they may also be more successful in manufacturing and marketing their products. We also face competition from third parties in obtaining allotments of fentanyl and dronabinol under applicable DEA production and procurement quotas, recruiting and retaining qualified personnel, establishing clinical trial sites and enrolling patients for clinical trials and in identifying and acquiring or in-licensing new products and product candidates.

SUBSYS®

SUBSYS® competes against numerous branded and generic products already being marketed and potentially those which are or will be in development. SUBSYS® is one of nine commercially available products in the TIRF market. In the BTCP market, physicians often treat patients with a variety of short-acting opioid medications, including morphine, morphine and codeine derivatives and fentanyl. Some currently marketed products against which we directly compete include Teva Pharmaceutical Industries Ltd.’s FENTORA® and ACTIQ®, Sentynl Therapeutics’ Abstral®, West Therapeutic Development, LLC’s Lazanda® and BioDelivery Science International, Inc.’s Onsolis®. Some generic fentanyl products against which SUBSYS® competes are marketed by Mallinckrodt, Inc., Par Pharmaceutical Companies and Actavis, Inc.

Cannabinoid Product Family

With respect to our dronabinol product candidates, the market in which we intend to compete is challenging in part because of the presence of generic products. We or our distributors may not be able to differentiate any products that we may market from those of our competitors, successfully develop or introduce new products that are less costly or offer better performance than those of our competitors, or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors. In addition, there are a number of established therapies and products already commercially available and under development by other companies that treat the indications which SYNDROS® and our dronabinol product candidates are intended to treat. Specifically, SYNDROS®, and our other dronabinol product candidates, will compete against therapies and products such as AbbVie, Inc.'s Marinol® and Marinol® generics. Par Pharmaceutical Companies markets an approved generic version of Marinol®, and Actavis, Inc. markets an authorized generic version of Marinol®. Moreover, our cannabinoid products may compete with non-synthetic cannabinoid drugs, including therapies such as GW Pharmaceuticals plc's Sativex® and Epidiolex®, especially in many countries outside of the United States where non-synthetic cannabinoids are legal. In addition, literature has been published arguing the benefits of natural cannabis, or marijuana, over dronabinol, and there are a number of states that have already enacted laws legalizing medicinal and recreational marijuana. There is some support in the United States for further legalization of marijuana. We also cannot assess the extent to which patients utilize marijuana illegally to alleviate CINV, instead of using prescribed therapies such as approved dronabinol products. Furthermore, in the treatment of CINV, physicians typically offer conventional anti-nausea agents prior to initiating chemotherapy, such as Sanofi's Anzemet®, Eisai Inc./Helsinn Group's Aloxi®, Roche Holding AG's Kytril®, Par Pharmaceutical Companies' Zuplenz® and GlaxoSmithKline plc's Zofran®, as well as Neurokinin 1 receptor antagonists on the market including Kyowa Hakko Kirin Co., Ltd.'s Sancuso® and Merck & Co., Inc.'s Emend®. To the extent that SYNDROS® and our dronabinol product candidates, if approved, compete in a broader segment of the CINV market, we will also face competition from these products.

Additionally, we are aware of companies that have received approval for the commercialization of CINV products, including Heron Therapeutics, Inc.'s (formerly A.P. Pharma, Inc.) Sustrol®, Tesaro, Inc.'s Varubi®, and Helsinn Therapeutics (U.S.), Inc.'s Akynzeo®. If these products are successfully marketed over the next few years, they could represent significant competition for SYNDROS®. Additionally, Aphios Corp.'s Zindol® is in late stage development (Phase 3), and if successfully developed and approved, could represent significant competition for SYNDROS®.

Intellectual Property

The success of most of our product candidates will depend in large part on our ability to:

- obtain and maintain patent and other legal protections for the proprietary technology, inventions and improvements we consider important to our business;
- prosecute our patent applications and defend our issued patents;
- preserve the confidentiality of our trade secrets; and
- operate without infringing the patents and proprietary rights of third parties.

We intend to continue to seek appropriate patent protection for certain of our product candidates, drug delivery systems, molecular modifications, as well as other proprietary technologies and their uses by filing patent applications in the United States and selected other countries. We intend for these patent applications to cover, where possible, claims for medical uses, processes for preparation, processes for delivery and formulations.

As of March 5, 2019, we owned or licensed from third parties a total of ninety-four worldwide patents and sixty-two patent applications including twenty-seven issued U.S. utility patents and twenty-nine pending U.S. utility patent applications. These U.S. patents and patent applications will expire between 2022 and 2039. Some of the issued patents and pending applications, if issued, may also be eligible for patent term adjustment and patent term restoration, thereby extending their patent terms.

SUBSYS®

Our SUBSYS® patent portfolio currently consists of nine Orange Book listed (with the FDA) U.S. Patent Nos. 8,486,972, 8,486,973, 8,835,459, 8,835,460, 9,241,935, 9,289,387, 9,642,797, 9,642,844, and 10,016,403, and two pending U.S. patent applications. These patents are directed to SUBSYS® brand fentanyl and/or the use of the SUBSYS® sublingual fentanyl spray for the treatment of pain and will expire in 2027 and 2030. We also currently have sixty-six issued foreign patents and four pending foreign patent applications covering formulations and methods of use relating to SUBSYS®. Any patents that issue from our pending foreign patents and applications are expected to expire no earlier than 2027.

Dronabinol

Our dronabinol patent portfolio currently consists of four issued U.S. patents and three pending U.S. patent applications. Two of the U.S. patents are directed to formulations of dronabinol and methods of manufacturing and packaging dronabinol in capsules. Two of the U.S. patents and the pending applications are directed to SYNDROS® brand oral solution formulations of dronabinol. Three of the issued dronabinol patents will expire in 2028, while the forth will expire in 2033. Any patents that issue from our pending patent applications will likely expire between 2028 and 2039.

Other

The rest of our patent portfolio relates to patents and applications owned or licensed by us and directed to other potential product candidates.

Although we believe our rights under these patents and patent applications provide a competitive advantage, the patent positions of pharmaceutical and biotechnology companies are highly uncertain and involve complex legal and factual questions. In addition, we may not be able to obtain issued patents from pending applications. Even if patents are granted, the allowed claims may not be sufficient to adequately protect the technology owned by or licensed to us. Any patents or patent rights that we obtain carry some risk of being circumvented, challenged or invalidated by our competitors. For example, a former officer of Insys Pharma sought unsuccessfully to rescind his assignment of his inventions concerning fentanyl and dronabinol patent applications described above. Ownership and inventorship disputes may arise for other patents and applications that we own or license.

We also rely on trade secrets, proprietary know-how and continuing innovation to develop and maintain our competitive position, especially when we do not believe that patent protection is appropriate or can be obtained. We require each of our employees, consultants and advisors to execute a proprietary information and inventions assignment agreement before they begin providing services to us. Among other things, this agreement obligates each employee, consultant or advisor to refrain from disclosing any of our confidential information received during the course of providing services and, with some exceptions, to assign to us any inventions conceived or developed during the course of these services. We also require confidentiality agreements from third parties that receive our confidential information.

The biotechnology and biopharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. As our current and potential product candidates and others based upon our proprietary technologies progress toward commercialization, the possibility of an infringement claim against us increases. While we attempt to be certain that our products and proprietary technologies do not infringe other parties' patents and other proprietary rights, competitors or other parties may assert that we infringe on their proprietary rights.

We have conducted certain clearance searches of issued U.S. patents for our fentanyl formulations but we have not conducted extensive clearance searches for SYNDROS® or our other product candidates, and cannot guarantee that the searches we have done were fully comprehensive and, therefore, whether SUBSYS®, SYNDROS® or any of our product candidates, delivery devices, or methods of using, making or delivering our product candidates infringe the patents searched, or that other patents do not exist that cover SUBSYS®, SYNDROS® or our product candidates, delivery devices or these methods. Interpreting patent claims involves complex legal and scientific questions and it is difficult to assess whether or not our product candidates would infringe any patent. Likewise, it is difficult to predict whether or not third-party patent applications will issue and

what claim scope they may obtain. If we conclude that any identified patents, or patent applications once issued as patents, cover SUBSYS®, SYNDROS® or any of our product candidates, we cannot guarantee that we will be able to formulate around such patents at all or without material delay or whether we can obtain reasonable license terms from the patent owners, if at all. There may also be other pending patent applications that are unknown to us and, if granted, may prevent us from making, using or selling SUBSYS®, SYNDROS® or our product candidates. Other product candidates that we may develop, either internally or in collaboration with others, could be subject to similar uncertainties. If a product is found to infringe a third-party patent, we could be prevented from developing and selling that product. Please see the section entitled “Risk Factors — Risks Relating to Intellectual Property.”

Environmental and Safety Matters

We use hazardous materials, including chemicals, biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations also produce hazardous waste products. Federal, state and local laws and regulations govern, among other things, the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental, health and safety laws and regulations may be expensive, and current or future environmental, health and safety laws and regulations may impair our product development efforts.

In addition, we cannot entirely eliminate the risk of accidental injury or environmental contamination from these materials. If one of our employees was accidentally injured as a result of the use, storage, handling or disposal of hazardous materials, the medical costs related to his or her treatment should be within the coverage terms of our workers’ compensation insurance policy. However, we do not carry specific biological or hazardous waste insurance coverage and our property and casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The FDCA and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. regulations may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending INDs, and NDAs or the issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Pharmaceutical product development in the United States typically involves, among other things, preclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease indicated for treatment.

Preclinical tests include laboratory evaluation of product chemistry, stability, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. The results of preclinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Certain nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may be conducted after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not placed a clinical hold on the IND within this 30-day period, the proposed clinical trial may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, GCP, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial, as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing in U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an IRB for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human volunteers, the drug is tested to assess safety, metabolism, PK, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to evaluate the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage, and identify possible adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to provide substantial evidence of clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to establish the efficacy and safety of the drug and to provide adequate information for the labeling of the drug. In some cases, the FDA may condition approval on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after approval. Such post-approval studies are typically referred to as Phase 4 studies.

The current FDA standards for approving new pharmaceutical products are more stringent than those that were applied in the past. These standards were not applied to many established products currently on the market, including certain opioid products. As a result, the FDA does not have as extensive safety databases on these products as on some products developed more recently. The FDA has recently expressed an intention to develop safety data for certain products, including many opioids. In particular, the FDA has expressed interest in specific impurities that may be present in a number of opioid narcotic APIs, such as oxycodone. Based on certain structural characteristics, these impurities may have the potential to cause mutagenic effects. If, after testing, such effects are ultimately demonstrated to exist, more stringent controls on the levels of these impurities may be required for FDA approval of products containing these impurities, such as oxymorphone. Any additional testing or remedial measures that may be necessary could result in increased costs for, or delays in, obtaining approval for certain of our products in development.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls, and proposed labeling, among other things. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment fees per product and per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the Agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. Under the PDUFA the FDA has agreed to certain performance goals in the review of NDAs. The FDA has a goal of reviewing applications for non-priority drug products within 12 months of NDA submission. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically comprised of a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The

FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless the facility demonstrates compliance with cGMPs and the NDA contains data that provides substantial evidence that the drug is safe and effective for the indication sought in the proposed labeling. Additionally, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs before approving an NDA.

After the FDA evaluates the data in the NDA and the manufacturing facilities, clinical sites, and the proposed product label, it may issue either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two to six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms that can materially affect the potential market and profitability of the drug. Further, if there are any modifications to the drug, including changes in indications, dosage, labeling, or manufacturing processes or facilities, a new or supplemental NDA may need to be submitted, which may require additional data or additional nonclinical studies and clinical trials. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The FDA may require sponsors of investigational drugs to submit proposed REMS in order to ensure that the benefits of the drugs continue to outweigh the risks associated with its use. Sponsors of certain drug applications approved without a REMS program may also be required to submit a proposed REMS program if the FDA becomes aware of new safety information and makes a determination that a REMS program is necessary.

The Hatch-Waxman Act

Abbreviated New Drug Applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the RLD and has been shown to be bioequivalent to the RLD. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, but are required to conduct bioequivalence testing, which compares the bioavailability of their drug product to that of the RLD to confirm chemical and therapeutic equivalence. Drugs approved in this way are commonly referred to as generic versions of the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA that any patents listed for the approved product in the FDA's Orange Book have expired or are not applicable. Specifically, the applicant must certify that: (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid or will not be infringed by the new product. 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 applicant does not challenge the listed patents via a Paragraph IV certification, the FDA will not approve the ANDA until all the listed patents claiming the referenced product have expired.

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 prevents the FDA from approving the ANDA until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant. As an incentive for the rapid development of generic drug products, the first ANDA(s) filed that challenges a listed patent by filing a Paragraph IV certification may be granted a 180-day marketing exclusivity period during which the FDA may not approve another ANDA for the same product. There may be multiple such “first filers.” The 180-day marketing exclusivity period is triggered either by commercial launch of any first-filed ANDA approved product or from the date of a court decision finding the challenged patent to be invalid, unenforceable or not infringed, whichever is first. The 180-day exclusivity can be forfeited, among other reasons, if the first filed and approved ANDA is not marketed, does not obtain tentative approval or the challenged patent expires.

The ANDA also will not be approved until any non-patent market exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. Federal law provides an exclusive period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law additionally provides for a period of three years of exclusivity following approval of a drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor. The FDA cannot grant effective approval of an ANDA based on that listed drug during this three-year period.

Section 505(b)(2) Regulatory Pathway

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA. Section 505(b)(2) of the FDCA enables the applicant to rely, in part, on the FDA’s findings of safety and efficacy for an existing product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved products. Specifically, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon the FDA’s findings from preclinical or clinical studies conducted for an approved product. The FDA may also require 505(b)(2) applicants to perform additional studies or measurements 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 findings of safety or efficacy for an already approved product, the applicant is subject to existing exclusivity for the reference product and 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. Thus 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.

Post-Approval FDA Requirements

Once an NDA is approved, a product is subject to extensive and ongoing post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. FDA post-market regulations also include, among other things, requirements relating to drug listing, recordkeeping, periodic reporting, product sampling and distribution, manufacturing and reporting of adverse events arising from use of the product. Failure to comply with these regulatory requirements may result in restrictions on the marketing or manufacturing of the product, recall or market withdrawal, fines, warning letters, refusal to approve pending applications, suspension or revocation of approvals, product seizure or detention, injunctions and/or the imposition of civil or criminal penalties.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and can take the same actions in reviewing NDA supplements as it does in reviewing original NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 commitments or requirements, a REMS program and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA 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. The FDA and comparable state 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.

The distribution of prescription pharmaceutical products is also subject to the PDMA, which governs the distribution of drugs and drug samples at the federal level, and sets minimum standards for the licensing and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Risk Evaluation and Mitigation Strategies

On December 29, 2011, the FDA approved a single shared REMS for TIRF products. TIRF products, which include the brand-name drugs Abstral®, ACTIQ®, FENTORA®, Lazanda®, Onsolis® and SUBSYS®, are narcotic pain medicines called opioids used to manage breakthrough pain in adults with cancer who routinely take other opioid pain medicines around-the-clock. The program officially began in March 2012.

The goals of the TIRF REMS Access Program are to ensure patient access to important medications and mitigate the risk of misuse, abuse, addiction, overdose and serious complications due to medication errors by:

- prescribing and dispensing TIRF products only to appropriate patients, including use only in opioid-tolerant patients;
- preventing inappropriate conversion between fentanyl products;
- preventing accidental exposure to children and others for whom TIRF products were not prescribed; and
- educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Healthcare professionals who prescribe TIRF products that will only be used in an inpatient setting (hospitals, hospices, or long-term care facilities) are not required to enroll in the TIRF REMS Access Program. Similarly, patients who receive TIRF products in an inpatient setting are not required to enroll in the program. Long-term care and hospice patients who obtain their medications from outpatient pharmacies, however, must be enrolled.

Controlled Substances; Drug Enforcement Administration

We sell products that are "controlled substances" as defined in the CSA, which establishes registration, security, recordkeeping, reporting, storage and other requirements administered by the DEA. States impose similar requirements. The DEA regulates entities that handle controlled substances and the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have high potential for abuse, no currently accepted medical use in the United States and lack accepted safety for use under medical supervision, and may not be marketed or sold in the United States. Except for research and industrial purposes, a pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances considered to present the lowest relative risk of abuse among such substances. Fentanyl, the active ingredient in our SUBSYS® product, is listed by the DEA as a Schedule II substance under the CSA. Consequently, its manufacture, shipment, storage, sale and use are subject to a high degree of regulation. For example, manufacturing of fentanyl is subject to a DEA regulated quota system. In addition, generally all Schedule II drug prescriptions must be signed by a physician and physically presented to a pharmacist before filling and may not be refilled without a new prescription.

DEA 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 to be handled under that registration.

The DEA typically inspects certain facilities to review their security controls, recordkeeping and reporting 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. Security measures required by the DEA include background checks on employees and physical control of inventory through measures such as vaults, 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, suspicious orders, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

A DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. This includes manufacturing of the API and production of dosage forms. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. Absent the Marinol®-like formulation and encapsulation exception, dronabinol is a Schedule I controlled substance and, therefore, subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for how much total dronabinol may be produced in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of dronabinol 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 manufacturing and procurement quotas. We or our partners, including our contract manufacturers, must obtain an annual quota from the DEA in order to produce or procure any Schedule I or Schedule II substance, including dronabinol and fentanyl. The DEA may adjust aggregate production quotas and individual manufacturing quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Our, or our contract manufacturers', quota of the active ingredient may not be sufficient to meet commercial demand or complete clinical trials. Any delay or refusal by the DEA in establishing our, or our contract manufacturers', quota for controlled substances could delay or stop our clinical trials or product launches which could have a material adverse effect on our business, financial position and results of operations.

The DEA conducts periodic inspections of certain registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in 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 proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could result in criminal proceedings.

Individual states also regulate controlled substances, and we and our contract manufacturers will be subject to state regulation on distribution of these products, including licensing, recordkeeping and security.

Controlled substances are also regulated pursuant to several international drug control treaties. These treaties are enforced by the United National Commission on Narcotic Drugs. The United States is a signatory to these treaties and thus must conform its laws and regulations to the international requirements, which generally include licensing, recordkeeping and reporting requirements. Both fentanyl and dronabinol are currently classified under the international treaties and current U.S. controls adequately address international requirements. Any change in the international treaties regarding classification of these products could affect regulation of these substances in the United States and in other countries.

Anti-Kickback and False Claims Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include Anti-Kickback and False Claims statutes. The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for statutory exemptions or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The reach of the Anti-Kickback Statute was also broadened by the PPACA which amends the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product. In addition, certain marketing practices, including off-label promotion, may also lead to violations of the False Claims Act. Many states also have statutes or regulations similar to the federal Anti-Kickback Statute

and False Claims Act, which state laws apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Moreover, qui tam suits filed under the False Claims Act can be brought by any individual on behalf of the government and such individuals, commonly known as “relators” or “whistleblowers,” may share in any amounts paid by the entity to the government in fines or settlement. The frequency of filing qui tam actions has increased significantly in recent years, causing greater numbers of healthcare companies to have to defend such qui tam actions and pay substantial sums to settle such actions.

Also, the HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

To the extent that any of our product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and Reimbursement

The commercial success of our products and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other third-party payers provide coverage for and establish adequate reimbursement levels for our products, product candidates, and related treatments.

Government health administration authorities, private health insurers and other organizations generally decide which drugs they will pay for and establish reimbursement levels for healthcare. In particular, in the U.S., private health insurers and other third-party payers often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the U.S., the European Union and other potentially significant markets for our product candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the U.S. and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. The cost containment measures that healthcare payers and providers are instituting, and the effect of any healthcare reform, could significantly reduce our revenues from the sale of any products or approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

The MMA imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payers. In 2018, CMS

published a roadmap outlining their efforts to address the opioid epidemic. Under this roadmap, new policies, which went into effect on January 1, 2019, were implemented for Part D plans that include improved safety alerts when opioid prescriptions are dispensed at the pharmacy, and drug management programs to better coordinate care when chronic high-risk opioid use is present. While CMS recognizes that a "one size fits all" approach does not take into account different circumstances related to opioid use, and has stated that patients being treated for active cancer-related pain are exempt from these interventions, further restrictions could be placed on opioid prescriptions.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payers, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our products or product candidates. If third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The U.S. and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including, most recently, the PPACA, which changes the way healthcare is financed by both governmental and private insurers.

Healthcare Privacy and Security Laws

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

Approval Outside the United States

In order to market any product outside of the United States, we must comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales and distribution of our products. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods, and may be otherwise complicated by our product candidates being controlled substances such as synthetic cannabinoids and fentanyl. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval and DEA classification. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

We have initiated early stage discussions with the Medicines Evaluation Board ("MEB") in the Netherlands to solicit feedback on potential approval pathway for SUBSYS®, and have entered into arrangements with third parties to pursue requisite regulatory approvals in the Middle East. As in the United States, the regulatory approval process in Europe and in other countries is a lengthy, challenging and inherently uncertain process.

Research and Development

Our operating results will also depend significantly on our research and development activities and related regulatory developments. Our research and development expenses were $57.6 million, $63.0 million and $73.9 for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018 and 2017, we had 50 and 61 full-time research and development personnel, respectively. We expect research and development expenses to fluctuate with the timing of our planned preclinical studies and clinical trials for our product candidates, particularly our proprietary cannabinoid product candidates and sublingual spray product candidates. We do not expect to realize net revenues from all of these research and development initiatives in the near term and may never realize net revenues from these investments. For additional information, see "Management's Discussion and Analysis of Financial Condition and Results of Operations—Factors Affecting Our Performance—Product Development and Related Regulatory Processes".

Employees

As of December 31, 2018, we employed 226 full-time employees, including 62 manufacturing employees, 66 sales and marketing employees, 50 employees in research and development, and 48 employees in administration. None of our employees are covered under a collective bargaining agreement and we consider our relationship with our employees to be good.

Scientific Advisory Board

We have established a scientific advisory board consisting of industry experts with knowledge of our target markets. Our scientific advisors generally meet twice a year as a group to assist us in formulating our research, development, clinical and sales and marketing strategies. Some individual scientific advisors consult with and meet informally with us on a more frequent basis. Our scientific advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Available Information

We make our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports available, free of charge, in the "Investors" section of our Internet website as soon as reasonably practicable after we electronically file these materials with, or furnish these materials to, the SEC. Our website is *www.insysrx.com*. Additionally, you will find these materials on the SEC Internet site at *http://www.sec.gov* that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC.

ITEM 1A. RISK FACTORS

Risks Related to Our Business and Industry

We are largely dependent on the commercial success of our two approved products, and although we have generated revenue from sales of these products, we may not be able to generate profits.

Our ability to generate profits depends upon the commercial success of our two main approved products, SUBSYS® and SYNDROS®. In addition to the risks discussed elsewhere in this section, our ability to generate revenues and profits from the sale of these products will depend on a number of factors, including, but not limited to:

- achievement of broad market acceptance and coverage by third-party payers for our products;
- the effectiveness of our efforts in marketing and selling our products;
- our and our contract manufacturers' ability to successfully manufacture commercial quantities of our products at acceptable cost levels and in compliance with regulatory requirements;
- our ability to maintain a cost-efficient commercial organization and, to the extent we seek to do so, successfully partner with additional third parties;
- our ability to successfully defend, expand and maintain intellectual property protection for our products;
- the efficacy and safety of our products; and
- our ability to comply with regulatory requirements.

Heightened attention on the use of opioids, including government litigation changes in policies, legislation and leadership at the federal and state level, could hinder or prevent the commercial success of SUBSYS® and any potential future opioid product candidates.

Many federal and governmental agencies are focused on the abuse of opioids in the United States and our current President and agencies such as the HHS have expressed their belief that the United States is in the midst of a prescription opioid abuse epidemic. Common prescription drugs that contain opioids are drugs such as oxycodone, hydrocodone, and fentanyl. The ongoing and heightened publicity surrounding the perceived national opioid epidemic continues to result in heightened sensitivity by many healthcare professionals to prescribe opioids, pharmacies to dispense opioids, patients to fill opioid prescriptions, distributors to distribute opioids and third-party payers to cover opioid prescriptions. Third-party payers, such as insurance companies and regulatory and government agencies, continue to scrutinize the prescription of opioids by healthcare professionals. In addition, we believe other high-profile initiatives, such as (i) President Trump's declaration of the opioid crisis as a public health emergency, (ii) Congressional efforts to examine the causes of the opioid epidemic in public, and (iii) states, cities and counties initiating multi-district litigation against manufacturers and distributors of opioids have likely added to this sensitivity around opioid prescribing. Consequently, these current and potential future trends have affected, and will likely continue to affect, the manner in which, and the situations when, opioids, including SUBSYS®, are being prescribed, dispensed and approved for coverage.

If SUBSYS®, SYNDROS®, or any of our product candidates for which we receive regulatory approval, do not maintain broad market acceptance or coverage by third-party payers, the revenues that we generate from these products will be limited.

The commercial success of SUBSYS®, SYNDROS® and any product candidates for which we obtain marketing approval from the FDA or other regulatory authorities, will depend upon the continued acceptance of these products by physicians, patients, healthcare payers and the medical community. Coverage and reimbursement of our approved products by third-party payers is also necessary for commercial success. The degree of market acceptance of SUBSYS®, SYNDROS® and any other product candidates for which we may receive regulatory approval will depend on a number of factors, including:

- patients' ability to obtain sufficient third-party payer coverage and reimbursement;
- our ability to provide acceptable evidence of safety and efficacy;

- acceptance by physicians and patients of the product as a safe and effective treatment;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- limitations or warnings contained in a product's FDA-approved labeling;
- the clinical indications for which the product is approved;
- the DEA scheduling classification for controlled substances, such as our dronabinol-based and fentanyl-based products;
- availability and perceived advantages of alternative treatments from competitors or otherwise;
- any negative publicity related to our or our competitors' products;
- any negative publicity related to our reputation;
- the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;
- pricing and cost effectiveness;
- the willingness of patients to pay out of pocket in the absence of third-party payer coverage; and
- our ability to maintain compliance with regulatory requirements.

For example, while we believe our sublingual spray delivery method for SUBSYS® appeals to patients, some patients may not view our sublingual spray device as easy to administer, safe and effective, and otherwise may not react favorably to sublingual delivery. In accordance with the REMS protocol for all TIRF products, physicians are advised to begin patients at the lowest dose available for the applicable TIRF product, which for SUBSYS® is 100 mcg. If patients do not experience pain relief at initial low-dose prescriptions of SUBSYS®, they or their physicians may conclude that SUBSYS® is ineffective in general and may discontinue use of SUBSYS® before titrating to an effective dose. In addition, many third-party payers require usage and failure on cheaper generic versions of ACTIQ® prior to providing reimbursement for SUBSYS® and other branded TIRF products, which limits SUBSYS®' use as a first-line treatment option.

In addition, products used to treat and manage pain, especially in the case of controlled substances, are from time to time subject to negative publicity, including illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny and in certain circumstances the FDA might even consider action to remove or revoke a product's approval. Controlled substances are classified by the DEA as Schedule I through V substances, with Schedule I substances being prohibited for sale in the United States, Schedule II substances considered to present the highest risk of abuse and Schedule V substances being considered to present the lowest relative risk of abuse. SUBSYS® contains fentanyl, an opioid, and is regulated as a Schedule II controlled substance, and despite the strict regulations on the marketing, distributing, prescribing and dispensing of such substances, illicit use and abuse of controlled substances is well-documented. SYNDROS® is also classified as a Schedule II controlled substance. Thus, the marketing of SUBSYS®, SYNDROS® and, if approved, our product candidates that contain controlled substances, may generate public controversy that may adversely affect market acceptance of SUBSYS®, SYNDROS® and, if approved, such product candidates.

Our efforts to educate the medical community and third-party payers on the benefits of SUBSYS®, SYNDROS® and any of our product candidates for which we obtain marketing approval from the FDA or other regulatory authorities and gain broad market acceptance requires significant resources and may not continue to be successful. If our products do not continue to receive an adequate level of acceptance by physicians, third-party payers and patients, we may not generate sufficient revenue from these products to be profitable.

In addition, fentanyl and dronabinol treatments can be costly to third-party payers and patients. Accordingly, hospitals and physicians may resist prescribing our products and third-party payers and patients may not purchase our products due to cost.

Furthermore, the potential market for SYNDROS® may not expand as we anticipate or may even decline based on numerous factors, including the introduction of superior alternative products and regulatory action negatively impacting the dronabinol market. Moreover, there is no guarantee that introduction of SYNDROS® will result in expansion of the dronabinol market or permit us to gain share in that market or maintain or increase any market share we may capture. New dronabinol products that we introduce could potentially replace SYNDROS®, thus not impacting the overall size of the market or increasing our overall share of that market. If we are unable to properly and compliantly expand the market for the medical use of dronabinol or gain, maintain or increase market share in that market, this failure would have a material adverse effect on our ability to execute on our business plan and ability to generate revenue.

The unpredictability and regulation surrounding reimbursement on SUBSYS® and SYNDROS® may affect our financial condition and results of operations.

Our sales of, and revenue from, SUBSYS® and SYNDROS® depend in significant part on the coverage and reimbursement policies of third-party payers, including government payers such as Medicare and Medicaid, and private health insurers. All third-party payers are sensitive to the cost of drugs and consistently implement efforts to control these costs, which efforts include, but are not limited to, establishing excluded or preferred drug lists. SUBSYS® has been, and will likely continue to be, subject to these restrictions and impediments from third-party payers, particularly PBMs and private health insurers. These PBMs, which administer prescription drug benefits for employers and health plans and runs large mail-order pharmacies, have significant influence in the insurance industry. While most PBMs have an exception process that physicians may pursue to have an off-formulary, medically necessary drug covered for patients, being placed on an exclusion list makes it difficult for many patients covered through a PBM administered plan to have SUBSYS® and SYNDROS® covered by insurance. In the future, we may not be able to work with other PBMs to evaluate price increases and to communicate with managed care and health-system decision-makers to ensure a balanced approach which takes into account the clinical performance and efficacy of our products. Moreover, in the United States, there have been, and we expect there will continue to be, a number of state and federal proposals that limit the amount that third-party payers may pay to reimburse the cost of drugs, particularly for state and federal government programs such as Medicare and Medicaid, as well as managed care providers and private insurance plans. We believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of SUBSYS® and SYNDROS®. For example, in 2018, CMS published a roadmap outlining their efforts to address the opioid epidemic. Under this roadmap, new policies, which went into effect on January 1, 2019, were implemented for Part D plans that include improved safety alerts when opioid prescriptions are dispensed at the pharmacy, and drug management programs to better coordinate care when chronic high-risk opioid use is present. While CMS recognizes that a “one size fits all” approach does not take into account different circumstances related to opioid use, and has stated that patients being treated for active cancer-related pain are exempt from these interventions, further restrictions could be placed on opioid prescriptions. Our ability to generate revenue is affected by the availability of third-party reimbursement for SUBSYS® and SYNDROS® and our results of operations will be negatively affected if we fail to manage adequate reimbursement levels for SUBSYS® and SYNDROS® from such third-party payers.

In addition, we outsource administrative reimbursement support assistance for patients, which function is critical to patients obtaining insurance coverage in connection with our products. The patient support assistance provided by third-parties, including specialty pharmacies, is subject to extensive and complex federal and state laws and varied third-party payers’ standards, procedures, processes and conditions. These third parties’ compliance with applicable laws, regulations and standards is expensive and time consuming and substantial governmental resources exist to enforce and prosecute these applicable laws, regulations and standards and companies that violate such laws, regulations and standards may face substantial penalties. The potential sanctions include significant civil, criminal and administrative penalties, damages and fines and exclusion from participation in federal healthcare programs. Because of the breadth of these laws and the lack of extensive legal guidance in the form of regulations or court decisions, it is possible that some of these third parties’ business activities could be subject to challenge or penalty under one or more of these laws and could materially affect our business in some way, including potentially vicarious liability if our employees violate our existing policies and procedures. Moreover, we may be subject to liability and regulatory sanctions in connection with the prior actions of former employees that operated in our patient service hub before we began outsourcing such function. Such aforementioned potential events could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payers to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payers is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our products.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage and adequate reimbursement will be obtained.

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

The manner by which we utilize our commercial sales force has evolved over time and may continue to evolve in the future. We or our collaborators may not be successful in executing sales and marketing strategies for SUBSYS®, SYNDROS®, or any additional product candidates for which we obtain regulatory approval. If such sales and marketing strategies are not successful, we may not be able to maintain or increase our revenues.

Our commercial organization including sales, marketing, managed markets, trade and distribution functions, which is now focused exclusively on marketing and selling SUBSYS® and SYNDROS® has evolved significantly since the launch of our first commercial product in March 2012. In response to the continuing decline in revenue, our management team has continued to examine potential cost reduction initiatives that could more closely align operating expenses with our reduced revenue. On July 12, 2018, we eliminated 45 positions through headcount reduction and role consolidation. The headcount reduction included 30 employees, the majority of which were sales and marketing employees, and represented approximately 9% of our workforce at the time. On and around November 1, 2018, we eliminated an additional 48 positions through further headcount reduction and role consolidation. The headcount reduction included 36 employees, the majority of which were sales and marketing employees, and represented approximately 13% of our workforce at the time. These reductions in our sales and marketing force may adversely affect the sales performance of our products. We may also need to consider alternatives that include entering into arrangements with third parties to market and sell our products in the United States or foreign territories. Any third-party arrangement may result in increased sales and marketing expenses or lower revenues than our current estimates and there can be no assurance that any current or future strategy will be successful.

We may continue to decrease the size of our sales force in the future based upon market conditions and actual sales performance, as well as in the event that we obtain regulatory approval for any of our product candidates. In addition, we could lose sales personnel, and the performance of our sales personnel as measured by actual sales has been, from time to time, and may in the future be disappointing.

Our business is subject to volatility and fluctuations in the number of employees we have across our enterprise. We may need to adjust the size and complexity of our organization in the future, depending upon the strategies we attempt to implement.

Our Company has evolved significantly since the launch of our first branded product in March 2012. Management and personnel, systems and facilities currently in place may not be adequate and/or appropriate to support our business plan.

Our need to effectively manage our operations and various business objectives requires that we adjust to ongoing challenges and needs and may require us to do one or more of the following:

- continue to improve our operational, financial, management and regulatory compliance controls and reporting systems and procedures;
- attract and retain sufficient numbers of talented employees;
- manage our commercialization activities for SUBSYS® and SYNDROS® effectively and in a cost-effective manner;
- manage our clinical trials effectively;
- manage our internal dronabinol production operations effectively and in a cost-effective manner;
- manage our development efforts effectively while carrying out our contractual obligations to contractors and other third parties; and
- continue to improve and expand our facilities.

In addition, historically, we have utilized and continue to utilize the services of part-time outside consultants to perform a number of tasks for us, including tasks related to compliance programs, clinical trial management, regulatory affairs, formulation development and other drug development functions. Our growth strategy may also entail expanding our use of consultants to implement these and other tasks going forward. Because we rely on consultants for certain functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. There can be no assurance that we will be able to manage our existing consultants or find other competent outside consultants, as needed, on economically reasonable terms, or at all. If we are not able to effectively manage our organization including our use of consultants, we may be unable to successfully implement the tasks necessary to effectively execute on our planned research, development and commercialization activities and, accordingly, may not achieve our research, development and commercialization goals.

We may encounter manufacturing failures that could impede or delay commercial production of SYNDROS® or the preclinical and clinical development or regulatory approval of our product candidates.

Any failure in our internal manufacturing operations could cause us to be unable to meet demand for SYNDROS® and lose potential revenue, delay the preclinical and clinical development or regulatory approval of our product candidates, and harm our reputation. Our internal manufacturing operations may encounter difficulties involving, among other things, production yields, regulatory compliance, contamination, quality control and quality assurance, obtaining DEA quotas which allow us to produce certain materials in the quantities needed to execute on our business plan, and shortages of qualified personnel. Our ability to support our existing product and our product candidates, could be impeded, delayed, limited or denied if we are unable to maintain the approval of our manufacturing processes and facilities. In addition, we have limited experience producing SYNDROS® in commercial quantities and may encounter difficulties with continuing to manufacture commercial quantities of SYNDROS® or the quantities of materials needed for our preclinical studies or clinical trials. Such difficulties could result in a delay in the commercial launch of our product candidates and cause delays in our preclinical studies, clinical trials and regulatory submissions.

We must comply with cGMPs enforced by the FDA through its facilities inspection program and review of submitted technical information. In addition, we must obtain and maintain necessary DEA and state registrations, and must establish and maintain processes to assure compliance with DEA and state requirements governing, among other things, the storage, handling, security, recordkeeping and reporting for controlled substances. We must also apply for, and receive, a quota from the DEA for dronabinol. Any failure to comply with these requirements may result in penalties, including fines and civil penalties, suspension of production, suspension or delay in product approvals, product seizure or recall, operating restrictions, criminal prosecutions or withdrawal of product approvals, any of which could significantly and adversely affect our business. If the safety of any product or product candidate or component is compromised due to a failure to adhere to applicable laws or for other reasons, we may not be able to successfully commercialize or obtain regulatory approval for the affected product or product candidate, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay or termination of commercialization, preclinical studies and clinical trials, regulatory submissions or approvals of our products or product candidates, entail higher costs or result in our being unable to effectively commercialize our approved

products. Certain changes in our manufacturing processes or procedures, including a change in the location where the material is manufactured, generally require prior FDA, or foreign regulatory authority, review and/or approval. We may need to conduct additional preclinical studies and clinical trials to support approval of such changes. This review and approval process may be costly and time-consuming, and could impede, delay, limit or prevent commercialization of a product.

We have expanded our SYNDROS® production capacity by constructing a second facility. We may encounter a number of challenges relating to the management and operation of such a facility, and we may never realize a return on our investment.

We have expanded our SYNDROS® production capacity by constructing a second facility designed to meet our expected future dronabinol API supply needs. The construction of the second facility has required significant capital expenditures and has resulted in significantly increased fixed costs. This second facility requires the maintenance of additional regulatory approvals and costs. We cannot guarantee we will receive the necessary approvals to operate this facility.

We cannot assure you that we will be able to successfully operate the second facility in a timely or profitable manner, or within the budget that we currently project. If the demand for SYNDROS® and any future related products never meets our expectations and forecasts, or if we do not produce the output we plan, we may not be able to realize the return on investment we anticipated, which would have a negative impact on our financial condition and results of operations.

Our ability to operate a new, larger facility successfully will greatly depend on our ability to hire, train and retain an adequate number of additional manufacturing employees, in particular employees with the appropriate level of knowledge, background and skills. Should we be unable to hire such employees, our business and financial results could be negatively impacted.

We are dependent on numerous third parties in our supply chain for the commercial supply of SUBSYS® and SYNDROS®, and if we fail to maintain our supply and manufacturing relationships with these third parties or fail to develop new relationships with other third parties, we may be unable to continue to commercialize SUBSYS® and SYNDROS®, or to develop other product candidates.

We rely on a number of third parties for the commercial supply of SUBSYS® and SYNDROS® and the clinical supply of certain of our product candidates. Our ability to commercially supply SUBSYS® and SYNDROS® and to develop our product candidates depends, in part, on our ability to successfully obtain the API for SUBSYS® and the materials for SYNDROS® and certain other of our product candidates, and outsource most if not all of the aspects of their manufacturing at competitive costs, in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. If we fail to develop and maintain supply relationships with these third parties, we may be unable to continue to commercialize SUBSYS® and SYNDROS® or certain of our other product candidates.

We purchase the fentanyl API utilized in connection with SUBSYS® from one vendor as our sole supplier of the API in this product. We purchase the starting materials for our dronabinol API utilized in connection with SYNDROS® from several third parties. We do not have long-term agreements with any of these parties, but rather purchase material on a purchase order basis. Moreover, some of the starting material for our dronabinol API is difficult to procure and produce. Our ability to obtain fentanyl API and the starting materials for our dronabinol API in sufficient quantities and quality, and on a timely basis, is critical to our continued commercialization of SUBSYS® and SYNDROS® and to our successful completion of preclinical studies and clinical trials for our product candidates. There is no assurance that these suppliers will continue to produce the materials in the quantities and quality and at the times they are needed, if at all, especially in light of the fact that we intend to significantly increase our orders for these materials in the near future. Moreover, the replacement of any of these suppliers, particularly the supplier of the starting material for our dronabinol API that is difficult to produce, could lead to significant delays and increase in our costs.

We do not own or operate manufacturing facilities for SUBSYS® and currently lack the in-house capabilities to manufacture SUBSYS®. Our SUBSYS® sub-component manufacturing is performed by Aptar. The final fill, assembly and packaging of SUBSYS® and SYNDROS® is performed by Renaissance and PCI Pharma Services. If there are problems relating to the equipment utilized by Aptar to manufacture SUBSYS® components, we will be responsible for fixing or replacing that equipment. Any requirement to do so could result in unexpected costs and expenses and delay the production of SUBSYS®, which could in turn negatively impact our business.

The manufacture of pharmaceutical products generally requires significant expertise and capital investment, often including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production. These problems can include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Additionally, our manufacturers may experience difficulties due to resource constraints, labor disputes, unstable political environments or natural disasters. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations for any reason, our ability to commercially supply SUBSYS® and SYNDROS® could be jeopardized. Any delay or interruption in our ability to commercially supply SUBSYS® and SYNDROS® will result in the loss of potential revenues and could adversely affect the market's acceptance of these products. We cannot guarantee that we will not encounter other manufacturing issues in the future. In addition, any delay or interruption in the supply of preclinical study or clinical trial supplies could delay the completion of those studies or trials, increase the costs associated with maintaining our programs and, depending upon the period of delay, require us to commence new studies or trials at additional expense or terminate studies or trials completely.

Manufacturers and suppliers are subject to regulatory requirements including cGMPs, which cover, among other things, manufacturing, testing, quality control and recordkeeping relating to our products and product candidates, and are subject to ongoing inspections by FDA, DEA and other regulatory agencies. Moreover, if we seek regulatory approval for any product candidate, the facilities to be used by us or our third-party manufacturers for the manufacture of the product candidate must be approved by the applicable regulatory authorities before the product candidate may be approved and marketed. We do not control the manufacturing processes of third-party manufacturers, and we are dependent upon them in material ways. If any of our third-party manufacturers cannot successfully manufacture product that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, they will not be able to secure or maintain regulatory approval for the manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve these facilities for the manufacture of our products or product candidates or if they withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to commercially supply SUBSYS® and SYNDROS® or develop or obtain regulatory approval for certain of our product candidates.

If our third-party manufacturers or suppliers fail to deliver the required commercial quantities of SUBSYS® and SYNDROS® and the respective sub-components and starting materials, on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers or suppliers capable of production at a substantially equivalent cost in substantially equivalent volumes and quality, and on a timely basis, the continued commercialization of SUBSYS® and SYNDROS® and the development of certain of our product candidates would be impeded, delayed, limited or prevented, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may encounter delays in the manufacturing of SUBSYS® or fail to generate revenue if our supply of the components of our sublingual spray delivery system is interrupted.

Our sublingual spray drug delivery system is sourced, manufactured and assembled by multiple third parties across different geographic locations in the United States and Europe. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up the sublingual spray system. The components of the spray system include the actuator subassembly, vial subassembly, and the setting mechanism. The actuator subassembly is comprised of nine individual components which are collectively supplied by six different third-party manufacturers. The vial subassembly that houses the drug formulation fentanyl is comprised of five different components supplied by four third-party manufacturers. Each of these third-party manufacturers is currently the single source of their respective components. If any of these manufacturers is unable to supply its respective component for any reason, including due to violations of cGMPs for

medical devices, known as QSR, our ability to both have the finished sublingual spray device manufactured and to commercially supply SUBSYS® will be adversely affected and we would lose potential revenue. Accordingly, a failure in any part of our supply chain may cause a material adverse effect on our ability to generate revenue from SUBSYS®, which in turn could have a material adverse effect on our business, results of operations, financial condition and prospects.

We face intense competition, including from generic products. If our competitors market or develop alternative treatments that are approved more quickly or marketed more effectively than our product candidates or are demonstrated to be safer or more effective than our products, our commercial opportunities will be reduced or eliminated.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our products or product candidates, such as pharmaceutical companies, including generic drug companies, biotechnology companies, drug delivery companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, including well-established sales forces, manufacturing capabilities, research and development capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us.

SUBSYS® competes against numerous branded and generic products already being marketed and potentially those which are or will be in development. Many of these competitive products are offered in the United States by large, well-capitalized companies. SUBSYS® is one of nine commercially available products in the TIRF market. In the BTCP market, physicians often treat BTCP with a variety of short-acting opioid medications, including morphine, morphine and codeine derivatives and fentanyl. Some currently marketed products against which we directly compete include Teva Pharmaceutical Industries Ltd.'s FENTORA® and ACTIQ®, Sentynl Therapeutics' Abstral®, West Therapeutic Development, LLC's Lazanda® and BioDelivery Sciences International, Inc.'s Onsolis®. Some generic fentanyl products against which SUBSYS® competes are marketed by Mallinckrodt, Inc., Par Pharmaceutical Companies, Inc. and Actavis, Inc. In addition, we are aware of numerous companies developing other treatments and technologies for rapid delivery of opioids to treat BTCP, including transmucosal, transdermal, nasal spray, and inhaled sublingual delivery systems. If these treatments and technologies are successfully developed and approved, they could represent significant additional competition to SUBSYS®.

With respect to SYNDROS® and our dronabinol product candidates, the market in which we intend to compete is challenging in part because generic products generally face greater price competition than branded products and the competition from generic products may have an effect on our product prices, market share, revenues and profitability. We may not be able to differentiate any products that we may market from those of our competitors, successfully develop or introduce new products that are less costly or offer better performance than those of our competitors, or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors. In addition, there are a number of established therapies and products already commercially available and under development by other companies that treat the indications that our dronabinol product candidates are intended to treat. Specifically, if approved, our dronabinol product candidates will compete, against therapies and products such as AbbVie, Inc.'s Marinol® and Marinol® generics. Par Pharmaceutical Companies markets an approved generic version of Marinol® and Actavis markets an authorized generic version of Marinol®. We cannot give any assurance that other companies will not obtain regulatory approval or acceptable DEA classification for, or commercialize additional generic dronabinol products.

Moreover, our dronabinol products may compete with non-synthetic cannabinoid drugs, including therapies such as GW Pharmaceuticals plc's Sativex®, especially in many countries outside of the United States where non-synthetic cannabinoids are legal. In addition, literature has been published arguing the benefits of natural cannabis, or marijuana, over dronabinol, and there are a number of states that have already enacted laws legalizing medicinal and recreational marijuana. There is some support in the United States for further legalization of marijuana. We also cannot assess the extent to which patients utilize marijuana illegally to alleviate CINV, instead of using prescribed therapies such as approved dronabinol products. Furthermore, in the treatment of CINV, physicians typically offer conventional anti-nausea drugs prior to initiating chemotherapy, such as Sanofi's Anzemet®, Eisai Inc./Helsinn Group's Aloxi®, Roche Holding AG's Kytril®, Par Pharmaceutical Companies' Zuplenz® and GlaxoSmithKline plc's Zofran®, as well as Neurokinin 1 receptor antagonists on the market including Kyowa Hakko Kirin Co., Ltd.'s Sancuso® and Merck & Co., Inc.'s Emend®. To the extent that SYNDROS® and our dronabinol product candidates compete in the broader CINV market, we will also face competition from these products and their generic equivalents, as applicable.

Additionally, we are aware of companies who have received approval for the commercialization of CINV products, including Heron Therapeutics, Inc.'s (formerly A.P. Pharma, Inc.) Sustrol®, Tesaro, Inc.'s Varubi®, and Helsinn Therapeutics (U.S.), Inc.'s Akynzeo®. If these products are successfully marketed over the next few years, they could represent significant competition for SYNDROS®. Additionally, Aphios Corp.'s Zindol® is in late stage development (Phase 3), and if successfully developed and approved could represent significant competition for SYNDROS®.

We also face competition from third parties in obtaining allotments of fentanyl and dronabinol under applicable DEA annual quotas, recruiting and retaining qualified personnel, establishing clinical trial sites and enrolling patients in clinical trials, and in identifying and acquiring or in-licensing new products and product candidates.

Our competitors may also develop products that are more effective, better tolerated, subject to fewer or less severe side effects, more useful, more widely-prescribed or accepted, or less costly than ours. For each product we commercialize, sales and marketing efficiency are likely to be significant competitive factors. We have built a commercial organization to market SUBSYS® and SYNDROS® in the United States without using third-party sales or marketing channels, but it is unclear what strategies we will utilize in the future in connection with our commercial organization in the United States for any additional proprietary product candidates that we may develop, and there can be no assurance that we can maintain and augment these capabilities in a manner that will be cost efficient and competitive with the sales and marketing efforts of our competitors, especially since some or all of those competitors could expend greater economic resources than we do and/or employ third-party sales and marketing channels.

We depend on wholesale distributors and specialty retail pharmacies for retail distribution of SUBSYS® and SYNDROS®; if we lose any of our significant wholesale distributors or specialty retail pharmacies, our business could be harmed.

The majority of our sales of SUBSYS® and SYNDROS® are to wholesale pharmaceutical distributors who, in turn, sell the products to pharmacies, hospitals and other customers, and to specialty retail pharmacies who sell the products directly to patients (collectively, our customers). For the year ended December 31, 2018, three wholesale pharmaceutical distributors, AmerisourceBergen Corporation, McKesson Corporation, and Cardinal Health, Inc., and two specialty retail pharmacies, individually and collectively comprised a material portion of our total gross sales of SUBSYS® and SYNDROS®. The loss by us of any of these wholesale distributors or specialty retail pharmacies' accounts, or a material reduction in their purchases, could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, the wholesale pharmaceutical distributors comprise a significant part of the distribution network for pharmaceutical products in the United States. This distribution network has undergone, and may continue to undergo, significant consolidation marked by mergers and acquisitions. As a result, a small number of large wholesale distributors control a significant share of the market. Consolidation of drug wholesalers has increased, and may continue to increase, competitive and pricing pressures on pharmaceutical products. We cannot assure you that we can manage these pricing pressures or that wholesaler purchases will not fluctuate unexpectedly from period to period.

Our sales of SUBSYS® and SYNDROS® can be greatly affected by the inventory levels our respective customers carry. We monitor wholesaler and specialty pharmacy inventory levels of SUBSYS® and SYNDROS® using a combination of methods. Pursuant to distribution service agreements with our three largest wholesale customers and two largest specialty pharmacies, we receive inventory level reports. For most other wholesalers where we do not receive inventory level reports, however, our estimates of wholesaler inventories may differ significantly from actual inventory levels. Significant differences between actual and estimated inventory levels may result in excessive production (requiring us to hold substantial quantities of unsold inventory, increasing the chance that this inventory would expire before it is sold), inadequate supplies of products in distribution channels, and insufficient product available at the retail level. These changes may cause our revenues to fluctuate significantly from quarter to quarter, and in some cases may cause our operating results for a particular quarter to be below our expectations or the expectations of securities analysts or investors. In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may result in substantial fluctuations in our results of operations from period to period. If our financial results are below expectations for a particular period, the market price of our common stock may drop significantly.

We rely on third parties to perform many necessary services for SUBSYS® and SYNDROS®, including services related to distribution, invoicing, storage and transportation, and expect to do so for any future branded proprietary products, if approved.

We have retained third-party service providers to perform a variety of functions related to the sale and distribution of SUBSYS® and SYNDROS®, key aspects of which are out of our direct control. For example, we rely on Specialty Pharmaceutical Services to provide key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management, and, as a result, most of our SUBSYS® and SYNDROS® inventory is stored at a single warehouse maintained by the service provider. We must rely on this provider as well as other third-party providers that perform services for us, including entrusting our inventories of SUBSYS® and SYNDROS® to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical damage or natural disaster at their facilities, our ability to deliver SUBSYS® and SYNDROS® to meet commercial demand would be significantly impaired. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market SUBSYS® and SYNDROS® could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial arrangements for these services on reasonable terms.

In addition to the level of commercial success of our approved products, our future growth is also dependent on our ability to successfully develop a pipeline of product candidates, and we cannot give any assurance that any of our product candidates will receive regulatory approval or acceptable DEA classification, if applicable, or that any approved products will be successfully commercialized.

Our long-term growth will be limited unless we can successfully develop a pipeline of additional product candidates. We do not have internal new drug discovery capabilities, and our primary focus is on developing improved formulations and delivery methods for existing FDA-approved products.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products containing controlled substances, among other things, are subject to extensive regulation by the FDA, the DEA and other regulatory authorities in the United States. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA also has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

- the FDA may not deem a product candidate safe and effective;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to support approval;
- the FDA may require additional pre-clinical studies or clinical trials;
- the FDA may not approve our third-party manufacturers' processes and facilities; or
- the FDA may change its approval policies or adopt new regulations.

Any of our product candidates may fail to achieve their specified endpoints in clinical trials. Furthermore, product candidates may not be approved even if they achieve their specified endpoints in clinical trials. The FDA may disagree with our trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials (i.e., Phase 4 trials). In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates.

If we are unable to expand our pipeline and obtain regulatory approval for our product candidates on the timelines we anticipate, we will not be able to execute our business strategy effectively and our ability to substantially grow our revenues will be limited, which would have a material adverse impact on our long-term business, results of operations, financial condition and prospects.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy of any of our product candidates, which could prevent or significantly delay their regulatory approval.

Our product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for the commercial sale of any product candidate, we must gather substantial evidence from well-controlled clinical trials that demonstrate to the satisfaction of the FDA that the product candidate is safe and effective for its proposed indication, and similar regulatory approvals would be necessary to commercialize the product candidate in other countries.

In light of widely publicized events concerning the safety risk of certain drug products, particularly drug products that contain controlled substances, regulatory authorities, members of Congress, the GAO, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the FDCA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require a REMS for certain drugs, including certain currently approved drugs. Under the FDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of our clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Clinical trials for our product candidates are expensive, time consuming, uncertain and susceptible to change, delay or termination.

Clinical trials are very expensive, time consuming and difficult to design and implement. Most of our product candidates are in clinical development. We estimate that clinical trials for these product candidates will continue for several years and may take significantly longer than expected to complete. In addition, we, the FDA, an IRB, or other regulatory authorities, including state and local, may suspend, delay or terminate our clinical trials at any time, or the DEA could suspend or terminate the registrations and quota allotments we require in order to procure and handle controlled substances, for various reasons, including:

- lack of effectiveness of any product candidate during clinical trials;
- discovery of serious or unexpected toxicities or side effects experienced by study participants or other safety issues;
- slower than expected rates of subject recruitment and enrollment rates in clinical trials;
- difficulty in retaining subjects who have initiated a clinical trial but may withdraw at any time due to adverse side effects from the therapy, insufficient efficacy, fatigue with the clinical trial process or for any other reason;
- delays or inability in manufacturing or obtaining sufficient quantities of materials for use in clinical trials, in particular obtaining sufficient quantities of dronabinol due to regulatory and manufacturing constraints;
- inadequacy of or changes in our manufacturing process or product formulation;
- delays in obtaining regulatory authorization to commence a study, or “clinical holds” or delays requiring suspension or termination of a study by a regulatory agency, such as the FDA, before or after a study is commenced;
- DEA-related recordkeeping, reporting, or security violations at a clinical site, leading the DEA or state authorities to suspend or revoke the site’s controlled substance license and causing a delay or termination of planned or ongoing studies;
- delays or inability to obtain DEA or FDA approval to operate our clinical sites;

- changes in applicable regulatory policies and regulations;
- delays or failure in reaching agreement on acceptable terms in clinical trial contracts or protocols with prospective clinical trial sites;
- uncertainty regarding proper dosing;
- unfavorable results from ongoing clinical trials and preclinical studies;
- failure of our CROs or other third-party contractors to comply with all contractual and regulatory requirements or to perform their services in a timely or acceptable manner;
- failure by us, our employees, our CROs or their employees to comply with all applicable FDA, DEA or other regulatory requirements relating to the conduct of clinical trials or the handling, storage, security and recordkeeping for controlled substances;
- scheduling conflicts with participating clinicians and clinical institutions;
- failure to design appropriate clinical trial protocols;
- insufficient data to support regulatory approval;
- inability or unwillingness of medical investigators to follow our clinical protocols;
- difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data; or
- regulatory concerns with cannabinoid or opioid products generally and the potential for abuse of the drugs.

Generally, there is a high rate of failure for drug candidates proceeding through clinical trials. We may suffer significant setbacks in our clinical trials similar to the experience of a number of other companies in the pharmaceutical and biotechnology industries, even after receiving promising results in earlier trials. Further, even if we view the results of a clinical trial to be positive, the FDA or other regulatory authorities may disagree with our interpretation of the data. In the event that we abandon or are delayed in our clinical development efforts related to our product candidates, we may not be able to execute on our business plan effectively, we may not be able to become profitable, our reputation in the industry and in the investment community would likely be significantly damaged and our stock price would likely decrease significantly.

We have in the past relied and expect to continue to rely on third parties to conduct and oversee our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

We have in the past relied and expect to continue to rely on third-party CROs to conduct and oversee our clinical trials. For example, we contracted with Worldwide Clinical Trials to conduct and oversee our pivotal bioequivalence study for our approved product SYNDROS®.

We also rely upon various medical institutions, clinical investigators and contract laboratories to conduct our trials in accordance with our clinical protocols and all applicable regulatory requirements, including the FDA's good clinical practice regulations and DEA and state regulations governing the handling, storage, security and recordkeeping for controlled substances. These CROs and third parties play a significant role in the conduct of these trials and the subsequent collection and analysis of data from the clinical trials. We rely heavily on these parties for the execution of our clinical and preclinical studies, and control only certain aspects of their activities.

If any of our clinical trial sites terminate their involvement in one of our clinical trials for any reason, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical trial site may be questioned by the FDA.

We have conducted and may in the future conduct clinical trials for our products or product candidates outside the United States and the FDA may not accept data from such trials.

We have conducted and may in the future choose to conduct one or more of our clinical trials outside the United States. For example, our Phase 3 SUBSYS® safety trial was conducted at 46 sites in the United States and ten sites in India. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data by the FDA is subject to certain conditions. For example, the study must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The study population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical studies conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, such studies would be subject to the applicable local laws and FDA acceptance of the data would be dependent upon its determination that the studies also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept any such data, it would likely result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan.

Since the starting materials we utilize to manufacture dronabinol are sourced out of India, we are exposed to a number of risks and uncertainties associated with that geographic region.

The suppliers of the starting materials we utilize to manufacture dronabinol are located in India. This exposes us to a number of risks and uncertainties outside our control. India has suffered political instability in the past due to various factors. There have also been armed conflicts between India and neighboring Pakistan. Moreover, extremist groups within India and neighboring Pakistan have from time to time targeted Western interests. In addition, India is susceptible to natural disasters such as earthquakes and floods. Political instability, future hostilities with countries such as Pakistan, targeting of our interests by extremist attacks, and earthquakes or other natural disasters in India could harm our operations and impede our ability to produce dronabinol on our anticipated timeline, or at all.

Our failure to successfully develop, acquire and market additional product candidates or approved products would impair our ability to grow our business.

As part of our growth strategy we intend to seek to expand our product pipeline by developing or exploring acquisition or in-licensing opportunities of proven drugs that can be paired with our sublingual spray drug delivery system. Some of these drugs may require reformulation to accommodate the approved doses in smaller volumes that are compatible with our delivery system. Any reformulation may increase the risk of failure during development, extend the development timelines, increase development costs and add complexity to the regulatory approval process and in some cases, reformulation may not be possible. If we are not able to identify additional drug compounds that can be delivered via the current version of our sublingual spray technology, or if we are unable to successfully develop higher dose versions of this technology, our ability to develop additional product candidates and grow our business would be adversely affected.

Furthermore, we intend to in-license, acquire, develop and/or market additional products and product candidates in the areas of supportive care. Because our internal research and development capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to license or sell products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including pre-clinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any approved products that we acquire will be manufactured or sold profitably or achieve market acceptance.

If we fail to attract and keep management and other key personnel, as well as our board members, we may be unable to continue to successfully commercialize SUBSYS® or SYNDROS®, develop our product candidates or otherwise implement our business plan.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific, medical and other personnel. We are highly dependent on our management, scientific and medical personnel, as well as our board members. The loss of the services of any of these individuals could impede, delay or prevent the continuing commercialization of SUBSYS® or SYNDROS® and the development of our product candidates and could negatively impact our ability to successfully implement our business plan. If we lose the services of any of these individuals, we may not be able to find suitable replacements on a timely basis or at all, and our business would likely be harmed as a result. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. We employ all of our executive officers and key personnel on an at-will basis and their employment can be terminated by us or them at any time, for any reason and without notice; provided, however, that under certain circumstances we may owe them additional compensation in connection with such termination.

In order to retain valuable employees at our Company, in addition to salary and cash incentives, we provide incentive stock options and restricted stock units that vest over time as well as certain other market-based benefits and compensation. The value to employees of stock options that vest over time will be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract offers from other companies.

We may not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the Chandler, Arizona area where we are headquartered. Our industry has experienced a high rate of turnover of management personnel in recent years. As such, we could have difficulty attracting experienced personnel to our Company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will impede significantly our ability to implement our business strategy and achieve our business objectives.

In addition, we have scientific and clinical advisors who assist us in formulating our development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability or loyalty to us. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Our current and former employees may engage, or have engaged, in misconduct or other improper activities, including noncompliance with regulatory standards.

We are exposed to the risk of fraud or other misconduct of our former and current employees, contractors or agents. Misconduct by our former or current employees, contractors or agents could include, and have included, intentional actions to circumvent our compliance protocols, intentional failures to comply with FDA regulations, provide accurate information by our employees, contractors and agents to the FDA, comply with applicable manufacturing standards, comply with federal and state healthcare privacy, fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations

intended to prevent fraud, misconduct, kickbacks, self-dealing, off-label promotion and other illegal or inappropriate practices. These laws and regulations may restrict or prohibit a wide range of pricing, false claims, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These laws also dictate the proper use of patient information and data which is subject to privacy laws such as HIPAA. Misconduct of our former or current employees could also involve the improper use of information obtained in the course of clinical trials, or illegal misappropriation of drug product, or illegal promotion of a drug product for off-label use, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics and maintain a compliance program that strives to meet existing guidance from regulators, but it is not always possible to identify and deter employee misconduct, and the precautions we currently take (or have taken) to detect and prevent this type of activity may not be (or may not have been) effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental sanctions and charges or third-party actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, we may be held accountable for the actions of bad actors that we may have employed, and those actions could have, and have had, a significant impact on our business, including the imposition of significant fines or other sanctions that could, among other things, significantly limit our ability to market our products. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of these legal matters.

We face potential exposure on various fronts, including securities class actions and derivative cases, as well as product and other liability exposure, and our existing and future insurance coverage may be inadequate to cover any successful claims brought against us, or settlements which we choose to resolve, which could result in substantial liability that could materially and adversely affect our financial condition and results of operations.

All of the activities of our organization, including our board of directors' oversight of management, the commercial use of our products, including any prior misdeeds of our former employees, and the clinical use of our product candidates expose us to the risk of liability claims and government sanctions and penalties. These risks are often varied and difficult to predict even in situations where we have continuing and protracted litigation since such litigation is inherently unpredictable. For instance, our Company and board of directors currently face several securities class action and derivative cases and our directors and officers ("D&O") insurance carrier has disputed the policy period into which certain matters should be placed or, in some instances, whether their policy applies.

In addition, because SUBSYS® is an opioid, we face significant risk of product liability for this product even though this product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA. Our products and product candidates are designed to affect important bodily functions and processes, but side effects, manufacturing defects, misuse or abuse associated with SUBSYS®, SYNDROS®, or our product candidates could result in injury to a patient or even death. For example, because our sublingual spray technology is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions and as a result, apply a dose in a manner that results in injury or death. In addition, SUBSYS® is an opioid pain reliever that contains fentanyl, and SYNDROS® is a synthetic cannabinoid, which are both regulated "controlled substances" under the CSA and could result in harm to patients relating to its potential for abuse. In addition, a liability claim may be brought against us even if our products or product candidates merely appear to have caused an injury or because our commercial activities are alleged to have impaired a prescriber's ability to independently act in the best interest of the patient. Product liability claims may be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products or product candidates, among others. If we cannot successfully defend ourselves against product liability claims, we will incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- the inability to commercialize our products or, if approved, our product candidates;
- decreased demand for our products or, if approved, product candidates;
- impairment of our business reputation;
- product recall or withdrawal from the market;
- withdrawal of clinical trial participants;
- costs of related litigation;

- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants; or
- loss of revenues.

Finally, we face other legal challenges for which we may not have any insurance coverage at all and which may entail settlement payments or litigation judgments that could individually, or in the aggregate, have a materially adverse effect on our financial condition and results of operations. For instance, we have disputes with insurance carriers regarding claims of insurance fraud by our former employees and we have investigations by federal and state governmental authorities for the alleged prior misconduct of our former employees.

With the assistance of a reputable and prominent insurance broker, we have attempted to maintain insurance coverage for our organization, which we believed to have appropriate aggregate coverage limits consistent with market practice at the time we obtained coverage. We also carry excess product liability insurance coverage that was determined to be appropriate. However, identifying appropriate coverage is difficult to manage and to predict and it is likely our historic and future insurance coverage will not be sufficient to cover all of our expenses or losses related to existing claims and cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and has provisions that limit that coverage under certain circumstances that may apply to our Company. For instance, as a result of the risks associated with marketing opioids, particularly as a result of the opioid epidemic, many insurance companies are limiting or eliminating certain policy coverage of opioids. In addition, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to, among other things, the challenges we have had with respect to the commercial activities of former employees and the past legal actions that our Company has endured or may endure in the future. If we determine that it is prudent to increase our product liability coverage, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all and insurance providers are increasingly putting limitations around coverage of opioid products and may not be willing to issue coverage at all. Large judgments have been awarded in class action, multi-district, and individual lawsuits related to opioids and we anticipate that significant judgements or settlements will occur in the future. A large successful product liability claim, or a series of smaller successful claims, brought against us could cause our stock price to decline and, if judgments or settlements exceed our insurance coverage or result in significant dollar amounts, could decrease our cash and have a material adverse effect our business, results of operations and financial condition.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our products and product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and wastes resulting from their use are stored at our and our manufacturers' facilities pending use and disposal. We cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, injury to our employees and others, and environmental liability. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of environmental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage and our property and casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our commercialization activities, drug development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on a large number of third parties to supply components for and manufacture our products and product candidates, warehouse and distribute SUBSYS® and SYNDROS® and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further commercialization and development of our products and product candidates could be delayed.

We may be adversely affected by natural disasters or other events that disrupt our business operations and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and other facilities are located in Chandler, Arizona and Round Rock, Texas, which are not areas that have experienced severe earthquakes. Accordingly, we do not carry earthquake insurance and an unexpected similar event in this region could be devastating to our business. However, other natural disasters or similar events, like hurricanes, fires or explosions or large-scale accidents or power outages, could severely disrupt our operations in Arizona or Texas, and may have a material adverse effect on our business, results of operations, financial condition and prospects.

Our enterprise financial systems are located in our Chandler, Arizona headquarters. Our manufacturing facilities are in Round Rock, Texas. If a disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or our Round Rock facilities, that damaged critical infrastructure, such as enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations at either location, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. For example, Texas, from time to time experiences natural disasters like hurricanes or tornadoes. In addition, Arizona has in the past experienced flash flooding. Due to the inherently unpredictable nature of these events, the disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Risks Related to Our Financial Position and Capital Requirements

The auditor's opinion on our audited financial statements for the fiscal year ended December 31, 2018, included in this annual report on Form 10-K, contains an explanatory paragraph relating to our ability to continue as a going concern.

The auditor's opinion on our audited financial statements for the year ended December 31, 2018 includes an explanatory paragraph stating that our losses and negative cash flows from operations and uncertainty in generating sufficient cash to meet our legal obligations and settlements and sustain our operations raise substantial doubt about our ability to continue as a going concern. While we are pursuing a variety of funding sources and transactions that could raise capital, there can be no assurances that we will be successful in these efforts or will be able to resolve our liquidity issues or eliminate our operating losses. If we are unable to obtain sufficient funding, we would need to significantly reduce our operating plans and curtail some or all of our product development, commercialization and strategic plans. Accordingly, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited consolidated financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial

doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding on commercially reasonable terms or at all.

If we fail to finalize our agreement in principle with the DOJ or comply with the final terms contained in the final written agreements with the DOJ and OIG, our results of operations and financial condition will be materially and adversely affected. In addition, even if we finalize such documentation with the federal government, the additional costs and burden to comply with the terms of such documents and the risks that exist if we fail to comply with such documents, such as exclusion from federal healthcare programs, are significant and present significant risk to our Company. Finally, we will also have additional financial payments and requirements associated with settlements with state authorities and offices of attorneys general which will result in significant costs and burdens for our Company.

On August 8, 2018, we announced that we reached an agreement in principle with the DOJ to settle the DOJ's civil and criminal investigation into inappropriate sales and commercial practices by some former company employees. This agreement in principle is subject to the negotiation of final settlement documents with the government. We expect that a final settlement, if completed, would include other material non-financial terms and conditions, including a fraud-based criminal felony plea by one of our subsidiaries and a deferred prosecution agreement with the Company related to the actions of our former employees. Additionally, we expect that a final settlement will include a corporate integrity agreement and conditional exclusion release between the Company and OIG that will require the Company to exit the opioid business within 12 months of the effective date, in addition to other provisions. We cannot be certain that a final agreement will be reached.

If executed, these agreements will require cooperation with the federal government's prosecutions, enhancements to our compliance program, fulfillment of reporting and monitoring obligations, and management certifications, among other requirements. In addition, compliance with the terms of these agreements will impose additional costs and burdens on us, including some form of employee training, third party reviews, compliance monitoring, reporting obligations and management attention. We estimate a minimum exposure of $150 million (plus interest) to be paid over 5 years. In addition, we also anticipate certain contingency payments estimated between $0 and $75 million. If we fail to comply with the final agreement with DOJ and OIG (including a potential requirement to exit the opioid business), the DOJ or OIG may impose substantial monetary penalties or exclude us from federal healthcare programs, including Medicare, Medicaid and Veterans Health Administration programs, which would have a material adverse effect on our business, financial condition and results of operations. Furthermore, we will also have additional financial payments and requirements associated with settlements with state authorities and offices of state attorneys general which will result in significant costs and burdens for our Company and we may be subject to new and unanticipated third-party claims and shareholder lawsuits in connection with all of these settlements with governmental authorities. See Note 7 of the Notes to our Consolidated Financial Statements for additional information regarding these legal matters.

We have had significant and increasing operating expenses, including litigation expenses and liabilities, and will require additional funding.

Our operations have consumed substantial amounts of cash since inception. In addition, our revenue has been declining and it has been difficult for us to stabilize our product sales so that we can predictably forecast future revenue. Furthermore, as our research and development activities mature and develop over the next several years, we will likely require substantial additional funds to continue such activities, depending upon events that are difficult to predict at this time. In addition, as we continue to contend with existing litigation (and resolve such proceedings as appropriate) and fund other legal expenses related to our former employees, we will require additional funding. In this regard, management's plans, in order to meet additional operating cash flow requirements, include the pursuit of potential strategic alternatives related to our opioid-related assets, as well as financing activities discussed further below.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the timing and amount of revenue from sales of our approved products, SUBSYS® and SYNDROS®, and any subsequently approved product candidates that are commercialized;

- the timing and amount of cash proceeds from the sale of the Company's opioid-related assets, if at all;
- the size and cost of our commercial infrastructure;
- the timing of FDA approval and DEA classification of our product candidates, if at all;
- the timing, rate of progress and cost of any future clinical trials and other product development activities for our dronabinol product candidates and any other product candidates that we may develop, in-license or acquire;
- costs associated with marketing and distributing SUBSYS®, SYNDROS®, and any subsequently approved product candidates;
- costs and timing of completion of any additional outsourced commercial manufacturing supply arrangements that we may establish;
- costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with SUBSYS®, SYNDROS®, and our product candidates;
- costs associated with prosecuting or defending any litigation (civil or criminal) and associated damages, regulatory fines, forfeitures, or sanctions as a result of such litigation or governmental investigations in which we are or may become involved;
- accrued but unpaid legal expenses claimed by John Kapoor;
- costs of operating as a public company;
- the effect of competing technological and market developments;
- our ability to acquire or in-license products and product candidates, technologies or businesses;
- personnel, facilities and equipment requirements;
- the terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish; and
- the uncertainty of the timing of a final settlement with the DOJ (and the payments associated therewith).

We will also need to raise additional funds to finance future cash needs through public or private equity offerings, debt financings, sale of assets, receivables or royalty financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership will be diluted. Any future debt financing into which we enter may impose upon us covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. In addition, if we raise additional funds through corporate collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to products or product candidates, or grant licenses on terms that are not favorable to us.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to significantly delay, scale back or discontinue one or more of our product development programs or commercialization efforts, or other aspects of our business plan. We also may be required to relinquish, license or otherwise dispose of rights to products or product candidates that we would otherwise seek to commercialize or develop ourselves on terms that are less favorable than might otherwise be available. In addition, our ability to achieve profitability or to respond to competitive pressures would be significantly limited.

Unanticipated changes in our tax provisions, the adoption of new tax legislation or exposure to additional tax liabilities could affect our financial performance.

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act (the “2017 Tax Act” or “U.S. Tax Reform”), which has significantly changed the U.S. federal income taxation of U.S. corporations by, among other things, reducing the U.S. corporate income tax rate from 35% to 21%, adopting elements of a territorial tax system, imposing a one-time transition tax (or "deemed repatriation tax") on all undistributed earnings and profits of

certain U.S. owned foreign corporations, revising the rules governing NOLs and the rules governing foreign tax credits, repealing the performance-based compensation exception to the $1 million deduction limit on executive compensation and expanding the scope of employees to whom the limit applies, eliminating the deductibility of certain fringe benefits, permitting immediate expensing of certain capital expenditures, limiting interest deductions, modifying the tax treatment of like-kind exchanges, and introducing new anti-base erosion provisions. Many of these changes were effective immediately upon the passage of the legislation, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementation of regulations by the Treasury and Internal Revenue Service ("IRS"), any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities, or how the changes will be viewed by foreign governments.

There may be other material adverse effects resulting from the legislation that we have not yet identified. While some of the changes made by the tax legislation may adversely affect the Company in one or more reporting periods and prospectively, other changes may be beneficial. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us.

We are subject to income and other taxes in the United States. Our tax liabilities in the United States are affected by, among other things, the amounts we charge in intercompany transactions for inventory, services, licenses, funding and other items. Tax authorities may disagree with our intercompany charges, cross-jurisdictional transfer pricing or other matters, and may assess additional taxes as a result. We regularly assess the likely outcomes of our various tax positions in order to determine the appropriateness of our tax provision. However, there can be no assurance that we will accurately predict the outcomes of an audit, and the amounts ultimately paid upon resolution of any audit could be materially different from the amounts previously included in our income tax expense and therefore could have a material impact on our tax provision, net income and cash flows.

Our ability to utilize our net operating loss carryforwards, or NOLs, and research and development income tax credit carryforwards may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, substantial changes in our ownership may limit the amount of NOLs and research and development income tax credit carryforwards that could be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our Company of more than 50% within a three-year period. Any such annual limitation, whether as the result of prior transactions, sales of common stock by our existing stockholders or additional sales of common stock by us, may significantly reduce the utilization of the NOLs and tax credits before they expire and could have an adverse effect on our future results of operations. As of December 31, 2018, we had approximately $112.3 million of federal NOLs, and $233.8 million of state NOLs. Based upon the Company's recent tax loss and current projections for future taxable income, the Company does not believe realization of these tax assets is more likely than not. As such, we continue to maintain a full valuation allowance against the deferred tax assets as of December 31, 2018.

In addition, the 2017 Tax Act eliminated the ability to carryback NOLs arising after 2017 and instead permits such NOLs to be carried forward indefinitely, and reduced the orphan drug credit to 25% from 50% of qualified clinical testing expenses. These provisions of the 2017 Tax Act may significantly alter the utilization of NOLs and orphan drug credits and could have an adverse effect on our future results of operations. See Note 10 of the Notes to our Consolidated Financial Statements for additional discussion related to the 2017 Tax Act.

Ongoing legal proceedings, whether or not the Company is a party, may result in challenges by the IRS to tax positions taken by the Company in prior tax years.

As disclosed elsewhere in this report, a number of health care professionals who previously interacted with our Company as members of our speaker bureau have been charged with, or have pled guilty to or been convicted of, criminal activity in connection with our sales, marketing and other commercial practices. See Note 7 of the Notes to our Consolidated Financial Statements for additional information regarding these matters. To the extent

that the Company has taken tax deductions in prior tax years by treating payments to these health care professionals or expenses associated with their speaker programs as deductible business expenses, the IRS could disallow these deductions and, were that disallowance to be sustained, the Company could be required to amend past tax returns, as well as to pay additional taxes, interest, and penalties. These additional payments could materially decrease our available cash and have a material adverse effect on our business, results of operations and financial condition.

We recently announced that we commenced a process to review strategic alternatives for our portfolio of opioid-related assets, including SUBSYS®, as well as formulations of buprenorphine and the combination of buprenorphine/naloxone. This and other strategic transactions we may pursue could impact our liquidity, increase our expenses and present significant distractions to our management, and which ultimately may not be successful.

We are evaluating strategic transactions, such as divestiture of existing product lines, including SUBSYS® and our remaining opioid-related assets, acquisitions of companies or products, asset purchases and out-licensing or in-licensing of products, product candidates or technologies, particularly those arrangements that seek to leverage other organizations' internal platforms or competencies for the benefit of our products or potential products. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic licensing and partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown or unanticipated liabilities, including foreign laws we are unfamiliar with;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- ability to successfully complete a divestiture of opioid assets within the 12-month period expected to be required by the OIG;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions, which we may not be able to obtain on favorable terms, if at all;
- higher than expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- entering into a long-term relationship with a partner that proves to be unreliable or counterproductive;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

In deciding whether to pursue a divestiture of a product line like SUBSYS®, we may consider (i) whether such asset is no longer critical or core to our ongoing operational strategy, (ii) whether we believe the opportunity to immediately monetize the asset is attractive and can be obtained on terms that are acceptable and (iii) whether regulatory requirements around the opioid or TIRF products, including requirements that may be contained in future agreements we enter into with governmental authorities, will make selling this product in the best interests of our Company and its stockholders.

In addition, the uncertainty related to consummating a strategic transaction of SUBSYS® or some other assets, including whether or not the anticipated benefits of such a transaction would be fully realized, is difficult to predict and there is no guarantee that we will consummate such a transaction at all or at the terms we would like. Divestitures or similar strategic transactions may prove to be complex and time consuming and require substantial resources and effort. We may be negotiating with certain strategic partners having greater financial resources than us or other advantages over us that may hinder or prevent us from consummating a transaction on acceptable terms.

Accordingly, although there can be no assurance that we will undertake or successfully complete any strategic transactions of the nature described above, any transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects if we are unable to execute on the planned objectives or capitalize on the relationship in the manner that was originally contemplated and the realization of the anticipated benefits of any strategic transaction, including a divestiture, could take longer than expected and may include contingent consideration and unforeseen expenses, complications and delays. In addition, we may be required to retain legal, regulatory, and other risks that occurred prior to the acquisition, whether known or unknown to us. Any one of these challenges or risks could impair our growth and ability to compete, require us to focus additional resources on these matters rather than more profitable activities, require us to reexamine our business strategy, or otherwise cause a material adverse effect on our business, financial condition, results of operations, cash flows, and/or share price.

Risks Related to Regulation of our Products and Product Candidates

If the FDA does not conclude that certain of our product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for such product candidates under Section 505(b)(2) are not as we expect, the approval pathway for those product candidates will likely take significantly longer, cost significantly more, and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We are developing several proprietary dronabinol product candidates for which we intend to seek FDA approval through the Section 505(b)(2) regulatory pathway. Section 505(b)(2), if applicable to us under the FDCA, would allow an NDA we submit to FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved compounds, which could expedite the development program for our product candidates by potentially decreasing the amount of clinical data that we would need to generate in order to garner FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for these product candidates, and complications and risks associated with these product candidates, would likely substantially increase. Additionally, we may need to obtain additional funding, which could result in significant dilution to the ownership interests of our then existing stockholders to the extent we issue equity securities or convertible debt. We cannot assure you that we would be able to obtain such additional financing on terms acceptable to us, if at all. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway would likely result in new competitive products reaching the market more quickly than our product candidates, which would likely materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain brand-name pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to accelerated product development or earlier approval.

Moreover, even if our product candidates are approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Annual DEA quotas on the amount of dronabinol and CBD allowed to be produced in the United States and our specific allocation of dronabinol and CBD by the DEA could significantly limit the production of SYNDROS® and our CBD product candidates for which we seek to obtain regulatory approval as well as significantly delay the clinical development of our CBD product candidates.

Dronabinol and CBD are subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for the amount of dronabinol and CBD that may be produced in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of dronabinol and CBD 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 are required to obtain an annual quota from the DEA in order to manufacture and produce dronabinol and CBD. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year and has substantial discretion in deciding whether or not to make such adjustments. For 2019, we were allocated what we believe is a sufficient quantity of dronabinol and CBD to meet our currently anticipated production and testing needs through 2019. However, we may need additional amounts of dronabinol and CBD in future years to implement our business plan and there is no certainty we will receive what we believe is the appropriate adjustments to our quotas. In addition, compliance with DEA quota requirements and restrictions can be complicated and, like any regulation, are subject to interpretations to the DEA's rules and regulations that may not always be clear. Ultimately, if we fail to stay within DEA quota guidelines we could be subject to potential actions by DEA including but not limited to fines, future restrictions and/or loss of registration.

Furthermore, we do not know what amounts of dronabinol or CBD other companies developing or marketing dronabinol products or CBD products or product candidates may have requested for 2019 or will request in future years. The DEA, in assessing factors such as medical need, abuse potential and other policy considerations, may have chosen to set the aggregate dronabinol quota for 2019 lower than the total amount requested by the companies, and may do so in the future. Though companies are permitted to petition the DEA to increase the aggregate quota for dronabinol or CBD in a given year after it is initially established, there is no guarantee the DEA would act promptly or favorably upon such a petition. The success of our business plan will depend in part on our being able to expand the overall market for the medical use of dronabinol or CBD, as appropriate, by introducing new formulations, and to sell significant amounts of our approved product(s). In order to do so, we will need to receive from the DEA significantly increased allotments of quotas over time and likely an increase in the aggregate annual quota. Any delay or refusal by the DEA in establishing quotas necessary for us to execute on our business plan could negatively impact our ability to sell SYNDROS® and any other dronabinol or CBD product candidate for which we obtain regulatory approval, if any, as well as our preclinical studies and clinical trials, which would in turn have a material adverse effect on our business, our ability to execute on our business plan, our financial position and results of operations, our prospects, and our ability to generate revenue to fund the development of our other product candidates.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. As a result of our previously disclosed DOJ Investigation, we anticipate we will be subject to sanctions and fines by the federal government and we believe certain ongoing state investigations could result in future sanctions and fines. The laws that may affect our ability to operate and that may be implicated in such foregoing sanctions or fines include:

- the federal Anti-Kickback Statute, which constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state and foreign law equivalents of each of the above federal laws, such as the Anti-Kickback Statute and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, 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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state healthcare programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results.

The FDA provides guidelines with respect to appropriate drug and product promotion, product labeling, and continuing medical and health education activities. Although we endeavor to follow these guidelines, the FDA or the Office of the Inspector General: U.S. Department of Health and Human Services may disagree, and we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. The Office of the Inspector General also has the authority to exclude us from participation in healthcare programs funded by the government. In addition, management's attention could be diverted, and our reputation could be damaged. See Note 7 under the heading "Legal Matters" in the Notes to our Consolidated Financial Statements for a discussion of these investigations by HHS, Office of Inspector General, the U.S. Attorney's Office for the District of Massachusetts and other attorney generals from several states, of potential violations involving our SUBSYS® marketing activities.

Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated, particularly the risks related to the actions of our former employees. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Our currently marketed products, SUBSYS® and SYNDROS®, and any of our product candidates that receive regulatory approval, will be subject to ongoing and continued regulatory review, which may result in significant expense and limit our ability to commercialize such products.

Even after we achieve U.S. regulatory approval for a product, the FDA may still impose significant restrictions on the approved indicated uses for which the product may be marketed or on the conditions of approval. For example, a product's approval may contain requirements for potentially costly post-approval studies and surveillance, including Phase 4 clinical trials, to monitor the safety and efficacy of the product. We are also subject to ongoing FDA obligations and continued regulatory review with respect to the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for our product. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and with GCPs and GLPs, which are regulations and guidelines enforced by the FDA for all of our products in clinical and pre-clinical development, and for any clinical trials that we conduct post-approval. To the extent that a product is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

In the case of SUBSYS®, SYNDROS®, and any of our product candidates containing controlled substances, we and our contract manufacturers will also be subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota allotments for the raw material for commercial production of our products. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations, QSR requirements for medical device components or similar requirements, if applicable. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where, or processes by which, the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring product recall, notice to physicians, withdrawal of the product from the market or suspension of manufacturing. In that regard, because certain of our contract manufacturers for SUBSYS® and SYNDROS® are located outside the United States, they may be subject to foreign laws and regulations governing the manufacture of drugs and devices, and any failure by them to comply with those laws and regulations may delay or interrupt supplies of our products.

If we, our products or product candidates or the manufacturing facilities for our products or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose fines or other civil or criminal penalties;
- suspend any ongoing clinical trials;
- deny or reduce quota allotments for the raw material for commercial production of our controlled substance products;
- delay or refuse to approve pending applications or supplements to approved applications filed by us;
- refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

In addition, our product labeling, advertising and promotion are subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription drug products. In particular, a drug product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling, although the FDA does not regulate the prescribing practices of physicians. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including substantial monetary penalties and criminal prosecution. For example, we have received subpoenas from the HHS, Office of Inspector General, the U.S. Attorney's Office for the District of Massachusetts and other attorney generals from several states. The subpoenas primarily request documents relating to the marketing of SUBSYS®. We are cooperating in responding to the subpoenas. See Note 7 under the heading "Legal Matters" in the Notes to our Consolidated Financial Statements for a discussion regarding these ongoing investigations.

The FDA's regulations, policies or guidance may change, and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. 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 achieve and maintain regulatory compliance, we may not be permitted to market our products, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

Our products and our product candidates may cause undesirable side effects or have other unexpected properties that could result in post-approval regulatory action.

If we or others identify undesirable side effects, or other previously unknown problems, caused by our products, other products with the same or related active ingredients or our product candidates, after obtaining U.S. regulatory approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require us to recall product;
- regulatory authorities may require the addition of warnings in the product label or narrowing of the indication in the product label;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered or modify the product in some other way;
- the FDA may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of the above events resulting from undesirable side effects or other previously unknown problems could prevent us from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our products.

Healthcare reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of our products and any of our product candidates that may be approved by the FDA.

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the MMA established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If SUBSYS® or any of our product candidates that are approved by the FDA are not widely included on the formularies of these plans, our ability to market our products to the Medicare population could suffer.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. For example, PPACA includes measures to significantly change the way healthcare is financed by both governmental and private insurers.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. On January 2, 2013, President Obama signed into law the ATRA which reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. For instance, President Trump's declaration of the opioid crisis as a public health emergency is anticipated by many to spur potential legislation or executive branch actions that could materially affect the manner in which federal healthcare programs operate.

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

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

In certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement and may, in some cases, be unavailable. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

In the United States, the commercial success of SUBSYS®, SYNDROS®, and our product candidates, if and when commercialized, will continue to depend, in part, upon the availability of coverage and reimbursement from third-party payers at the federal, state and private levels. Third-party payers include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payers may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Also, third-party payers have attempted 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.

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

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

Risks Related to Intellectual Property

We may not be able to obtain and enforce patent rights or other intellectual property rights that cover SUBSYS®, SYNDROS®, and our other products or product candidates, that are of sufficient breadth to prevent third parties from competing against us.

Our success with respect to SUBSYS®, SYNDROS®, and our other products and product candidates, will depend in part on our ability to obtain and maintain patent protection in both the United States and other countries, to preserve our trade secrets, and to prevent third parties from infringing upon our proprietary rights on our product candidates. Our ability to protect any of our approved drug products from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Fentanyl and dronabinol have been approved for many years and therefore our ability to obtain any patent protection is limited. Composition of matter patents on APIs are a particularly effective form of intellectual property protection for pharmaceutical products as they apply without regard to any method of use. However, we will not be able to obtain composition of matter patents or methods of use patents that cover the APIs in any of our products or product candidates. As a result, competitors who obtain the requisite regulatory approval can offer products with the same active ingredients as our products or product candidates so long as the competitors do not infringe any formulation patents that we may obtain or license, if any.

Our patent portfolio related to our sublingual spray technology that is used in SUBSYS® includes patents and patent applications in the United States, Australia, Brazil, Canada, China, Europe, India, Japan, Mexico, New Zealand and Russia. The covered technology and the scope of coverage vary from country to country. For those countries where we do not have granted patents, we may not have any ability to prevent the unauthorized use of our sublingual spray technology.

In addition, the only patent protection that we can expect will otherwise cover SUBSYS® and dronabinol products and product candidates consists of patents relating to formulations, methods of treatment using certain formulations and methods of manufacturing and packaging. Formulation patents preclude competitors from using a similar formulation. Manufacturing or packaging patents preclude competitors from using the same manufacturing or packaging methods. However, these type of patents do not preclude a competitor from making and marketing the same composition of matter unless they use the same formulation or manufacturing or packaging methods. Any patents that we may obtain may be too narrow in scope and thus easily circumvented by competitors.

Further, in countries where we do not have granted patents directed to our formulations or manufacturing or packaging, third parties may be able to make, use, or sell products identical to, or substantially similar to, SUBSYS®, our dronabinol products or product candidates.

We have multiple pending patent applications in the United States and in some foreign jurisdictions directed to formulations for our fentanyl and dronabinol products and product candidates. We have a number of pending applications and issued patents in the United States and in many foreign countries that pertain to either fentanyl or dronabinol formulations. We can give no assurances that any patents will issue, that if they do issue or have issued, they will provide sufficient protection against competitors, or that they would be valid and enforceable.

Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any patents we may obtain or license may not provide us with sufficient protection for our products and product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies. In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be held valid or enforceable by the courts or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us.

Patent applications in the United States are generally maintained in confidence for up to 18 months after their filing. Similarly, publication of discoveries in scientific or patent literature often lag behind actual discoveries. Consequently, we cannot be certain that we or our licensors were the first to invent, or the first to file patent applications on our products or product candidates. In the event that a third-party has also filed an U.S. patent application relating to our drug product or a similar invention, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U.S. patent position.

In addition, third parties may challenge our in-licensed patents and any of our own patents that we may obtain, which could result in the invalidation or unenforceability of some or all of the relevant patent claims. Litigation or other proceedings to enforce or defend intellectual property rights is very complex, expensive, and may divert our management's attention from our core business and may result in unfavorable results that could adversely affect our ability to prevent third parties from competing with us.

The laws of some foreign jurisdictions do not provide intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property in foreign jurisdictions, our business prospects could be substantially harmed. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain evolving or unresolved. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

The degree of future protection of our proprietary rights is uncertain. Patent protection may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we might not have been the first to invent or the first to file the inventions covered by each of our pending patent applications and issued patents;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- the patents of others may have an adverse effect on our business;
- it is possible that some or none of our or our licensors' pending patent applications will result in issued patents;
- any patents we obtain or our licensors' issued patents may not encompass commercially viable products, may not provide us with any competitive advantages, or may be challenged by third parties;
- any patents we obtain or our in-licensed issued patents may not be valid or enforceable; or
- we may not develop additional proprietary technologies that are patentable.

If we or our licensors fail to prosecute, maintain and enforce patent protection for our products or product candidates, our ability to develop and commercialize our products or product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. This failure to properly protect the intellectual property rights relating to our products or product candidates could have a material adverse effect on our business, financial condition and results of operation. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how, by entering into confidentiality agreements with third parties, and proprietary information and invention agreements with certain employees, consultants and advisors, third parties may still obtain this information or we may be unable to protect our rights. We also have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. There can be

no assurance that binding agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets and unpatented know-how will not otherwise become known or be independently discovered by our competitors. If trade secrets are independently discovered, we would not be able to prevent their use. Enforcing a claim that a third-party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secret information.

Our products and the intellectual property related to such products face competition from lower cost generic or follow-on products.

Manufacturers of generic drugs are seeking to compete with our drugs and will do so with our product candidates if they are approved. These generic drug manufacturers present a significant challenge to us and they may challenge the scope, validity or enforceability of our patents in court, requiring us to engage in complex, lengthy and costly litigation. If any of our owned or licensed patents are infringed or challenged, we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would have a material adverse effect on our sales of that product.

In addition, manufacturers of innovative drugs as well as generic drug manufacturers may be able to design their products around our owned or licensed patents and compete with us using the resulting alternative technology. For more information concerning certain pending proceedings relating to our intellectual property rights, including a discussion on our Paragraph IV challenges, see Note 7 under the heading “Legal Matters” in the Notes to our Consolidated Financial Statements.

Upon the expiration or loss of patent protection for a product, or upon the “at-risk” launch (despite pending patent infringement litigation against the generic product) by a manufacturer of a generic version of one of our products, we could quickly lose a significant portion of our sales of that product and the value of that product line could be significantly reduced. In addition, if our branded products lose their market exclusivity, our products may face increased competition or pricing pressure.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our rights to our products and technology.

If we or our collaborators or licensors choose to go to court to stop a third-party from using the inventions claimed in our own or in-licensed patents, that third-party may ask the court to rule that the patents are invalid and/or should not be enforced against that third-party. These lawsuits are expensive and would consume time and other resources even if we or they, as the case may be, were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we or they, as the case may be, do not have the right to stop others from using the inventions.

There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third-party on the ground that such third-party’s activities do not infringe our owned or in-licensed patents. In addition, our own or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in a reexamination or opposition proceeding before a governmental patent agency, or during litigation.

We may also not be able to detect infringement of our own or in-licensed patents, which may be especially difficult for methods of manufacturing or formulation products. While we intend to take actions reasonably necessary to enforce our patent rights, we depend, in part, on our licensors and collaborators to protect a substantial portion of our proprietary rights.

If we are sued for alleged infringement of intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to our products and product candidates. As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our products or product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of medical devices, drugs, products or their methods of use. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our products, product candidates, technology or methods.

In addition, there may be issued patents of third parties of which we are currently unaware, that are infringed or are alleged to be infringed by our products, product candidates or proprietary technologies. Because some patent applications in the United States may be maintained in secrecy until the patents are issued, because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our own and in-licensed issued patents or our pending applications. Our competitors may have filed, and may in the future file, patent applications covering our products, product candidates or technology similar to ours. Any such patent application may have priority over our own and in-licensed patent applications or patents, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate, in the United States, in an interference proceeding to determine priority of invention.

If another party has reason to assert a substantial new question of patentability against any of our claims in our own and in-licensed U.S. patents, the third-party can request that the patent claims be reexamined, which may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential infringement suits and, interference and reexamination proceedings, we may become a party to patent opposition proceedings where either the patentability of the inventions subject of our patents are challenged, or we are challenging the patents of others. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful.

We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our products and/or product candidates and/or proprietary technologies infringe their intellectual property rights. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third-party's patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages for having violated the other party's patents.

If a third-party's patents was found to cover our products and/or product candidates, proprietary technologies or their uses, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to continue to commercialize our products or our product candidates or use our proprietary technologies unless we or they obtained a license to the patent. A license may not be available to us or our collaborators on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, technologies or methods pending a trial on the merits, which could be years away.

There is a substantial amount of litigation involving patent and other intellectual property rights in the device, biotechnology and pharmaceutical industries generally. If a third-party claims that we or our collaborators infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes or violates the third-party's rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court prohibiting us from selling or licensing the product unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed to us alleged trade secrets of their other clients or former employers.

As is common in the biotechnology and pharmaceutical industry, certain of our employees were formerly employed by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Moreover, we engage the services of consultants to assist us in the development of our products and product candidates, many of whom were previously employed at or may have previously been or are currently providing consulting services to, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees and consultants or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers or their former or current customers. For example, we have in the past received letters from third parties asserting that one of our employees may have used proprietary information of his former employers in connection with our prior regulatory filings. Litigation may be necessary to defend against these types of claims. Even if we are successful in defending against any such claims, any such litigation would likely be protracted, expensive, a distraction to our management team, not viewed favorably by investors and other third parties, and may potentially result in an unfavorable outcome.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on our own and in-licensed patents are due to be paid to the governmental patent agencies over the lifetime of the patents. Future maintenance fees will also need to be paid on other patents which may be issued to us. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our licensor to pay annuity fees due to patent agencies on our patents and pending patent applications. The various governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Risks Relating to an Investment in Our Stock

Our principal stockholder has placed his shares in an independently controlled trust and depending upon the results of his criminal trial in 2019, his ownership stake may be subject to forfeiture or compelled divestiture.

Effective as of February 27, 2018, our Company entered into a voting trust agreement with Dr. John N. Kapoor (and certain of his beneficiaries) and an independent trustee. During the term of this voting trust, Dr. John N. Kapoor (and certain of his beneficiaries) will not have control over voting decisions (except under limited circumstances) over the shares of the Company's common stock beneficially owned by Kapoor and the beneficiaries. As of the effective date of the voting trust agreement, the shares subject to the trust represented approximately 59% of the outstanding shares of common stock of the Company. Until the voting trust agreement is

terminated, the shares subject to the trust shall generally be voted on any matter by the trustee as directed by an independent voting committee (the "Voting Committee") whose members meet certain independence standards with respect to Kapoor. If at any time the shares subject to the trust represent less than 40% of the outstanding shares of common stock of the Company, such shares shall be voted on any matter by the trustee in the same proportion that the shares of the Company's common stock that are not subject to the trust are voted on such matter, which is commonly referred to as "mirror voting."

By virtue of this trust, the Voting Committee can and will be able to effectively control the election of the members of our Board of Directors, our management and our affairs and prevent corporate transactions, such as mergers, consolidations or the sale of all or substantially all of our assets, that may be favorable from our standpoint or that of our other stockholders or cause a transaction that we or our other stockholders may view as unfavorable. In addition, pursuant to an exception included in the voting trust agreement, Kapoor retains a veto right which permits him to veto change of control transactions. Accordingly, this concentration of ownership may harm the market price of our common stock by:

- delaying, deferring or preventing a change in control;
- impeding a merger, consolidation, takeover or other business combination involving us;
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us; or
- otherwise effectively limiting the rights of other stockholders because the voting committee of the trust has the ability to approve matters submitted to stockholders, including the election of directors, approval of significant transactions and the amendment of our certificate of incorporation.

The existence and nature of this voting trust could be viewed negatively by third parties and have a negative impact on our stock price. Moreover, if Kapoor's ownership falls below 40% of the outstanding shares and the shares subject to the trust are now subject to "mirror voting," it is possible that a group of shareholders representing a relatively small percentage of ownership in the company could work together to effectively control key decisions. Finally, upon Kapoor's passing, we cannot assure you as to how these shares will be distributed and subsequently voted.

In addition, Kapoor is currently in the midst of a criminal trial as a result of his indictment on or about October 26, 2017 by the U.S. Attorney's Office for the District of Massachusetts, as superseded on September 11, 2018 by a second superseding indictment. This indictment provides that upon conviction, the government could seek forfeiture of Kapoor's ownership interest in the Company. Furthermore, depending upon the outcome of the trial, mandatory or permissive exclusion under OIG rules and regulations may prevent Kapoor from participating in government programs which would result in a requirement by OIG for Kapoor to divest his ownership in the Company. Finally, depending upon the outcome of the trial, NASDAQ could require Kapoor to divest his ownership in order for the Company to continue to be listed on the exchange. If this occurs, it may be considered a change in control under Section 382 of the Code and our ability to utilize our NOLs and tax credits may be further limited.

Our common stock price has been volatile, which could result in substantial losses for stockholders.

Our common stock is currently traded on The NASDAQ Global Market. We have in the past experienced, and may in the future experience, limited daily trading volume. The trading price of our common stock has been and may continue to be volatile. The market for pharmaceutical companies, in particular, has at various times experienced extreme volatility that often has been unrelated to the operating performance of particular companies. These broad market and industry fluctuations may significantly affect the trading price of our common stock, regardless of our actual operating performance. The trading price of our common stock could be affected by a number of factors, including, but not limited to, changes in expectations of our future performance, changes in estimates by securities analysts (or failure to meet such estimates), quarterly fluctuations in our sales and financial results and a variety of risk factors, including the ones described elsewhere in this report. Periods of volatility in the market price of a company's securities sometimes result in securities class action litigation, which regardless of the merit of the claims, can be time-consuming, costly and divert management's attention. In addition, if we needed to raise equity funds under adverse conditions, it would be difficult to sell a significant amount of our stock without causing a significant decline in the trading price of our stock.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Future sales of our common stock or securities convertible into our common stock may depress our stock price.

Sales of a substantial number of shares of our common stock or securities convertible into our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. The exercise of outstanding stock options could result in increased sales of our common stock in the market, which could exert significant downward pressure on our stock price. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price we deem appropriate.

If a large number of shares of our common stock or securities convertible into our common stock are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Anti-takeover provisions in our stockholder rights plan, charter documents and Delaware law might deter acquisition bids for us that you and other stockholders might consider favorable.

On August 15, 2014, after approval by our stockholders, we entered into a rights agreement traditionally referred to as a poison pill. This rights agreement will have certain anti-takeover effects which will cause substantial dilution to a person or group that attempts to acquire the Company on terms not approved by our Board. In addition, our amended and restated certificate of incorporation and bylaws contain provisions that may make the acquisition of our Company more difficult without the approval of our Board of Directors. These provisions:

- establish a classified Board of Directors so that not all members of our board are elected at one time;
- authorize the issuance of undesignated preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval, and which may include rights superior to the rights of the holders of common stock;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- provide that the Board of Directors is expressly authorized to make, alter, or repeal our bylaws; and
- establish advance notice requirements for nominations for elections to our board or for proposing matters that can be acted upon by stockholders at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law which, subject to certain exceptions, prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. These anti-takeover provisions and other provisions under Delaware law could discourage, delay or prevent a transaction involving a change in control of our Company, even if doing so would benefit our stockholders. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing so as to cause us to take certain corporate actions you desire.

We may be a "controlled company" under NASDAQ's rules and, as a result, may qualify for, and may rely on, exemptions from certain NASDAQ independence rules, which could make our common stock less attractive to investors.

As a result of the independent voting trust holding Kapoor's shares and controlling the related voting power, we believe we are potentially a "controlled company" as defined in the NASDAQ Listing Rules and, therefore we may avail ourselves of certain exemptions under applicable NASDAQ rules, including exemptions from the rules that require us to have (i) a majority of independent directors on the Board; (ii) independent director oversight of executive officer compensation; and (iii) independent director oversight of director nominations.

We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

The continued operation and expansion of our business may require substantial funding. Accordingly, we do not anticipate that we will pay any cash dividends on shares of our common stock for the foreseeable future. Any determination to pay dividends in the future will be at the discretion of our Board of Directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions imposed by applicable law and other factors our Board of Directors deems relevant.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

We lease a total of approximately 88,000 square feet of office and lab space in Chandler, Arizona under lease agreements that expire in June 2021. We believe that the Chandler, Arizona facilities are adequate to meet our current needs, and that suitable additional or alternative space will be available for our foreseeable future needs. Additionally, we lease a total of approximately 93,000 square feet for our U.S.-based, state-of-the-art dronabinol manufacturing facilities, which are both located in Round Rock, Texas under lease agreements that expire between January 2022 and February 2032. We have the option to extend our primary manufacturing facility lease for two 5-year periods following March 2024. We believe that the Round Rock, Texas manufacturing facilities are adequate to meet our current needs and that suitable additional or alternative space will be available for our foreseeable future needs.

ITEM 3. LEGAL PROCEEDINGS

The information included in Note 7 under the heading "Legal Matters" in the Notes to our Consolidated Financial Statements in Part II, Item 8. *Financial Statements and Supplementary Data* is incorporated herein by reference.

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

Beginning with our initial public offering on May 7, 2013, our common stock is traded on the NASDAQ Global Market under the symbol INSY.

Holders

As of March 4, 2019, there were approximately 35 holders of record of our common stock and 74,428,260 shares of our common stock outstanding. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividends

Since our initial public offering, we have not declared nor paid dividends on our common stock and we do not expect to pay cash dividends on our common stock in the foreseeable future.

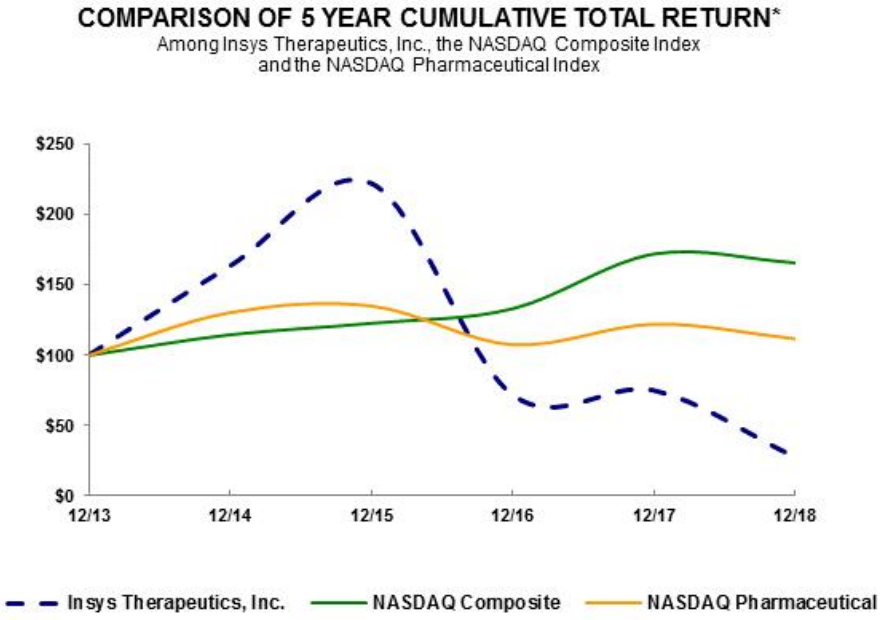
Issuer Purchases of Equity Securities

Stock Repurchase Program

On November 5, 2015, we announced a stock repurchase program which authorizes up to $50 million in repurchases of common stock. As of December 31, 2018, we had $17.4 million remaining under this program. There were no repurchases of our common stock during the year ended December 31, 2018. Also see Note 8 of the Notes to our Consolidated Financial Statements for additional information on this repurchase program.

Company Stock Performance

The following graph compares our total cumulative shareholder return as compared to the NASDAQ Composite Index and the NASDAQ Pharmaceutical Index for the period beginning on December 31, 2013 and ending on December 31, 2018. Total shareholder return assumes $100.00 invested at the beginning of the period in our common stock, the stocks represented by the NASDAQ Composite Index and the NASDAQ Pharmaceutical Index, respectively. Total return assumes reinvestment of dividends.



This stock performance graph shall not be considered soliciting material and shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, whether made on, before or after the date of this filing and irrespective of any general incorporation language in such filing.

ITEM 6. SELECTED FINANCIAL DATA

The following table sets forth certain financial data with respect to our business. The selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and related Notes and Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other information contained elsewhere in this Annual Report on Form 10-K. The selected financial data in the table below as of December 31, 2016, 2015 and 2014 and for the years ended December 31, 2015 and 2014, were derived from our audited Consolidated Financial Statements not included in this Annual Report on Form 10-K.

	Years Ended December 31,				
	2018	2017	2016	2015	2014
	(In thousands, except share and per share data)				
		(As Revised)	(As Revised)		
Consolidated Statements of Comprehensive Income (Loss) Data:					
Net revenue (1)	$ 82,080	$ 140,693	$ 242,275	$ 330,323	$ 219,092
Gross profit	71,277	120,050	216,882	301,469	196,514
Operating income (loss)	(127,723)	(219,031)	7,326	90,456	60,990
Income tax expense (benefit) (2) (3)	(1,900)	9,640	834	32,941	25,089
Net income (loss)	(124,507)	(226,835)	7,590	58,053	36,054
Net income (loss) per common share					
Basic	$ (1.68)	$ (3.12)	$ 0.11	$ 0.81	$ 0.52
Diluted	$ (1.68)	$ (3.12)	$ 0.10	$ 0.77	$ 0.49
Weighted average common shares outstanding (2)					
Basic	74,073,665	72,636,780	71,639,856	71,592,581	68,759,070
Diluted	74,073,665	72,636,780	74,166,981	75,707,651	73,335,132
Dividends declared per common share	$ —	$ —	$ —	$ —	$ —

(1) Net revenue for 2018 is presented under ASC 606, all other years are presented under ASC 605

(2) See Note 2 of the Notes to our Consolidated Financial Statements for a discussion of revisions to previously issued financial statements.

(3) The year ended December 31, 2017 includes the recording of a full valuation allowance against the deferred tax assets.

	December 31,				
	2018	2017	2016	2015	2014
			(In thousands)		
		(As Revised)			
Consolidated Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 95,678	$ 117,188	$ 182,880	$ 159,091	$ 82,863
Total current assets	126,292	175,942	229,643	252,051	146,465
Total assets	192,527	279,080	332,893	351,285	215,635
Total current liabilities, including debt	106,860	207,179	78,614	90,436	48,709
Total liabilities	235,627	212,871	86,547	98,980	52,445
Total stockholders' equity (deficit)	(43,100)	66,209	269,589	252,305	163,190

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Forward-Looking Statements

The information in this Annual Report on Form 10-K, or this Form 10-K, including this discussion in Management's Discussion and Analysis of Financial Condition and Results of Operations, or MD&A, contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections. All statements, other than statements of historical facts, included or incorporated in this Form 10-K could be deemed forward-looking statements, particularly statements about our plans, strategies and prospects under this MD&A heading and under the heading "Business." In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," "intend" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these identifying words. All forward-looking statements in this Form 10-K are made based on our current expectations, forecasts, estimates and assumptions, and involve risks, uncertainties and other factors that could cause results or events to differ materially from those expressed in the forward-looking statements. In evaluating these statements, you should specifically consider various factors, uncertainties and risks that could affect our future results or operations as described from time to time in our SEC reports, including those risks outlined under the heading "Risk Factors" in Part I, Item 1A of this Form 10-K. These factors, uncertainties and risks may cause our actual results to differ materially from any forward-looking statement set forth in this Form 10-K. You should carefully consider the trends, risks and uncertainties described below and other information in this Form 10-K and subsequent reports filed with or furnished to the SEC before making any investment decision with respect to our securities. All forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by this cautionary statement.

These forward-looking statements include, but are not limited to, statements concerning:

- *our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management;*
- *our ability to continue as a going concern;*
- *the source and sufficiency of our liquidity and capital resources to fund our operations;*
- *the impact and potential outcomes of pending claims, litigation, and other legal proceedings, along with our strategies and actions relating thereto;*
- *our expectations regarding completion of the settlement in principle with the DOJ;*
- *our belief that PBM formulary changes relative to SUBSYS® or SYNDROS® may have a material impact on future net revenue;*
- *our intent to file an NDA for the treatment of epilepsy with cannabidiol;*
- *our belief regarding the sufficiency of our manufacturing capacity;*
- *our beliefs regarding the beneficial attributes of our product candidates and delivery mechanisms;*
- *our expectation that our suppliers are equipped to supply us with our current and future chemical needs;*
- *our expectation that changes in healthcare laws will result in reduced Medicaid and Medicare payments for prescription drugs;*
- *our expectation that legal expenses and research and development costs will be our largest categories of expenses;*
- *our expectation that sales and marketing expenses will fluctuate based on changes in SUBSYS® or SYNDROS® net revenue;*
- *our plans for the development of different delivery systems for our product candidates;*

- *our beliefs regarding net revenue for SUBSYS® and SYNDROS® and our strategies relating thereto;*
- *our sales and marketing strategy for future products and delivery systems;*
- *our pursuit of strategic transactions such as the divestiture of existing or candidate product lines, acquisitions of other companies or asset purchases, out- or in-licensing of products, strategic partnerships, joint ventures, business combinations and investments;*
- *our ability to obtain foundation materials and manufacture dronabinol and CBD in light of government quotas;*
- *the beliefs about the expected pathway of drug applications we expect to file in the future;*
- *our expectation that physicians and payers will continue to gain familiarity about and accept the features of SUBSYS® and SYNDROS®;*
- *our plans and strategies for obtaining future international approvals;*
- *our plans and strategies to protect our intellectual property;*
- *our intention of not paying dividends;*
- *possible capital raising transactions that we may pursue;*
- *factors that relate to our status as a controlled company;*
- *our projections that research and development and operating costs will fluctuate;*
- *our belief that any investments in our sales and research and development infrastructure will result in increased sales;*
- *our belief that reductions in our sales and marketing force could result in decreased sales;*
- *accounting estimates and the impact of new or recently issued accounting pronouncements;*
- *our projections that cash flows from operations will fluctuate as a result of the fluctuation of sales of SUBSYS® and SYNDROS®;*
- *trends in restrictions and impediments relating to reimbursement policies imposed by PBMs;*
- *our projections that we will not recognize revenue in the near term from current research and development initiatives;*
- *our exposure to interest rate changes and market risks related to our investment;*
- *the effects of U.S. tax reform;*
- *and the potential impact of Section 382 limitations on our NOLs.*

The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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 that we make. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements.

The following discussion and analysis of the results of operations and financial condition of Insys Therapeutics, Inc. for the years ended December 31, 2018 and 2017 should be read in conjunction with the Consolidated Financial Statements and the notes thereto, and other financial information contained elsewhere in this Form 10-K.

Overview

We are a specialty pharmaceutical company that develops and commercializes innovative drugs and novel drug delivery systems of therapeutic molecules that improve patients' quality of life. As of December 31, 2018, we have two commercially marketed products:

- SUBSYS® — a proprietary, single-use product that delivers fentanyl, an opioid analgesic, for transmucosal absorption underneath the tongue, offered in 100, 200, 400, 600, 800, 1,200 and 1,600 mcg dosages. SUBSYS® is approved for the management of BTCP patients 18 years of age and older who are already receiving and are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. We received FDA approval for SUBSYS® in January 2012 and commercially launched SUBSYS® in March 2012. On November 5, 2018, we announced that we commenced a process to review strategic alternatives for our portfolio of opioid-related assets, including SUBSYS®, as well as formulations of buprenorphine and the combination of buprenorphine/naloxone.
- SYNDROS® — a proprietary, orally administered liquid formulation of dronabinol for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments and anorexia associated with weight loss in patients with AIDS. We received FDA approval for SYNDROS® in July 2016. In March 2017, the DEA issued an interim final ruling that would result in SYNDROS® being placed in Schedule II of the CSA. We received final labeling approval by the FDA in May 2017 and commercially launched SYNDROS® in July 2017.

We market SUBSYS® and SYNDROS® through our U.S.-based field sales force focused on supportive care physicians. Consistent with most pharmaceutical manufacturing companies, we sell and distribute SUBSYS® and SYNDROS® primarily to pharmaceutical wholesalers and collect sales proceeds from those wholesalers. For the year ended December 31, 2018, our three largest wholesale customers accounted for 58% of product shipments. We also sell SUBSYS® and SYNDROS® directly to certain specialty pharmaceutical retailers who distribute our product. For the year ended December 31, 2018 direct sales to specialty pharmaceutical retailers accounted for 39% of product shipments. We do not own or have any ownership stake in any pharmaceutical wholesaler or specialty pharmacy, nor do we have an option to acquire any wholesaler or specialty pharmacy. All pharmacies that fulfill SUBSYS® and SYNDROS® prescriptions are fully independent. Our relationships with every pharmacy that fulfills SUBSYS® and SYNDROS® prescriptions are non-exclusive in that each of these pharmacies may also fulfill prescriptions for other pharmaceutical manufacturers, including our competitors. For the year ended December 31, 2018, over 290 independent pharmacies have fulfilled at least one SUBSYS® prescription.

Our sales of, and revenue from, SUBSYS® and SYNDROS® depend in significant part on the coverage and reimbursement policies of third-party payers, including government payers such as Medicare and Medicaid, and private health insurers. All third-party payers are sensitive to the cost of drugs and consistently implement efforts to control these costs, which efforts include, but are not limited to, establishing excluded or preferred drug lists. SUBSYS® has been, and will likely continue to be, subject to these restrictions and impediments from third-party payers, particularly PBMs and private health insurers. We provide administrative reimbursement support assistance, in large part through our insurance reimbursement support group, which provides administrative support assistance to help patients coordinate with their insurance companies.

We are also developing other product candidates, such as cannabinoid line extensions and sublingual spray product candidates.

We produce the API for SYNDROS® at our U.S.-based, state-of-the-art dronabinol manufacturing facility. While we believe that this facility has the capacity to supply sufficient commercial quantities of dronabinol API for SYNDROS®, and support the continued development of our other dronabinol product candidates in the near-term, we have opened and expanded a second dronabinol manufacturing facility, which we anticipate will enable us to supply sufficient commercial quantities of dronabinol API for the anticipated commercialization of our proprietary dronabinol product candidates, if approved.

We have the capability to manufacture pharmaceutical CBD, an over 99.5% pure form of cannabidiol, in our Round Rock, Texas manufacturing facility.

Factors Affecting Our Performance

We believe that our performance and future success are dependent upon a number of factors, including our approved product sales, investments in our infrastructure and growth, and our ability to successfully develop product candidates and complete related regulatory processes. While each of these areas presents significant opportunities for us, they also pose significant risks and challenges that we must successfully address. In addition, our ability to ensure that our products, policies and practices adhere to the extensive national, state, and local regulations applicable to our industry is critical to our success. Finally, we believe that as our ongoing federal and state investigations and litigation proceedings have continued to accumulate, these challenges in the aggregate have led to significant legal costs and pressure on our cash flows, liquidity, and our business with respect to factors like reputational damage in the healthcare community and industry.

As management seeks to continue to provide insight into known material trends and uncertainties related to our net revenue and other factors affecting our performance, we note that the macro trend of the continuing and heightened publicity surrounding the national opioid epidemic continues to result in sensitivity by many healthcare professionals to prescribe opioids, pharmacies to dispense opioids, distributors to distribute opioids and third-party payors to cover opioid prescriptions, particularly those that are off-label. Third-party payers, such as insurance companies and regulatory and government agencies, continue to scrutinize the indications and uses for which opioid prescriptions are being written and dispensed. In addition, we believe other high-profile initiatives, such as (i) President Trump's declaration of the opioid crisis as a public health emergency, (ii) Congressional efforts to examine the causes of the opioid epidemic in public, and (iii) states, cities and counties initiating multi-district litigation against manufacturers and distributors of opioids have likely added to this sensitivity around opioid prescribing. Consequently, these current and potential future trends and events have affected, and will likely continue to affect, the manner in which, and the situations when, opioids, including SUBSYS®, are being prescribed, dispensed and approved for coverage.

Our product, and the TIRF class in which it is classified, has experienced a significant downward trend for the past several years. Based upon industry data available to us, since 2015, TIRF class prescriptions have declined approximately 75% and it is difficult to predict if this trend will continue or whether the prescriptions for this class of product will stabilize. Our product, SUBSYS®, is declining at a faster rate than the overall market and we have not been able to stabilize the trajectory of our revenue. We believe that the nature of the pricing on our branded products such as SUBSYS® (as well as SYNDROS®) has adversely affected our overall market share decline, and accordingly, our revenue generated from such products, especially since pharmaceutical product pricing has received significant governmental and media attention and we believe that migration to lower-cost generics has resulted from this focus.

In addition to the macro trends discussed above, our Company continues to have issues more specific to our business that have affected, and will likely continue to adversely affect, our net revenue and may be causing the decrease in overall market share for SUBSYS®. For instance, our Company has significant reputational issues primarily driven by ongoing state and federal investigations into our sales, marketing and other commercial practices, as well as criminal developments related thereto, and media reports covering such activity. We have had numerous former employees who have either been charged with, or have pled guilty to, criminal activity in connection with our sales, marketing, and other commercial practices. In addition, we have had various healthcare professionals who previously interacted with our Company, either through our speaker bureau, as a prescriber, or both, that have either been charged with, or have pled guilty to, or been convicted of, criminal activity in connection with our sales, marketing and other commercial practices. These developments, which may continue to worsen, have significantly and adversely affected our reputation within the healthcare industry and with some potential prescribers of our products.

On November 5, 2018, we announced that we commenced a process to review strategic alternatives for our portfolio of opioid-related assets, including SUBSYS®, as well as formulations of buprenorphine and the combination of buprenorphine/naloxone. Our decision to pursue this process is consistent with our ongoing negotiations in connection with the agreement in principle relating to the DOJ Investigation, wherein we expect the OIG to require us to exit the opioid business within 12 months of executing the final settlement agreements. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of these legal matters. Furthermore, this dovetails with our strategy to become a leader in pharmaceutical cannabinoids and novel drug delivery systems and to continue shifting our focus away from opioids in our product pipeline. We anticipate that our Company has a number of clinical and regulatory milestones to achieve over the next few quarters, including the completion of the CBD and epinephrine studies and filing the naloxone NDA, that are consistent with our objectives. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships and licensing, joint ventures, restructurings, divestitures, business combinations and investments.

In response to the continuing decline in revenue, our management team has continued to examine potential cost reduction initiatives that could more closely align operating expenses with our reduced revenue. On July 12, 2018, we eliminated 45 positions through headcount reduction and role consolidation. The headcount reduction included 30 employees, the majority of which were sales and marketing employees, and represented approximately 9% of our workforce at the time. On and around November 1, 2018, we eliminated an additional 48 positions through further headcount reduction and role consolidation. The headcount reduction included 36 employees, the majority of which were sales and marketing employees, and represented approximately 13% of our workforce at the time. These reductions in our sales and marketing force may adversely affect the sales performance of our products.

Due to factors including the cost pressure and impact on liquidity of significant litigation expenses and settlement costs, including those associated with the DOJ agreement in principle, if completed, management may in the future need to take additional cost reduction measures to the extent that our revenue does not stabilize or decisions that management makes in connection with this strategic alternative process materially affect our liquidity and our primary revenue generating asset, SUBSYS®. In addition, our Company may need to seek liquidity from outside sources including debt and equity in order to continue to meet management's operating plans and objectives and there can be no assurances that we will be able to do so at all or on terms that we believe are favorable to us. The Company has engaged Lazard Freres & Co. LLC to advise the Company on capital planning and the evaluation of strategic alternatives.

Approved Product Sales. Our operating results will depend significantly upon sales of approved products. During the year ended December 31, 2018, a substantial portion of our net revenues were generated from the sale of our approved product, SUBSYS®. We generated minimal revenues from the sale of SYNDROS® during the year ended December 31, 2018. Our results depend on prescription volume generally, which we believe will be driven primarily by achievement of broad market acceptance and coverage by third-party payers and effectiveness of the marketing and selling efforts with respect to SUBSYS® and SYNDROS®. Importantly, the proportion of prescriptions written for repeat SUBSYS® patients is approximately 91% of prescriptions as of December 31, 2018. Generally, repeat SUBSYS® patients receive significantly higher doses of SUBSYS® on average than first-time patients as patients are titrated from a starter dose of SUBSYS® to their effective dose in accordance with the TIRF REMS protocol.

According to IQVIA, the total market for TIRF products declined approximately 40% during the year ended December 31, 2018, to approximately 26,000 prescriptions during the year ended December 31, 2018 from approximately 43,000 prescriptions during the year ended December 31, 2017. SUBSYS® prescriptions were approximately 24% of the TIRF market on a prescription basis for the year ended December 31, 2018, compared to 29% market share for the year ended December 31, 2017. As noted above, TIRF class prescriptions have declined approximately 75% since 2015.

The ongoing and heightened publicity surrounding the perceived national opioid epidemic continues to result in heightened sensitivity by many healthcare professionals to prescribe opioids, pharmacies to dispense opioids, patients to fill opioid prescriptions, distributors to distribute opioids and third-party payers to cover opioid prescriptions. Third-party payers, such as insurance companies and regulatory and government agencies, continue to scrutinize the prescription of opioids by healthcare professionals. In addition, we believe other high-profile initiatives, such as (i) President Trump's declaration of the opioid crisis as a public health emergency, (ii)

Congressional efforts to examine the causes of the opioid epidemic in public, and (iii) states, cities and counties initiating multi-district litigation against manufacturers and distributors of opioids have likely added to this sensitivity around opioid prescribing. Consequently, these current and potential future trends have affected, and will likely continue to affect, the manner in which, and the situations when, opioids, including SUBSYS®, are being prescribed, dispensed and approved for coverage.

While we continue to sell directly into wholesalers and retail pharmacies for our revenue, the direct pressures discussed above related to the retail demand-side components of our business contributed to the decline in full-year 2018 SUBSYS® revenue when compared to 2017, and we expect this trend to continue during 2019.

Third-Party Payer Interactions and Government Programs Associated with Reimbursement. Acceptance of our products by third-party payers is critical to the success of our business and financial condition. Our relationships with these third-party payers evolves on a regular basis and is often difficult to predict. By way of example, from time to time, third-party payers modify which drugs they choose to reimburse. For instance, on or around August 1, 2014, ESI officially released its exclusion list of drugs, effective January 1, 2015, in connection with its national preferred formulary. While SUBSYS® was removed from this list in 2017, other PBMs may take similar actions and these actions may have a material impact on our net revenue in the future. As we have in the past, we will continue working with PBMs to evaluate price increases and to communicate with managed care and health-system decision-makers to ensure a balanced approach, which takes into account the clinical performance and efficacy of our products.

In addition, from time to time, our business may be affected by evolving or new governmental programs in the reimbursement landscape. For instance, CMS, which is part of the HHS, has instituted The Recovery Audit Program. The program's mission is to identify and correct improper Medicare payments through the efficient detection and collection of overpayments made on claims of healthcare services provided to Medicare beneficiaries, and the identification of underpayments to providers so that CMS can implement actions that will prevent future improper payments in all 50 states. We are aware that in January 2016, certain specialty pharmacies received written correspondence from Humana indicating that as a result of a CMS audit, Humana was initiating a deletion of certain PDEs related to SUBSYS® which will result in a reversal and recovery of identified claims paid to certain pharmacies. This audit by CMS may have been part of The Recovery Audit Program or a similar initiative of CMS. Based upon information available to us, all of these claims involve Medicare Part D patients whose prescriptions were in connection with off-label indications and related to approximately $5.6 million in SUBSYS® claims in the aggregate. Upon our inquiry for more information about these matters, Humana notified us that these deletions of certain PDEs resulting from the CMS audit also involve TIRF medications other than SUBSYS® and Humana intends to resolve these matters with the pharmacies. We believe that some affected pharmacies may alter their processes and or protocols related to dispensing off label TIRF prescriptions to Medicare patients as a result of these and similar events.

Investments in Our Infrastructure and Growth. Our ability to increase our sales and to further penetrate our target market segments is dependent in part on our ability to invest in our infrastructure and in our sales and marketing efforts. In order to drive growth, we may hire additional sales and marketing personnel and invest in marketing our products to our target physician prescriber base. While we would anticipate that any increase in sales force would result in increased product sales and net revenue, this would also lead to corresponding increases in our operating expenses. Conversely, a decrease in sales force may lead to decreased product sales, net revenue, and operating expenses. During the year ended December 31, 2018, we had reductions in our sales force due to market conditions. For additional information, see "Factors Affecting Our Performance – Cost Savings Initiatives" below. While this led to corresponding decreases in our sales and marketing expenses, the reduction in sales force may also result in future decreased product sales and net revenues. We have constructed a second dronabinol manufacturing facility, which we anticipate will supply us with sufficient commercial quantities of dronabinol API for the commercialization of our proprietary dronabinol product candidates, if approved. This second facility has, and will continue to, increase our operating expenses.

Product Development and Related Regulatory Processes. Our operating results will also depend significantly on our research and development activities and related regulatory developments. Our research and development expenses were $57.6 million and $63.0 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018 and 2017, we had 50 and 61 full-time research and development personnel, respectively. We expect research and development expenses to fluctuate with the timing of our planned preclinical studies and clinical trials for our product candidates, particularly our proprietary cannabinoid product candidates and sublingual spray product candidates. We do not expect to realize net revenues from all of these research and development initiatives in the near term and may never realize net revenues from these investments. Due to the risks inherent in conducting preclinical studies and clinical trials, the regulatory approval process and the costs of preparing, filing and prosecuting patent applications, our development completion dates and costs will vary significantly for each product candidate and are very difficult to estimate. The lengthy process of seeking regulatory approvals and the subsequent compliance with applicable regulations require the expenditure of substantial additional resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals or acceptable DEA classifications for our product candidates, could cause our research and development expenditures to increase significantly and, in turn, have a material adverse effect on our results of operations.

In addition, dronabinol and CBD are subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for the amount of dronabinol and CBD that may be produced in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of dronabinol and CBD 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 are required to obtain an annual quota from the DEA in order to manufacture and produce dronabinol and CBD. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year and has substantial discretion in deciding whether or not to make such adjustments. For 2018, we received all needed quota and all batches were produced consuming that quota before year-end. For 2019, we have received sufficient quota to meet current production plans for dronabinol and CBD.

Legal Expenses. As our ongoing federal and state investigations and litigation proceedings have continued to accumulate, these challenges have led to significant legal costs and expenses, which have had, and will continue to have, a material adverse effect on our financial condition and results of operations. It is difficult to predict such legal costs, and in some ways these costs are not within our control. For instance, consistent with the practice of many publicly-traded companies, we have entered into, and continue to enter into, indemnity agreements with our executive officers and certain members of our board of directors. These indemnity agreements broadly provide for us to advance expenses (including attorneys' fees) incurred in connection with any legal proceeding, as well as indemnification for any and all expenses, actually and reasonably incurred, in connection with the investigation, defense, settlement or appeal of such a proceeding, in connection with matters related to their position. As has been previously disclosed, two of our former executive officers, who have indemnity agreements with us based upon their prior employment and membership on our board of directors, have been criminally charged. Our satisfaction of our obligations pursuant to these executives' indemnity agreements, as well as the payment of legal fees for other former employees in connection with these legal proceedings, has resulted in significant expense. Moreover, our board of directors has been subject to securities class action and derivative cases which has resulted, and may in the future result, in significant and continuing legal costs and expenses related to separate legal counsel for individuals. The Company continues to analyze, and in some instances dispute the reasonableness of a portion of, the costs and expenses associated with the defense and representation of Dr. Kapoor. If such disputed amounts are subsequently determined not to be due and payable, we would recognize a reversal of these expenses in a future period. The reversal of these expenses could have a material impact on any of our Consolidated Statements of Operations and Comprehensive Income (Loss) (either on a quarterly or annual basis). If it is subsequently determined that all of these costs are reasonable, and the Company is required to pay the remaining balance, this could have a material adverse impact on our cash position and liquidity.

Cost Savings Initiatives. As a result of the declining TIRF market, combined with the DOJ Investigation and other legal matters, we have implemented a number of cost savings initiatives. Some of these initiatives include prioritizing research and development projects, reducing discretionary spending, and renegotiating long-term commitment contracts. On July 12, 2018, we eliminated 45 positions through headcount reduction and role consolidation. The headcount reduction included 30 employees, the majority of which were sales and marketing employees, and represented approximately 9% of our workforce at the time. On and around November 1, 2018, we eliminated an additional 48 positions through further headcount reduction and role consolidation. The headcount

reduction included 36 employees, the majority of which were sales and marketing employees, and represented approximately 13% of our workforce at the time. The affected employees received certain severance benefits, for which we incurred one-time severance-related charges totaling approximately $0.9 million during the year ended December 31, 2018. The majority of these charges were recorded within sales and marketing expenses. We may also incur other charges or cash expenditures not currently contemplated due to events that may occur as a result of, or associated with, the headcount reduction. We expect to continue to incur losses from operations, and w e may take additional actions to reduce our immediate cash expenditures. Although management has been successful in renegotiating long-term contracts and reducing expenses, there can be no assurance that we will be successful or that any needed financing will be available in the future at terms acceptable to the Company.

Basis of Presentation

Net Revenue

We sell SUBSYS® and SYNDROS® in various dosing packages to wholesale pharmaceutical distributors and specialty retail pharmacies (collectively, our customers), on a wholesale basis. Sales to our customers are subject to specified rights of return. We recognize revenue when we transfer control of our products to our customers, as our contracts have a single performance obligation (delivery of our product to their preferred location). Net revenue is measured as the amount of consideration we expect to receive in exchange for transferring goods.

Cost of Revenue, Gross Profit and Gross Margin

Cost of revenue consists primarily of materials, third-party manufacturing costs, freight in, direct and indirect personnel costs, and other overhead costs based on units dispensed through patient prescriptions. Also included in cost of revenue are charges for reserves for excess, dated or obsolete commercial inventories and production manufacturing variances.

Gross profit is net revenue less cost of revenue. Gross margin is gross profit expressed as a percentage of net revenue.

Sales and Marketing Expenses

Our sales and marketing expenses consist primarily of salaries, commissions, benefits, travel, consulting fees, costs of obtaining prescription and market data, and market research studies related to SUBSYS® and SYNDROS®. As of December 31, 2018 and 2017, we had 66 and 180 full-time sales and marketing personnel, respectively. Because we use an incentive-based compensation model for our sales professionals, we expect our sales and marketing expenses to fluctuate from period to period based on changes in SUBSYS® and SYNDROS® net revenue.

Research and Development Expenses

Research and development expenses consist of costs associated with our preclinical studies and clinical trials, and other expenses related to our drug development efforts. Our research and development expenses consist primarily of:

- external research and development expenses incurred under agreements with third-party CROs and investigative sites, third-party manufacturers and consultants;
- employee-related expenses, which include salaries, benefits and stock-based compensation for the personnel involved in our drug development activities; and
- materials, facilities, equipment and laboratory supplies, depreciation, impairment and other allocated expenses.

Our recent research and development efforts have been focused primarily on our cannabidiol, naloxone, dronabinol, buprenorphine, and epinephrine programs. As of December 31, 2018 and 2017, we had 50 and 61 full-time research and development personnel, respectively. We expect research and development expenses to fluctuate

with the timing of our planned preclinical studies and clinical trials for our product candidates. We determine which research and development projects to pursue, as well as the level of funding available for each project, based on the scientific, preclinical and clinical results of each product candidate, as well as the related regulatory action and the risk adjusted economic benefit to the company.

The following table provides a breakdown of our research and development expenses (in millions):

	Years Ended December 31,		
	2018	2017	2016
Cannabidiol	$ 21.5	$ 15.0	$ 15.3
Buprenorphine	0.6	8.6	9.4
Fentanyl	0.3	2.8	4.5
Epinephrine	2.7	1.2	0.4
Naloxone	5.4	2.4	3.0
Dronabinol	4.2	3.6	3.9
Buprenorphine/Naloxone	1.0	0.9	1.0
Internal research and development costs	20.9	25.9	29.5
Other	1.0	2.6	6.9
Total research and development expenses	$ 57.6	$ 63.0	$ 73.9

General and Administrative Expenses

Our general and administrative expenses consist primarily of:

- salaries and related costs for personnel in executive, finance, accounting, tax, human resources, information technology, and business development;
- regulatory fees for commercialized products;
- insurance premiums;
- fees for investor relations services and internal support functions;
- facility costs not otherwise included in research and development expenses; and
- professional fees for consulting and accounting services.

As of December 31, 2018 and 2017, we had 48 and 50 full-time general and administrative personnel, respectively. We expect general and administrative expense to fluctuate with market changes.

Legal Expenses

Our legal expenses consist primarily of salaries and related costs for legal personnel and professional fees for legal services. We expect legal expense to fluctuate due to timing of litigation and legal defense activities. See "Factors Affecting Our Performance – Legal Expenses" for additional information.

Charges Related to Litigation Award and Settlements

Charges related to litigation award and settlements for the year ended December 31, 2018 were $16.8 million and include a $14.0 million accrual in connection with the potential settlement of insurance litigation matters and a $1.7 million interest expense accrual in connection with the DOJ Investigation. Charges related to litigation award and settlements for the year ended December 31, 2017 include a $150.0 million accrual in connection with the DOJ Investigation and $4.5 million in connection with the investigation by the State of Illinois. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of our ongoing disputes and other legal matters.

Income Tax Expense (Benefit), Deferred Income Taxes, and Net Operating Loss Carryforwards

We account for income taxes based upon an asset and liability approach. Deferred tax assets and liabilities represent the future tax consequences of the differences between the financial statement carrying amounts of assets and liabilities versus the tax basis of assets and liabilities. Under this method, deferred tax assets are recognized for deductible temporary differences, and operating loss and tax credit carryforwards. Deferred tax liabilities are recognized for taxable temporary differences. Deferred tax assets are reduced by a valuation allowance when, in our opinion, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The impact of tax rate changes on deferred tax assets and liabilities is recognized in the year that the change is enacted. We also account for the uncertainty in income taxes by utilizing a comprehensive model for the recognition, measurement, presentation, and disclosure in financial statements of any uncertain tax positions that have been taken or are expected to be taken on an income tax return.

During the three months ended September 30, 2018, we identified an error related to the accounting for the uncertain income tax positions in 2017. We assessed the materiality of this error on our prior annual financial statements, assessing materiality both quantitatively and qualitatively, in accordance with the SEC's Staff Accounting Bulletin ("SAB") No. 99 and SAB No. 108 and concluded that the error was not material to our audited financial statements for the year ended December 31, 2017, the Unaudited Condensed Consolidated Financial Statements for any of the quarterly periods within the year ended December 31, 2017, nor to the quarterly periods ended March 31, 2018 and June 30, 2018. To correctly present uncertain income tax position liabilities, income tax expense (benefit), and net loss per share in the appropriate periods, management revised its previously issued Consolidated Balance Sheet and Statement of Stockholders' Equity as of December 31, 2017, the Consolidated Statement of Operations and Comprehensive Income (Loss) for the year ended December 31, 2017, and the Unaudited Condensed Consolidated Statements of Operations and Comprehensive Income (Loss) for the three months ended December 31, 2017. See Note 2 of the Notes to our Consolidated Financial Statements for additional information.

Under Section 382 of the Code, substantial changes in our ownership may limit the amount of NOLs that can be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our Company of more than 50% within a three-year period as determined under the Code, which we refer to as an ownership change. As of December 31, 2018, we had approximately $112.3 of federal NOLs, and $233.8 million of state NOLs. Based upon the Company's recent tax loss and current projections for future taxable income, the Company does not believe realization of these tax assets is more likely than not. As such, we maintain a full valuation allowance against the deferred tax assets as of December 31, 2018.

The 2017 Tax Act reduced the federal statutory income tax rate from 35% to 21% effective January 1, 2018, eliminated the ability to carryback NOLs arising after 2017 and instead permits such NOLs to be carried forward indefinitely, and reduced the orphan drug credit to 25% from 50% of qualified clinical testing expenses, among other changes. As a result of the 2017 Tax Act, we remeasured our net deferred tax assets and recognized a provisional net tax expense of $7.5 million during the year ended December 31, 2017. The Company completed its analysis of the 2017 Tax Act in conjunction with the completion of the Company's tax returns for 2017 and recorded a $1.0 million reduction of tax expense during the year ended December 31, 2018. See Note 10 of the Notes to our Consolidated Financial Statements for additional discussion related to the 2017 Tax Act.

Significant Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our Consolidated Financial Statements, which have been prepared in conformity with U.S. GAAP. The preparation of these Consolidated Financial Statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. Actual results could differ from those estimates.

While our significant accounting policies are more fully described in Note 2 to our Consolidated Financial Statements appearing elsewhere in this document, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our Consolidated Financial Statements.

Revenue Recognition

SUBSYS® was commercially launched in March 2012 and is monitored by an FDA-mandated REMS program known as the TIRF REMS. SYNDROS® was commercially launched in July 2017. We sell all of our products to customers in the United States. See Note 12 of the Notes to our Consolidated Financial Statements for information on revenues disaggregated by product line and route to market.

To determine revenue recognition for contractual arrangements that we identify are within the scope of ASC Topic 606, we perform the following five steps: (i) identify each contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to our performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the relevant performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods we transfer to the customer. We recognize revenue from the sale of our commercially approved products, SUBSYS® and SYNDROS®, when we transfer control of our products to our customers, as our contracts have a single performance obligation (delivery of our product to their preferred location). Revenue is measured as the amount of consideration we expect to receive in exchange for transferring goods. Any shipping and handling activities that we perform, whether before or after a customer has obtained control of the products, are considered activities to fulfill our obligation to transfer the products, and are recorded as incurred within sales and marketing expenses. We offer the following discounts to our customers:

Wholesaler and Retailer Discounts. We offer discounts to certain wholesale distributors and specialty retailers based on contractually determined rates. We record receivables due from the wholesalers and retailers net of these discounts upon transfer of control to the respective wholesale distributors and retail pharmacies.

Prompt Pay Discounts. We offer cash discounts to our customers, generally 2% of the sales price, as an incentive for prompt payment. We record receivables net of these cash discounts.

Stocking Allowances. We may offer discounts and extended payment terms, generally in the month of the initial commercial launch of a new product and on the first order made by certain wholesale distributors and retail pharmacies based on contractually determined rates. We record receivables due from the wholesalers and retailers net of these discounts upon transfer of control to the respective wholesale distributors and retail pharmacies. The extended payment terms are not greater than 12 months and therefore do not include a financing component.

As is customary in the pharmaceutical industry, it is common for our contracts to include product sales allowances that can decrease the transaction price and are therefore considered to be variable consideration. Product sales allowances, which include product returns, patient discount programs, rebates and chargebacks, are variable consideration and are based on amounts owed or to be claimed on the related sales. We estimate variable consideration when determining the transaction price using the expected value method. We assess whether variable consideration is constrained and only include estimated amounts in the transaction price to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Our estimates of variable consideration and determination of whether to include estimated amounts in the transaction price are based largely on historical data, and take into consideration the terms of our agreements with customers and third-party payers and the levels of inventory within the distribution channels that may result in future discounts taken. In certain cases, such as patient assistance programs, our estimates are based on estimated utilization. If actual future results vary, we may need to adjust these estimates, which could have an effect on revenue in the period of adjustment. During the year ended December 31, 2018, we recognized revenue of $8.5 million related to changes in the estimated transaction price allocated to performance obligations satisfied in prior periods. Our product sales allowances include:

Product Returns. We allow customers to return product for credit beginning six months prior to, and ending 12 months following, the product expiration date. SUBSYS® currently has a shelf life of 36 or 48 months from the date of manufacture, depending on the manufacture date, and SYNDROS® currently has a shelf life of 24 or 36 months from the date of manufacture, depending on the manufacture date. We have monitored actual return history since product launch, which provides us with a basis to reasonably estimate future product returns, taking into consideration the shelf life of product at the time of shipment, shipment and prescription trends, estimated distribution channel inventory levels and consideration of the introduction of competitive products.

Because of the shelf life of our products and our return policy of issuing credits on returned product that is within six months before, and up to 12 months following, the product expiration date, there may be a significant period of time between when the product is shipped and when we issue credits on returned products. Accordingly, we may have to adjust these estimates, which could have a material effect on net revenue and earnings in the period of adjustment. The allowance for product returns is included in accrued sales allowances.

Patient Discount Programs. We offer discount card programs to patients, in which patients receive discounts on their prescriptions that are reimbursed by us to the retailer. We estimate the total amount that will be redeemed based on a percentage of actual redemptions applied to inventory in the distribution and retail channels. The allowance for patient discount programs is included in accrued sales allowances.

Rebates. We participate in certain rebate programs, which provide discounted prescriptions to qualified insured patients. Under these rebate programs, we pay a rebate to the third-party administrator of the program, generally two to three months after the quarter in which prescriptions subject to the rebate are filled. We estimate and accrue these rebates based on current and estimated future contract prices, historical and estimated future percentages of products prescribed to qualified patients and estimated levels of inventory in the distribution channel. The allowance for rebates is included in accrued sales allowances.

Chargebacks. We provide discounts primarily to authorized users of the FSS of the General Services Administration under an FSS contract negotiated by the Department of Veterans Affairs and various organizations under Medicaid contracts and regulations. These organizations purchase products from the wholesale distributors at a discounted price, and the wholesale distributors then charge back to us the difference between the current retail price and the price the organization paid for the product. We estimate chargebacks based on estimated wholesaler inventory levels, current contract and estimated future prices and historical chargeback activity.

As of December 31, 2018, the majority of our accounts receivables were related to product sales. For the year ended December 31, 2018, the Company had no material bad-debt write-offs and there were no contract assets, contract liabilities or deferred contract costs recorded on the Consolidated Balance Sheets as of December 31, 2018.

A roll-forward of our product sales allowances for the years ended December 31, 2018 and 2017 is as follows (in thousands):

	Wholesale Discounts (1)	Patient Discount Programs	Rebates	Returns	Total
Balance at December 31, 2016	$ 5,459	$ 10,120	$ 16,283	$ 2,552	$ 34,414
Product sales allowances:					
Provision related to current period sales	14,525	10,569	35,466	8,332	68,892
Provisions related to sales made in prior years	—	—	(4,468)	—	(4,468)
Payment and credits related to sales made in current period	(10,793)	(9,298)	(23,871)	—	(43,962)
Payment and credits related to sales made in prior periods	(5,359)	(10,120)	(11,815)	(7,460)	(34,754)
Balance at December 31, 2017	$ 3,832	$ 1,271	$ 11,595	$ 3,424	$ 20,122
Provision related to current period sales	9,292	4,891	21,613	2,497	38,293
Provisions related to sales made in prior years	—	—	—	8,464	8,464
Payment and credits related to sales made in current period	(6,082)	(4,200)	(17,427)	(1,911)	(29,620)
Payment and credits related to sales made in prior periods	(3,732)	(1,271)	(9,283)	(11,501)	(25,787)
Balance at December 31, 2018	$ 3,310	$ 691	$ 6,498	$ 973	$ 11,472

(1) Includes wholesaler discounts, prompt pay discounts, stocking allowances and government chargebacks.

Inventories, Net

Inventories consist of raw materials, work-in-process and finished product and are stated at the lower of cost or NRV. Cost, which includes amounts related to materials and costs incurred by our contract manufacturers, is determined on a first-in, first-out basis. Non-current inventories are those that are not expected to be consumed or sold within 12 months of the balance sheet date and are included in other assets in our Consolidated Balance Sheets. In evaluating whether inventory should be classified as current or noncurrent, management considers factors such as historical and anticipated future sales compared to quantities on hand and the remaining shelf life of products on hand. Inventory costs are capitalized prior to regulatory approval and product launch based on management's judgment of probable future commercial use and NRV of the inventory. Such judgment incorporates our knowledge and best estimate of where the relevant product is in the regulatory process, our required investment in the product, market conditions, competing products and our economic expectations for the product post-approval relative to the risk of manufacturing the product prior to approval. In evaluating the recoverability of inventories produced in preparation for product launches, we consider the probability that revenue will be obtained from the future sale of the related inventory together with the status of the product within the regulatory approval process, as well as the market for the product in its current state. We could be required to permanently write down previously capitalized costs related to pre-approval or pre-launch inventory upon a change in such judgment, due to a denial or delay of approval by regulatory bodies, a delay in commercialization, or other potential factors including product expiration. Inventories are reviewed periodically for potential excess, dated or obsolete status. Management evaluates the carrying value of inventories on a regular basis, taking into account such factors as historical and anticipated future sales compared to quantities on hand, the price we expect to obtain for products in their respective markets compared with historical cost and the remaining shelf life of goods on hand.

Stock-Based Compensation

Stock-based compensation expense is measured at the grant date, based on the estimated fair value of the award. The cost is recognized in our Consolidated Financial Statements as expense ratably over the requisite service period or vesting period, which is generally three to four years, on a straight-line basis. We account for forfeitures when they occur.

We currently use the Black-Scholes option-pricing model to estimate the fair value of our stock-based payment awards. This model requires the input of highly subjective assumptions, including the fair value of the underlying common stock, the expected volatility of the price of our common stock, risk-free interest rates, the expected term of the option and the expected dividend yield of our common stock. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future. These assumptions are estimated as follows:

- Expected Volatility — Prior to our IPO, we did not have a reliable history of market prices for our common stock. Following our IPO, while we have an active trading market, we do not have sufficient historical data to accurately estimate volatility for the period equivalent to the expected term of the stock option grants. Accordingly, we estimate the expected stock price volatility for our common stock by taking the median historical stock price volatility for industry peers based on daily price observations over a period equivalent to the expected term of the stock option grants. Industry peers consist of other public companies in the pharmaceutical industry that are similar in size, stage of life cycle and financial leverage. We intend to incorporate the volatility of our own common stock share price in future periods as we begin to have sufficient historical data available.
- Risk-Free Interest Rate — The risk-free interest rate assumption is based on observed interest rates appropriate for the expected terms of our awards. The risk-free interest rate assumption is based on the yields of U.S. Treasury securities with maturities similar to the expected term of the options for each option group.
- Expected Term — The expected term represents the period that our stock-based awards are expected to be outstanding. The expected terms of all of our awards is based on a simplified method allowed by the SEC due to insufficient historical data, and defines the term as the average of the contractual term of the options and the weighted-average vesting period for all open tranches.
- Expected Dividend Yield — We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future. Consequently, we used an expected dividend yield of zero.

Deferred Tax Valuation Allowance

We record a valuation allowance to reduce our deferred tax assets to the amount that is more likely than not to be realized. In assessing the realization of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. The Company also considers the scheduled reversal of deferred tax liabilities, projected future taxable income or losses, and tax planning strategies in making this assessment. Based upon the Company's recent tax loss and current projections for future taxable income, the Company does not believe realization of these tax assets is more likely than not. As such, we maintain a full valuation allowance against the deferred tax assets as of December 31, 2018.

Recently Issued Accounting Pronouncements

Recent accounting pronouncements which may be applicable to us are described in Note 2 of the Notes to our Consolidated Financial Statements contained herein in Part II, Item 8.

Results of Operations

The following table presents certain selected consolidated financial data expressed as a percentage of net revenue:

	Years Ended December 31,		
	2018	2017 (As Revised)	2016
Net revenue	100.0%	100.0%	100.0%
Cost of revenue	13.2	14.7	10.5
Gross profit	86.8	85.3	89.5
Operating expenses:			
Sales and marketing	38.2	34.7	28.8
Research and development	70.1	44.7	30.5
General and administrative	47.9	33.1	17.3
Legal	65.8	15.0	8.3
Charges related to litigation award and settlements	20.4	113.5	1.6
Total operating expenses	242.4	241.0	86.5
Operating income (loss)	(155.6)	(155.7)	3.0
Other income:			
Interest income	2.4	1.3	0.4
Other income (expense)	(0.8)	—	0.1
Total other income	1.6	1.3	0.5
Income (loss) before income taxes	(154.0)	(154.4)	3.5
Less: income tax expense (benefit)	(2.3)	6.9	0.3
Net income (loss)	(151.7)%	(161.3)%	3.2%

Comparison of year ended December 31, 2018 to year ended December 31, 2017

Net Revenue. Net revenue decreased $58.6 million, or 41.6%, to $82.1 million for the year ended December 31, 2018 compared to $140.7 million for the year ended December 31, 2017. The decrease in net revenue was primarily attributable to a 47.0% decrease in SUBSYS® shipments to our customers for the year ended December 31, 2018 due primarily to reduced demand for SUBSYS®, as compared to the year ended December 31, 2017, partially offset by a 3.6% increase in net sales price due to changes in mix of prescribed dosages and changes in provisions for wholesaler discounts, patient discounts, rebates and returns, as well as price increases in January 2017, August 2017, and January 2018. Provisions for patient discounts, wholesaler discounts, rebates and returns were $4.9 million, $9.7 million, $21.6 million and $10.9 million, respectively, or 36.4% on a combined basis of gross revenue from the sale of our products for the year ended December 31, 2018, compared to $10.6 million, $14.5 million, $31.0 million and $8.3 million, respectively, or 31.4% on a combined basis of gross revenue from the sale of our products for the year ended December 31, 2017. The decrease in product sales allowances was primarily attributable to lower sales of SUBSYS®, partially offset by an increase in product returns due to expiry. As described in “Factors Affecting Our Performance – Approved Product Sales”, the continuing sensitivity by some healthcare professionals to prescribe, and pharmacies to dispense, opioids, scrutiny by third-party payers and governmental agencies, ongoing state and federal investigations, and media reports related thereto, contributed to the decrease in full-year SUBSYS® revenue when compared to 2017.

Cost of Revenue, Gross Profit and Gross Margin. Cost of revenue decreased $9.8 million to $10.8 million for the year ended December 31, 2018 compared to $20.6 million for the year ended December 31, 2017. The decrease in cost of revenue was primarily attributable to lower sales of SUBSYS® during the year ended December 31, 2018, partially offset by a $3.1 million decrease in charges to excess and obsolete inventory reserves and a $0.7 million decrease in losses on firm purchase commitments. Gross profit decreased $48.8 million to $71.3 million for the year ended December 31, 2018 compared to $120.1 million for the year ended December 31, 2017. Gross margin for the year ended December 31, 2018 was approximately 87% compared to approximately 85% for the year ended December 31, 2017.

Sales and Marketing Expense. Sales and marketing expense decreased $17.5 million to $31.4 million for the year ended December 31, 2018 compared to $48.9 million for the year ended December 31, 2017. The decrease in sales and marketing expense was due primarily to lower sales of SUBSYS® and decreases in personnel costs resulting from the headcount reductions and role consolidations in July and November 2018 as a part of our cost savings initiatives.

Research and Development Expense. Research and development expense decreased $5.4 million to $57.6 million for the year ended December 31, 2018 compared to $63.0 million for the year ended December 31, 2017. The decrease in research and development expense was due primarily to timing of clinical and development expenses and decreases in personnel costs.

General and Administrative Expense. General and administrative expense decreased $7.2 million to $39.3 million for the year ended December 31, 2018 compared to $46.5 million for the year ended December 31, 2017. The decrease in general and administrative expense was due primarily to our efforts to reduce expenses as part of our cost savings initiatives and a decrease in stock-based compensation costs.

Legal Expense. Legal expense increased $32.9 million to $54.0 million for the year ended December 31, 2018, compared to $21.1 million for the year ended December 31, 2017. The increase was due to increases in legal expense incurred in connection with various ongoing government investigations and prosecutions of our former employees, and other legal proceedings. See “Factors Affecting our Performance – Legal Expenses” for additional information.

Charges Related to Litigation Award and Settlements . Charges related to litigation award and settlements were $16.8 million for the year ended December 31, 2018 and include a $14.0 million accrual in connection with the potential settlement of insurance litigation matters and a $1.7 million interest expense accrual in connection with the DOJ Investigation. Charges related to litigation award and settlements for the year ended December 31, 2017 include a $150.0 million accrual in connection with the DOJ Investigation and $4.5 million in connection with the investigation by the State of Illinois. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of these legal matters.

Other Income. Other income decreased $0.5 million to $1.3 million for the year ended December 31, 2018, compared to $1.8 million for the year ended December 31, 2017. The decrease is primarily to due to a loss on the disposal of property and equipment.

Income Tax Expense (Benefit). Provision (benefit) for income taxes was $(1.9) million for the year ended December 31, 2018 representing an effective tax rate of 1.5%. Provision for income taxes was $9.6 million for the year ended December 31, 2017 representing an effective tax rate of (4.4)%. The change in the effective rate for the year ended December 31, 2018, compared with the year ended December 31, 2017, was primarily due to the recording of a full valuation allowance against the deferred tax assets during the year ended December 31, 2017, as well as the resolution of a previously recorded uncertain tax position for legal costs during the year ended December 31, 2018.

Comparison of year ended December 31, 2017 to year ended December 31, 2016

Net Revenue. Net revenue decreased $101.6 million, or 41.9%, to $140.7 million for the year ended December 31, 2017 compared to $242.3 million for the year ended December 31, 2016. The decrease in net revenue was attributable to a decrease in net revenue of SUBSYS®, which was the result of a 40.5% decrease in SUBSYS® shipments to pharmaceutical wholesalers and specialty pharmaceutical retailers for the year ended December 31, 2017 due primarily to reduced demand for SUBSYS®, as compared to the year ended December 31, 2016, combined with a 2.0% decrease in net sales price due to changes in mix of prescribed dosages and changes in provisions for wholesaler discounts, patient discounts, rebates and returns, partially offset by price increases in July 2016, January 2017, and August 2017. Provisions for patient discounts, wholesaler discounts, rebates and returns were $10.6 million, $14.5 million, $31.0 million and $8.3 million, respectively, or 31.4% on a combined basis of gross revenue from the sale of SUBSYS® for the year ended December 31, 2017, compared to $95.6 million, $28.0 million, $40.7 million and $0.7 million, respectively, or 40.5% on a combined basis of gross revenue from the sale of SUBSYS® for the year ended December 31, 2016. The decrease in product sales allowances was primarily attributable to lower volumes of patient assistance, partially offset by an increase in product returns. We generated minimal revenues from the sale of SYNDROS® during the year ended December 31, 2017. As described in “Factors Affecting Our Performance – Approved Product Sales”, the continuing sensitivity by some healthcare professionals to prescribe, and pharmacies to dispense, opioids, scrutiny by third-party payers and governmental agencies, and

ongoing state and federal investigations, and media reports related thereto contributed to the decrease in full-year SUBSYS® revenue when compared to 2016.

Cost of Revenue, Gross Profit and Gross Margin. Cost of revenue decreased $4.8 million to $20.6 million for the year ended December 31, 2017 compared to $25.4 million for the year ended December 31, 2016. The decrease in cost of revenue was primarily attributable to the decrease in sales of SUBSYS® during the year ended December 31, 2017, partially offset by a loss of $1.0 million which represented firm, non-cancellable and unconditional purchase commitments for quantities in excess of our current forecasts for future demand. Gross profit decreased $96.8 million to $120.1 million for the year ended December 31, 2017 compared to $216.9 million for the year ended December 31, 2016 due primarily to the decrease in sales of SUBSYS®. Gross profit was also impacted by a $6.2 million increase in our reserve for excess and obsolete inventory to $13.6 million for the year ended December 31, 2017 compared to $7.4 million during the year ended December 31, 2016 related to SUBSYS®. Gross margin for the year ended December 31, 2017 was approximately 85% compared to approximately 90% for the year ended December 31, 2016.

Sales and Marketing Expense. Sales and marketing expense decreased $20.8 million to $48.9 million for the year ended December 31, 2017 compared to $69.7 million for the year ended December 31, 2016. The decrease in sales and marketing expense was due primarily to lower sales compensation expense and incremental product selling and marketing expense associated with the decrease in sales of SUBSYS® and corresponding reduction in sales force.

Research and Development Expense. Research and development expense decreased $10.9 million to $63.0 million for the year ended December 31, 2017 compared to $73.9 million for the year ended December 31, 2016. The decrease in research and development expense was due primarily to timing of clinical and development expenses. Also contributing to the decrease in research and development expense was a charge of $2.4 million for product not commercially viable during the year ended December 31, 2016 related to SYNDROS®. There was no similar charge for the year ended December 31, 2017.

General and Administrative Expense. General and administrative expense increased $4.4 million to $46.5 million for the year ended December 31, 2017 compared to $42.1 million for the year ended December 31, 2016. The increase in general and administrative expense was due primarily to charitable contributions of $5.6 million and an increase in personnel costs due to increased headcount, partially offset by a decrease in stock-based compensation costs.

Legal Expense. Legal expense increased $1.1 million to $21.1 million for the year ended December 31, 2017, compared to $20.0 million for the year ended December 31, 2016. The increase was due to increases in legal expense incurred in connection with various ongoing government investigations and prosecutions of our former employees, and other legal proceedings. See “Factors Affecting our Performance – Legal Expenses” for additional information.

***Charges Related to Litigation Award and Settlements*.** Charges related to litigation award and settlements for the year ended December 31, 2017 include a $150.0 million accrual in connection with the DOJ Investigation and $4.5 million in connection with the investigation by the State of Illinois. Charges related to litigation award and settlements for the year ended December 31, 2016 include legal expense accruals of $3.4 million related to a settlement reached with the State of New Hampshire and $0.5 million in connection with the investigation by the State of Massachusetts. See Note 7 of the Notes to our Consolidated Financial Statements for a discussion of these legal matters.

Other Income. We reported other income of $1.8 million for the year ended December 31, 2017 and $1.1 million for the year ended December 31, 2016 due primarily to higher returns from previously invested excess cash.

Income Tax Expense (Benefit). Provision for income taxes was $9.6 million for the year ended December 31, 2017 representing an effective tax rate of (4.4)%. Provision for income taxes was $0.8 million for the year ended December 31, 2016 representing an effective tax rate of 9.9%. The increase in income tax expense relates primarily to the increase in valuation allowance during the year ended December 31, 2017. The decrease in the effective tax rate for the year ended December 31, 2017 was due primarily to the $150.0 million accrual related to the DOJ Investigation that does not currently meet the more likely than not standard for recognizing a tax benefit, the re-measurement of our net deferred tax assets as a result of the 2017 Tax Act, and the increase in the valuation allowance. See Note 10 of the Notes to our Consolidated Financial Statements for a discussion of the 2017 Tax Act.

Liquidity and Capital Resources

Sources of Liquidity

Current operations are financed principally with existing cash on hand, investments in marketable securities, and cash flows from operations. We will also need to raise additional funds to finance future cash needs through public or private equity offerings, debt financings, sale or licensing of assets, receivables or royalty financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership will be diluted. Any future debt financing into which we enter may impose upon us covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. In addition, if we raise additional funds through corporate collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to products or product candidates, or grant licenses on terms that are not favorable to us.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to significantly delay, scale back or discontinue one or more of our product development programs or commercialization efforts, or other aspects of our business plan. We also may be required to relinquish, license or otherwise dispose of rights to products or product candidates that we would otherwise seek to commercialize or develop ourselves on terms that are less favorable than might otherwise be available. In addition, our ability to achieve profitability or to respond to competitive pressures would be significantly limited. These factors, and the factors described below under the heading “Funding Requirements”, continue to raise substantial doubt about our ability to continue as a going concern.

Cash Flows

The following table shows a summary of our cash flows for the years indicated (in millions):

	Years Ended December 31,		
	2018	2017	2016
Net cash provided by (used in) operating activities	$ (55.9)	$ (60.6)	$ 58.9
Net cash provided by (used in) investing activities	53.4	(17.8)	(22.0)
Net cash provided by (used in) financing activities	2.1	5.8	(11.8)
Net increase (decrease) in cash and cash equivalents	(0.4)	(72.6)	25.1
Cash and cash equivalents, beginning of period	32.0	104.6	79.5
Cash and cash equivalents, end of period	$ 31.6	$ 32.0	$ 104.6

Cash Flows from Operating Activities. Net cash used in operating activities was $55.9 million and $60.6 million for the years ended December 31, 2018 and 2017, respectively, compared to net cash provided by operating activities of $58.9 million for the year ended December 31, 2016. The net cash used during the year ended December 31, 2018 primarily reflects the net loss for the period driven by a reduction in SUBSYS® net sales and changes in working capital and payments in connection with litigation costs and expenses, adjusted in part by depreciation and amortization, stock-based compensation expense, and an impairment loss on property and equipment. The net cash used during the year ended December 31, 2017 primarily reflects the net loss for the period driven by a reduction in SUBSYS® net sales, adjusted in part by deferred income tax benefit, depreciation and amortization and stock-based compensation expense, and is also impacted by changes in working capital and payments in connection with the settlement of the investigations by the States of New Hampshire and Illinois, and the settlement with Dr. Kottayil. The net cash provided during the year ended December 31, 2016 primarily reflects the net income for the period and changes in working capital, adjusted in part by depreciation and amortization and stock-based compensation expense.

Cash Flows from Investing Activities. Net cash provided by investing activities was $53.4 million for the year ended December 31, 2018, compared to net cash used in investing activities of $17.8 million and $22.0 million for the years ended December 31, 2017 and 2016, respectively. Cash provided by investing activities during 2018 consisted primarily of the net sale and maturity of investments, partially offset by purchases of property and

equipment. During 2017, we invested $1.1 million of excess cash in short-term and long-term investments, net of proceeds, and we also invested $16.7 million for purchases of equipment and leasehold improvements. During 2016, we invested $11.4 million of excess cash in short-term and long-term investments, net of proceeds, and we also invested $10.6 million for purchases of equipment and leasehold improvements.

Cash Flows from Financing Activities. Net cash provided by financing activities was $2.1 million and $5.8 million for the years ended December 31, 2018 and 2017, respectively, as compared to net cash used in financing activities of $11.8 million for the year ended December 31, 2016. During the year ended December 31, 2018, we received proceeds of $1.1 million from the exercise of stock options and proceeds of $1.0 million from shares issued under our employee stock purchase plan. During the year ended December 31, 2017, we received proceeds of $4.5 million from the exercise of stock options and proceeds of $1.3 million from shares issued under our employee stock purchase plan. During the year ended December 31, 2016, we expended approximately $16.1 million to repurchase shares of our common stock and recognized $1.7 million due to tax deficiencies on stock options and awards, partially offset by proceeds from the exercise of stock options of $3.8 million and proceeds from shares issued under our employee stock purchase plan of $2.3 million.

We invoice pharmaceutical wholesalers and specialty pharmaceutical retailers upon delivery of SUBSYS® and SYNDROS®. To date, our customers have typically paid us 30 to 60 days from their applicable invoice dates.

Our cash flows for 2019 and beyond will depend on a variety of factors, including sales of SUBSYS® and SYNDROS®, regulatory approvals, investments in manufacturing and production, capital equipment, research and development, general and administrative expenses, strategic alternatives related to our opioid-related assets, and legal costs and expenses associated with litigation proceedings and settlements.

Funding Requirements

As our research and development activities mature and develop over the next several years, the Company will likely require substantial additional funds to continue such activities, depending upon events that are difficult to predict at this time. In addition, as the Company continues to contend with existing litigation (and resolve such proceedings as appropriate) and fund other legal expenses related to our former employees, we will require additional funding. In this regard, management's plans, in order to meet any additional operating cash flow requirements, include the pursuit of potential strategic alternatives related to our opioid-related assets, as well as financing activities such as public offerings and private placements of our common stock, preferred stock offerings, and issuances of debt and convertible debt instruments.

In the ordinary course of business, we are involved in litigation, claims, government inquiries, investigations, charges and proceedings. Refer to Note 7 under the heading "Legal Matters" in the Notes to our Consolidated Financial Statements . The legal fees and expenses required to successfully defend ourselves and our former executives against pending and future litigation, criminal trials and investigations has, and will likely continue to, materially impact cash flows. In addition, the uncertainty of the timing of a final settlement with the DOJ (and the payments associated therewith) will likely impact our liquidity and may require us to sell or license assets, sell investments before the recovery of their amortized cost basis, or raise capital at potentially unfavorable terms or rates, particularly when aggregated with other potential state and multi-district litigation investigation settlements that may occur in the future, as well as potential future settlements related to ongoing litigation with insurance payers or other third parties.

Because of the numerous risks and uncertainties associated with the commercialization of SUBSYS®, SYNDROS® and the development of our other product candidates, outcomes of litigation or liabilities for indemnification, and the pursuit of strategic alternatives related to our opioid-related assets discussed elsewhere in this report, it is difficult to predict the amounts of increased capital outlays and operating expenditures associated with our current anticipated product introduction, clinical trials and preclinical studies. The timing and amounts of our funding requirements will depend on numerous factors, including but not limited to:

- costs and actions associated with litigation and government investigations, including any settlement amounts or required divestitures;

- indemnification obligations for former executives, including the outcome of the disputed indemnification costs for the Company's founder, John Kapoor;
- the levels and mix of our product sales;
- the rates of progress, costs and outcomes of our clinical trials and other product development programs, including product candidates that we may develop, in-license or acquire;
- regulatory approvals, DEA classifications and other regulatory related events;
- personnel, facilities, equipment and other similar requirements;
- costs of operating as a public company;
- the effects of competing technological and market developments;
- costs and judgements of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates;
- our ability to divest, acquire, or in-license products and product candidates, technologies or businesses; and
- terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish.

We cannot be sure that our existing cash and cash equivalents or investments will continue to be adequate to fund our operations, or that additional financing will be available when needed, or that, if available, financing will be obtained on terms favorable to us or our stockholders. Having insufficient funds may require us to delay, scale back or eliminate some or all of our research or development programs or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. If we raise additional funds by issuing equity or convertible securities, substantial dilution to existing stockholders will likely result. If we raise additional funds by incurring new debt obligations, the terms of the debt will likely require significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business.

As discussed in Note 1 of the Notes to the Consolidated Financial Statements under ASU 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40), or, ASC 205-40, we have the responsibility to evaluate whether conditions or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. Under ASC 205-40, this evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Since we currently anticipate that our existing capital resources, along with management's plans described above, will enable us to meet our planned operational expenses and capital expenditures, based on our current operating plans, into early 2020, we have determined that this cash runway of less than 12 months, along with our losses and negative cash flows from operations and uncertainty in generating sufficient cash to meet our legal obligations and settlements, meet the ASC 205-40 standard for raising substantial doubt about our ability to continue as a going concern within one year of the issuance date of these financial statements. While we have plans to mitigate this risk, which primarily consist of raising additional capital through a combination of equity or debt financings, and reducing cash expenditures, there is no guarantee that we will be successful in these mitigation efforts and substantial doubt about our ability to continue as a going concern has not been alleviated as of December 31, 2018.

Contractual Obligations (in thousands)

Contractual Obligations	Total	Payments Due in Less Than 1 Year	Payments Due in 1-3 Years	Payments Due in 3-5 Years	Payments Due in More Than 5 Years
Operating leases	$ 22,941	$ 3,044	$ 5,468	$ 2,578	$ 11,851
Purchase obligations	10,000	4,000	6,000	—	—
	$ 32,941	$ 7,044	$ 11,468	$ 2,578	$ 11,851

Off-Balance Sheet Arrangements

During the year ended December 31, 2018, we did not have any relationships with unconsolidated organizations or financial partnerships, such as structured finance or special purpose entities, that would have been established for the purpose of facilitating off-balance sheet arrangements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

At December 31, 2018, $6.4 million of our cash equivalent investments was in money market securities that are reflected as cash equivalents because all original maturities are within 90 days. Our money market securities may consist of commercial paper, Federal agency discount notes and money market funds. We believe our interest rate risk with respect to these investments is limited due to the short-term duration of these arrangements and the yields earned, which approximate current interest rates.

Our policy for our short-term and long-term investments is to establish a high-quality portfolio that preserves principal, meets liquidity needs, avoids inappropriate concentrations and delivers an appropriate yield in relationship to our investment guidelines and market conditions. Our investment portfolio, consisting of fixed income securities that we hold on an available-for-sale basis, was approximately $78.4 million as of December 31, 2018 and $136.4 million as of December 31, 2017. These securities, like all fixed income instruments, are subject to interest rate risk and would likely decline in value if market interest rates increase. Currently, we have the ability to hold our fixed income investments until maturity and, therefore, we would not expect to recognize any material adverse impact in income or cash flows if market interest rates increase.

The following table provides information about our available-for-sale securities that are sensitive to changes in interest rates. We have aggregated our available-for-sale securities for presentation purposes since they are all very similar in nature (dollar amounts in millions):

Interest Rate Sensitivity
Principal Amount by Expected Maturity as of December 31, 2018

	Financial instruments mature during year ended:					
	2019	2020	2021	2022	2023	Thereafter
CD's, commercial paper and available-for-sale securities	$ 70.7	$ 8.0	$ —	$ —	$ —	$ —
Weighted-average yield rate	2.26%	0.24%	0.00%	0.00%	0.00%	0.00%

We have not entered into derivative financial instruments. We do not have operations outside of the U.S. and, accordingly, we have not been susceptible to significant risk from changes in foreign currencies.

During the normal course of business, we could be subjected to a variety of market risks, examples of which include, but are not limited to, interest rate movements and foreign currency fluctuations, as we discussed above, and collectability of accounts receivable. We continuously assess these risks and have established policies and procedures to protect against the adverse effects of these and other potential exposures. Although we do not anticipate any material losses in these risk areas, no assurance can be made that material losses will not be incurred in these areas in the future.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Insys Therapeutics, Inc.
Chandler, Arizona

Opinion on the Consolidated Financial Statements

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

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 12, 2019, expressed an unqualified opinion thereon.

Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered losses and negative cash flows from operations and expects uncertainty in generating sufficient cash to meet its legal obligations and settlements and sustain its operations. These factors raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Change in Accounting Method Related to Revenue

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for revenue in 2018 due to the adoption of the Accounting Standards Codification 606, "*Revenue from Contracts with Customers* ."

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the 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 consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2007.

Phoenix, Arizona

March 12, 2019

INSYS THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2018	2017 (As Revised)
Assets		
Current Assets:		
Cash and cash equivalents	$ 31,552	$ 31,999
Short-term investments	64,126	85,189
Accounts receivable, net of allowances of $3,832 at December 31, 2017	12,610	21,513
Inventories, net	8,608	17,408
Prepaid expenses and other current assets	9,396	19,833
Total current assets	126,292	175,942
Property and equipment, net	52,086	55,174
Long-term investments	8,446	46,733
Other assets	5,703	1,231
Total assets	$ 192,527	$ 279,080
Liabilities and Stockholders' Equity (Deficit)		
Current Liabilities:		
Accounts payable and accrued expenses (including accrued legal expenses of $32,625 and $4,847 at December 31, 2018 and 2017, respectively	$ 50,859	$ 30,438
Accrued compensation	6,437	8,808
Accrued sales allowances	8,162	16,290
Deferred revenue	—	1,109
Accrued litigation awards and settlements	41,402	150,534
Total current liabilities	106,860	207,179
Noncurrent accrued litigation awards and settlements	125,000	—
Uncertain income tax position (Note 1)	3,767	5,692
Total liabilities	235,627	212,871
Commitments and Contingencies (Note 7)		
Stockholders' Equity (Deficit):		
Preferred stock (par value $0.01 per share; 10,000,000 shares authorized; 0 shares issued and outstanding as of December 31, 2018 and 2017, respectively)	—	—
Common stock (par value $0.01 per share; 100,000,000 shares authorized; 74,381,303 and 73,612,052 shares issued and outstanding as of December 31, 2018 and 2017, respectively)	744	736
Additional paid in capital	292,508	278,356
Unrealized loss on available-for-sale securities, net of tax	(269)	(438)
Notes receivable from stockholders	—	(21)
Accumulated deficit (Note 1)	(336,083)	(212,424)
Total stockholders' equity (deficit)	(43,100)	66,209
Total liabilities and stockholders' equity	$ 192,527	$ 279,080

See accompanying notes to Consolidated Financial Statements.

INSYS THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands, except share and per share data)

	Years Ended December 31,		
	2018	2017 (As Revised)	2016 (As Revised)
Net revenue	$ 82,080	$ 140,693	$ 242,275
Cost of revenue	10,803	20,643	25,393
Gross profit	71,277	120,050	216,882
Operating expenses:			
Sales and marketing	31,372	48,870	69,651
Research and development	57,572	62,954	73,913
General and administrative	39,268	46,487	42,098
Legal	54,011	21,086	19,994
Charges related to litigation award and settlements	16,777	159,684	3,900
Total operating expenses	199,000	339,081	209,556
Operating income (loss)	(127,723)	(219,031)	7,326
Other income:			
Interest income	1,984	1,881	1,039
Other income (expense), net	(668)	(45)	59
Total other income	1,316	1,836	1,098
Income (loss) before income taxes	(126,407)	(217,195)	8,424
Income tax expense (benefit) (Note 1)	(1,900)	9,640	834
Net income (loss)	$ (124,507)	$ (226,835)	$ 7,590
Unrealized gain (loss) on available-for-sale securities, net of tax of $50, $0, and $0	169	(136)	(150)
Total comprehensive income (loss)	$ (124,338)	$ (226,971)	$ 7,440
Net income (loss) per common share:			
Basic	$ (1.68)	$ (3.12)	$ 0.11
Diluted	$ (1.68)	$ (3.12)	$ 0.10
Weighted average common shares outstanding (Note 1)			
Basic	74,073,665	72,636,780	71,639,856
Diluted	74,073,665	72,636,780	74,166,981

See accompanying notes to Consolidated Financial Statements.

INSYS THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Common Stock		Additional Paid in Capital	Unrealized Gain (Loss) on Available-For-Sale Securities	Notes Receivable From Stockholders	Retained Earnings (Accumulated Deficit)	Total
	Shares	Amount					
Balance at December 31, 2015	71,907,858	$ 719	$ 246,685	$ (152)	$ (21)	$ 5,074	$ 252,305
Exercise of stock options	637,721	6	3,797	—	—	—	3,803
Issuance of common stock- employee stock purchase plan	221,046	2	2,278	—	—	—	2,280
Tax deficiency on stock options and awards	—	—	(1,729)	—	—	—	(1,729)
Stock based compensation - stock options and awards	—	—	21,589	—	—	—	21,589
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(150)	—	—	(150)
Repurchase of common stock	(843,075)	(8)	(16,091)	—	—	—	(16,099)
Net income	—	—	—	—	—	7,590	7,590
Balance at December 31, 2016	71,923,550	719	256,529	(302)	(21)	12,664	269,589
Exercise of stock options	1,476,448	15	4,530	—	—	—	4,545
Issuance of common stock- employee stock purchase plan	202,597	2	1,324	—	—	—	1,326
Stock based compensation - stock options and awards	—	—	16,015	—	—	—	16,015
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(136)	—	—	(136)
Vesting of restricted stock units	14,000	—	—	—	—	—	—
Shares withheld for future payment of employees' withholding tax liability	(4,543)	—	(42)	—	—	—	(42)
Impact of adoption of ASU 2016-09 (As Revised)	—	—	—	—	—	1,747	1,747
Net loss (As Revised) (Note 2)	—	—	—	—	—	(226,835)	(226,835)
Balance at December 31, 2017 (As Revised)	73,612,052	736	278,356	(438)	(21)	(212,424)	66,209
Adoption of new accounting standard ASC 606	—	—	—	—	—	848	848
Exercise of stock options	442,191	5	1,091	—	—	—	1,096
Issuance of common stock- employee stock purchase plan	220,858	2	1,046	—	—	—	1,048
Stock based compensation - stock options, awards, and restricted stock units	—	—	12,016	—	—	—	12,016
Unrealized gain on available-for-sale securities, net of tax	—	—	—	169	—	—	169
Vesting of restricted stock units	106,202	1	(1)	—	—	—	—
Write-off of notes receivable from stockholders	—	—	—	—	21	—	21
Net loss	—	—	—	—	—	(124,507)	(124,507)
Balance at December 31, 2018	74,381,303	$ 744	$ 292,508	$ (269)	$ —	$ (336,083)	$ (43,100)

See accompanying notes to Consolidated Financial Statements.

INSYS THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2018	2017 (As Revised)	2016
Cash flows from operating activities:			
Net income (loss)	$ (124,507)	$ (226,835)	$ 7,590
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Inventory obsolescence reserve	3,095	6,186	7,397
Depreciation and amortization	7,579	7,337	6,249
Stock-based compensation	12,016	16,015	21,589
Deferred income tax benefit	—	23,243	(5,636)
Loss on disposal of assets	440	—	—
Impairment on property and equipment	1,487	—	—
Excess tax deficiency on stock options and awards	—	—	1,729
Write-off of notes receivable and other assets due from stockholders	26	—	—
Amortization of investment discount	26	1,125	2,029
Changes in operating assets and liabilities:			
Accounts receivable, net	8,903	(859)	26,618
Inventories	2,260	2,251	7,647
Prepaid expenses and other current and noncurrent assets	9,464	(14,518)	(1,721)
Accounts payable, accrued expenses and other current and noncurrent liabilities	15,802	(118)	(12,409)
Accrued sales allowances	(8,448)	(12,665)	(6,078)
Deferred revenue	—	1,109	—
Accrued litigation award and settlements	15,868	137,067	3,900
Net cash provided by (used in) operating activities	(55,989)	(60,662)	58,904
Cash flows from investing activities:			
Purchase of investments	(61,726)	(132,068)	(115,375)
Proceeds from sales of investments	16,747	32,471	7,948
Proceeds from maturities of investments	104,472	98,448	96,009
Purchases of property and equipment	(6,095)	(16,661)	(10,614)
Net cash provided by (used in) investing activities	53,398	(17,810)	(22,032)
Cash flows from financing activities:			
Proceeds from issuance of common stock	1,048	1,326	2,280
Excess tax deficiency on stock options and awards	—	—	(1,729)
Shares withheld for future payment of employees' withholding tax liability	—	(42)	—
Proceeds from exercise of stock options	1,096	4,545	3,803
Repurchase of common stock	—	—	(16,099)
Net cash provided by (used in) financing activities	2,144	5,829	(11,745)
Change in cash and cash equivalents	(447)	(72,643)	25,127
Cash and cash equivalents, beginning of period	31,999	104,642	79,515
Cash and cash equivalents, end of period	$ 31,552	$ 31,999	$ 104,642
Supplemental cash flow disclosures:			
Cash paid (refunded) for income taxes, net	$ (13,392)	$ 2,110	$ 10,742
Non-cash capital expenditures	$ 323	$ 2,678	$ 425

See accompanying notes to Consolidated Financial Statements.

INSYS THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

Insys Therapeutics, Inc., which was incorporated in Delaware in June 1990, and our subsidiaries (collectively, "we," "us," and "our") maintain headquarters in Chandler, Arizona.

We are a specialty pharmaceutical company that develops and commercializes innovative drugs and novel drug delivery systems of therapeutic molecules that improve patients' quality of life. We have two commercially marketed products: SUBSYS®, a proprietary sublingual fentanyl spray for BTCP in opioid-tolerant adult patients; and SYNDROS®, a proprietary, orally administered liquid formulation of dronabinol for the treatment of CINV and anorexia associated with weight loss in patients with AIDS.

Going Concern Uncertainty Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 205-40, Presentation of Financial Statements - Going Concern (ASC 205-40), requires management to assess the Company's ability to continue as a going concern for one year after the date the financial statements are issued. Under ASC 205-40, management has the responsibility to evaluate whether conditions and/or events raise substantial doubt about the Company's ability to meet future financial obligations as they become due within one year after the date that the financial statements are issued. As required by this standard, management's evaluation shall initially not take into consideration the potential mitigating effects of management's plans that have not been fully implemented as of the date the financial statements are issued.

As of December 31, 2018, the Company had an accumulated deficit of $336.1 million, negative cash flows from operating activities for the year ended December 31, 2018, and significant ongoing legal expenses.

While we have no outstanding debt and $104.1 million in cash and cash equivalents and investments as of December 31, 2018, the Company expects its negative cash flows from operating activities to continue and thus have determined that the Company's losses and negative cash flows from operations and uncertainty in generating sufficient cash to meet our legal obligations and settlements and sustain our operations raise substantial doubt about the Company's ability to continue as a going concern within one year of the issuance date of these Consolidated Financial Statements. As our research and development activities mature and develop over the next several years, the Company will likely require substantial funds to continue such activities, depending upon events that are difficult to predict at this time. In addition, as the Company continues to contend with existing litigation (and resolve such proceedings as appropriate) and to fund other legal expenses related to our former employees, we will require additional funding. In this regard, management's plans, in order to meet any additional operating cash flow requirements, include the pursuit of strategic alternatives related to our opioid-related assets, sale or licensing of assets, as well as financing activities such as public offerings and private placements of our common stock, preferred stock offerings, and issuances of debt and convertible debt instruments.

There are no assurances that such additional funding will be obtained and that the Company will succeed in its future operations. If the Company cannot successfully raise additional capital and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected. The Company has engaged Lazard Freres & Co. LLC to advise the Company on capital planning and the evaluation of strategic alternatives.

2. Significant Accounting Policies

Revision of Previously Issued Financial Statements for Correction of Immaterial Errors

During the three months ended September 30, 2018, we identified an error related to the accounting for uncertain income tax positions in the interim and annual financial statements for the year ended December 31, 2017. We determined that we had incorrectly applied the accounting guidance when implementing ASU No. 2016-09, "Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting" on January 1, 2017 by inadvertently omitting the impact on the unrecognized tax benefit ("UTB") reserves for state

taxes. In addition, we identified errors in the calculation of weighted average shares outstanding for the years ended December 31, 2017 and 2016. The error in the calculation of weighted average shares outstanding impacted net loss per share for the year ended December 31, 2017; there was no impact on net income per share for the year ended December 31, 201 6. We assessed the materiality of these errors on our prior annual financial statements, assessing materiality both quantitatively and qualitatively, in accordance with the SEC's Staff Accounting Bulletin ("SAB") No. 99 and SAB No. 108 and concluded that the errors were not material to our audited financial statements for the year ended December 31, 2017. However, to correctly present uncertain income tax position liabilities, income tax expense (benefit), and net loss per share in the appropriate periods, management revised its previously issued financial statements for the year ended December 31, 2017. Certain amounts in prior periods as previously reported have been reclassified to conform to the current period presentation.

The following tables summarize the impact and financial statement line items impacted by the revision adjustments as of and for the year ended December 31, 2017 (in thousands, except share and per share data):

	As of December 31, 2017		
	As previously reported	Adjustments	As Revised
Consolidated Balance Sheet:			
Uncertain income tax positions	$ 8,619	$ (2,927)	$ 5,692
Total liabilities	215,798	(2,927)	212,871
Accumulated deficit	(215,351)	2,927	(212,424)
Total stockholders' equity	63,282	2,927	66,209

	Year Ended December 31, 2017		
	As previously reported	Adjustments	As Revised
Consolidated Statement of Operations and Comprehensive Income (Loss):			
Income tax expense	$ 10,820	$ (1,180)	$ 9,640
Net loss	(228,015)	1,180	(226,835)
Total comprehensive loss	(228,151)	1,180	(226,971)
Net loss per common share:			
Basic	$ (3.16)	$ 0.04	$ (3.12)
Diluted	$ (3.16)	$ 0.04	$ (3.12)
Weighted average common shares outstanding			
Basic	72,259,063	377,717	72,636,780
Diluted	72,259,063	377,717	72,636,780

	Year Ended December 31, 2017			
	As previously reported	Adjustments	Reclassifications	As Revised
Consolidated Statement of Cash Flows:				
Net loss	$ (228,015)	$ 1,180	$ —	$ (226,835)
Change in operating assets and liabilities:				
Accounts payable, accrued expenses and other current and noncurrent liabilities	(11,603)	(1,180)	12,665	(118)
Accrued sales allowances	—	—	(12,665)	(12,665)

	Year Ended December 31, 2017		
	As previously reported	Adjustments	As Revised
Consolidated Statement of Stockholders' Equity:			
Impact of adoption of ASU 2016-09	$ —	$ 1,747	$ 1,747
Net loss	(228,015)	1,180	(226,835)
Accumulated deficit	(215,351)	2,927	(212,424)
Total stockholders' equity	63,282	2,927	66,209

The following tables summarize the impact and financial statement line items impacted by the revision adjustments as of and for the year ended December 31, 2016:

	Year Ended December 31, 2016		
	As previously reported	Adjustments	As Revised
Consolidated Statement of Operations and Comprehensive Income (Loss):			
Weighted average common shares outstanding			
Basic	71,618,793	21,063	71,639,856
Diluted	74,145,918	21,063	74,166,981

Principles of Consolidation

The Consolidated Financial Statements include the accounts of Insys Therapeutics, Inc. and its wholly-owned subsidiaries. All significant intercompany balances and transactions have been eliminated in the accompanying Consolidated Financial Statements.

Reclassification

Certain amounts in prior periods have been reclassified to conform to the current period presentation.

Fair Value of Financial Instruments

The carrying values of certain of our financial instruments, including cash and cash equivalents, accounts receivable, accounts payable, and accrued expenses approximate their fair value due to the short-term nature of these financial instruments.

FASB ASC No. 820, “Fair Value Measurement,” defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. It also establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets;

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

Revenue Recognition for 2018

SUBSYS® was commercially launched in March 2012 and is monitored by an FDA-mandated REMS program known as the TIRF REMS. SYNDROS® was commercially launched in July 2017. We sell all of our products to customers in the United States. See Note 12, Product Lines, Concentration of Credit Risk and Significant Customers, for information on revenues disaggregated by product line and route to market.

To determine revenue recognition for contractual arrangements that we identify are within the scope of ASC Topic 606, we perform the following five steps: (i) identify each contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to our performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the relevant performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods we transfer to the customer. We recognize revenue from the sale of our commercially approved products, SUBSYS® and SYNDROS®, when we transfer control of our products to our customers, as our contracts have a single performance obligation (delivery of our product to their preferred location). Revenue is measured as the amount of consideration we expect to receive in exchange for transferring goods. Any shipping and handling activities that we perform, whether before or after a customer has obtained control of the products, are considered activities to fulfill our obligation to transfer the products, and are recorded as incurred within sales and marketing expenses. We offer the following discounts to our customers:

Wholesaler and Retailer Discounts. We offer discounts to certain wholesale distributors and specialty retailers based on contractually determined rates. We record receivables due from the wholesalers and retailers net of these discounts upon transfer of control to the respective wholesale distributors and retail pharmacies.

Prompt Pay Discounts. We offer cash discounts to our customers, generally 2% of the sales price, as an incentive for prompt payment. We record receivables net of these cash discounts.

Stocking Allowances. We may offer discounts and extended payment terms, generally in the month of the initial commercial launch of a new product and on the first order made by certain wholesale distributors and retail pharmacies based on contractually determined rates. We record receivables due from the wholesalers and retailers net of these discounts upon transfer of control to the respective wholesale distributors and retail pharmacies. The extended payment terms are not greater than 12 months, and therefore do not include a financing component.

As is customary in the pharmaceutical industry, it is common for our contracts to include product sales allowances that can decrease the transaction price and are, therefore, considered to be variable consideration. Product sales allowances, which include product returns, patient discount programs, rebates and chargebacks, are variable consideration and are based on amounts owed or to be claimed on the related sales. We estimate variable consideration when determining the transaction price using the expected value (probability weighted estimate) method. We assess whether variable consideration is constrained and only include estimated amounts in the transaction price to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Our estimates of variable consideration and determination of whether to include estimated amounts in the transaction price are based largely on historical data, and take into consideration the terms of our agreements with customers and third-party payers and the levels of inventory within the distribution channels that may result in future discounts taken. In certain cases, such as patient assistance programs, our estimates are based on estimated utilization. If actual future results vary, we may need to adjust these estimates, which could have an effect on revenue in the period of adjustment. During the year ended December 31, 2018, we recognized revenue of $8.5 million related to changes in the estimated transaction price allocated to performance obligations satisfied in prior periods. Our product sales allowances include:

Product Returns. We allow customers to return product for credit beginning six months prior to, and ending 12 months following, the product expiration date. SUBSYS® currently has a shelf life of 36 or 48 months from the date of manufacture, depending on the manufacture date, and SYNDROS® currently has a shelf life of 24 or 36 months from the date of manufacture, depending on the manufacture date. We have monitored actual return history since product launch, which provides us with a basis to reasonably estimate future product returns, taking into consideration the shelf life of product at the time of shipment, shipment and prescription trends, estimated distribution channel inventory levels and consideration of the introduction of competitive products.

Because of the shelf life of our products and our return policy of issuing credits on returned product that is within six months before, and up to 12 months following, the product expiration date, there may be a significant period of time between when the product is shipped and when we issue credits on returned products. Accordingly, we may have to adjust these estimates, which could have a material effect on net revenue and earnings in the period of adjustment. The allowance for product returns is included in accrued sales allowances.

Patient Discount Programs. We offer discount card programs to patients, in which patients receive discounts on their prescriptions that are reimbursed by us to the retailer. We estimate the total amount that will be redeemed based on a percentage of actual redemptions applied to inventory in the distribution and retail channels. The allowance for patient discount programs is included in accrued sales allowances.

Rebates. We participate in certain rebate programs, which provide discounted prescriptions to qualified insured patients. Under these rebate programs, we pay a rebate to the third-party administrator of the program, generally two to three months after the quarter in which prescriptions subject to the rebate are filled. We estimate and accrue these rebates based on current and estimated future contract prices, historical and estimated future percentages of products prescribed to qualified patients and estimated levels of inventory in the distribution channel. The allowance for rebates is included in accrued sales allowances.

Chargebacks. We provide discounts primarily to authorized users of the FSS of the General Services Administration under an FSS contract negotiated by the Department of Veterans Affairs and various organizations under Medicaid contracts and regulations. These organizations purchase products from the wholesale distributors at a discounted price, and the wholesale distributors then charge back to us the difference between the current retail price and the price the organization paid for the product. We estimate chargebacks based on estimated wholesaler inventory levels, current contract and estimated future prices and historical chargeback activity.

We do not have any significant extended payment terms as payment is received shortly after the point of sale. As of December 31, 2018, the majority of our accounts receivables were related to product sales. For the year ended December 31, 2018, the Company had no material bad-debt write-offs in the Consolidated Statement of Operations and Comprehensive Income (Loss) and there were no contract assets, contract liabilities or deferred contract costs recorded on the Consolidated Balance Sheets as of December 31, 2018.

Revenue Recognition for 2017 and 2016

Prior to January 1, 2018 we recognized revenue under ASC Topic 605. Revenue is recognized when (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred and title has passed, (iii) the price is fixed or determinable and (iv) collectability is reasonably assured. We record revenue for SUBSYS® at the time the customer receives the shipment. Given the limited sales history of SYNDROS®, the Company currently cannot reliably estimate expected returns of the product at the time of shipment. Accordingly, the Company defers recognition of revenue on product shipments of SYNDROS® until the right of return no longer exists, which occurs at the earlier of the time SYNDROS® units are sold to health care facilities or dispensed through patient prescriptions, or expiration of the right of return. Units dispensed are generally not subject to return, except in the rare cases where the product malfunctions or the product is damaged in transit. The Company estimates patient prescriptions dispensed using an analysis of third-party market research data. If this third-party data underestimates or overestimates actual patient prescriptions dispensed for a given period, adjustments to revenue may be necessary in future periods. To date, such adjustments have not been material.

We recognize estimated product sales allowances as a reduction of product sales in the same period the related revenue is recognized. Product sales allowances are based on amounts owed or to be claimed on the related sales. These estimates take into consideration the terms of our agreements with customers and third-party payers and the levels of inventory within the distribution channels that may result in future discounts taken. In certain cases, such as patient assistance programs, we recognize the cost of patient discounts as a reduction of revenue based on estimated utilization. If actual future results vary, we may need to adjust these estimates, which could have an effect on product revenue in the period of adjustment.

Restricted Cash

At times, we may have cash that serves as collateral for corporate credit cards to provide financial assurance that the Company will fulfill its obligations. The cash may be held in custody by the issuing bank and restricted as to withdrawal or use. As of December 31, 2018, the Company had no restricted cash.

Cash and Cash Equivalents

We consider all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. The carrying value of those investments approximates their fair market value due to their short maturity and liquidity. Cash and cash equivalents include cash on hand and amounts on deposit with financial institutions, which at times may exceed current FDIC coverage limits of $250,000.

Short-Term and Long-Term Investments

Our policy for short-term and long-term investments is to establish a high-quality portfolio that preserves principal, meets liquidity needs, avoids inappropriate concentrations and delivers an appropriate yield in relationship to our investment guidelines and market conditions. Short-term and long-term investments consist of corporate, various government agency and municipal debt securities, as well as certificates of deposit that have maturity dates that are greater than 90 days. Certificates of deposit and commercial paper are carried at cost which approximates fair value. We classify our marketable debt securities as available-for-sale in accordance with FASB ASC Topic 320, “Investments — Debt and Equity Securities”. Available-for-sale debt securities are carried at fair value with unrealized gains and losses reported in stockholders’ equity (deficit), net of related tax effects. There were no reclassifications on available-for-sale debt securities during the years ended December 31, 2018 and 2017. A decline in the market value of any available-for-sale debt security below cost that is deemed to be other than temporary results in impairment of the fair value of the investment. We did not have any unrealized gains or losses or decline in values judged to be other than temporary during the years ended December 31, 2018, 2017 and 2016. If we had unrealized gains and losses and declines in value judged to be other than temporary, we would have been required to include those changes in other expense in the Consolidated Statements of Comprehensive Income (Loss). Premiums and discounts are amortized or accreted over the life of the related available-for-sale debt security. The cost of securities sold is calculated using the specific identification method. At December 31, 2018, our certificates of deposit and commercial paper as well as our marketable securities have been recorded at an estimated fair value

of $6,390,000, $64,126,000 and $8,446,000 in cash and cash equivalents, short-term investments and long-term investments, respectively.

Accounts Receivable, Net

Trade accounts receivable are recorded at the transaction price, net of wholesaler and retailer discounts, prompt pay discounts, and stocking allowances. See “Revenue Recognition” above for a description of our wholesaler discounts, prompt pay discounts, and stocking allowances. We evaluate the collectability of our accounts receivable based on a variety of factors including the length of time the receivables are past due, the financial health of the customer and historical experience. We write off accounts receivable against the allowance when a balance is determined to be uncollectable.

Inventories, Net

Inventories consist of raw materials, work-in-process and finished product and are stated at the lower of cost or NRV. Cost, which includes amounts related to materials and costs incurred by our contract manufacturers, is determined on a first-in, first-out basis. Non-current inventories are those that are not expected to be consumed or sold within 12 months of the balance sheet date and are included in other assets in our Consolidated Balance Sheets. In evaluating whether inventory should be classified as current or noncurrent, management considers factors such as historical and anticipated future sales compared to quantities on hand and the remaining shelf life of products on hand. Inventory costs are capitalized prior to regulatory approval and product launch based on management’s judgment of probable future commercial use and NRV of the inventory. Such judgment incorporates our knowledge and best estimate of where the relevant product is in the regulatory process, our required investment in the product, market conditions, competing products and our economic expectations for the product post-approval relative to the risk of manufacturing the product prior to approval. In evaluating the recoverability of inventories produced in preparation for product launches, we consider the probability that revenue will be obtained from the future sale of the related inventory together with the status of the product within the regulatory approval process, as well as the market for the product in its current state. We could be required to permanently write down previously capitalized costs related to pre-approval or pre-launch inventory upon a change in such judgment due to a denial or delay of approval by regulatory bodies, a delay in commercialization, or other potential factors including product expiration. Inventories are reviewed periodically for potential excess, dated or obsolete status. Management evaluates the carrying value of inventories on a regular basis, taking into account such factors as historical and anticipated future sales compared to quantities on hand, the price we expect to obtain for products in their respective markets compared with historical cost and the remaining shelf life of goods on hand.

Property and Equipment, Net

Property and equipment are recorded at cost and depreciated using the straight-line method over their estimated useful lives. Maintenance and repairs that do not extend the life of assets are charged to expense when incurred. When property and equipment is disposed of, the related costs and accumulated depreciation are removed from the accounts and any gain or loss is reported in other income (expense) in the period the transaction takes place. During the year ended December 31, 2018, we recorded losses on the disposal of property and equipment of $440,000. There were no such charges during the year ended December 31, 2017.

Property and equipment are reviewed for impairment whenever events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted cash flows expected to be generated by the asset. If the carrying amount exceeds its estimated future undiscounted cash flows, an impairment charge is recognized by the amount by which the carrying amount exceeds the fair value of the asset. The fair value is measured on a nonrecurring basis using unobservable (Level 3) inputs. Impairment charges are reported in the period the impairment is identified. During the year ended December 31, 2018, we recorded impairment charges in research and development of $1,487,000 as the result of a decision to abandon a partially constructed device manufacturing machine with a cost of $1,487,000 and no associated depreciation, which was written down to its fair value of $0. There were no such charges during the year ended December 31, 2017.

Income Taxes

We account for our deferred income tax assets and liabilities based on differences between the financial reporting and tax bases of assets and liabilities, and NOLs and other tax credit carry forwards. These items are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in the period that includes the enactment date.

We record a valuation allowance to reduce the deferred income tax assets to the amount that is more likely than not to be realized. In making such determinations, management considers all available positive and negative evidence, including scheduled reversals of deferred tax liabilities, projected future taxable income, tax planning strategies and recent financial operating results.

We recognize a tax benefit from uncertain tax positions when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits of the position.

Our policy is to classify interest and penalties associated with income tax liabilities as income tax expense (benefit) in the Consolidated Statements of Comprehensive Income (Loss).

Research and Development Expenses

Research and development ("R&D") costs are expensed when incurred. Research and development expenses consist of costs associated with our preclinical studies and clinical trials, and other expenses related to our drug development efforts. Our research and development expenses consist primarily of:

- external research and development expenses incurred under agreements with third-party CROs and investigative sites, third-party manufacturers and consultants;
- employee-related expenses, which include salaries, benefits and stock-based compensation for the personnel involved in our drug development activities; and
- materials, facilities, equipment and laboratory supplies, depreciation, impairment and other allocated expenses.

Advertising and Marketing

Advertising and marketing costs are expensed as incurred. Advertising expense totaled $800,000, $993,000 and $1,572,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

Legal Expenses

Legal costs are expensed as incurred. Our legal expenses consist primarily of salaries and related costs for legal personnel and professional fees for legal services.

Stock-Based Compensation Expenses

Stock-based compensation cost is estimated at the grant date based on the fair value of the award, and the cost is recognized as expense ratably over the service or vesting period, which is generally three to four years, on a straight-line basis. We account for forfeitures when they occur. We use the Black-Scholes option pricing model for estimating the grant date fair value of stock options using the following assumptions:

- Volatility - Prior to our IPO, we did not have a reliable history of market prices for our common stock. Following our IPO, while we have an active trading market, we do not have sufficient historical data to accurately estimate volatility for the period equivalent to the expected term of the stock option grants. Accordingly, we estimate the expected stock price volatility for our common stock by taking the median historical stock price volatility for industry peers based on daily price observations over a period equivalent to the expected term of the stock option grants. We intend to incorporate the volatility of our own common stock share price in future periods as we begin to have sufficient historical data available.

- Expected term - The expected term is based on a simplified method allowed by the SEC due to insufficient historical data, and defines the term as the average of the contractual term of the options and the weighted-average vesting period for all open employee awards.
- Risk-free rate - The risk-free interest rate for the expected term of the option is based on the average market rate on U.S. treasury securities in effect during the quarter in which the options were granted.
- Dividends - The dividend yield assumption is based on our history and expectation of paying no dividends.

Foreign currency transactions

Some of our vendors are located outside of the United States, and at times we enter into transactions that are denominated in a foreign currency. The foreign currency transaction gains and losses on these transactions are reported in other income (expense), net. Foreign currency gains (losses) totaled $(198,000) and $(89,000) for the years ended December 31, 2018 and 2017, respectively. There were no material foreign currency gains (losses) during the year ended December 31, 2016.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") requires management to 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 amounts of revenue and expense during the reporting period. On an on-going basis, we evaluate our estimates, including those related to revenue recognition (which is affected by prescriptions dispensed, wholesaler discounts, patient discount programs, rebates, and chargebacks), inventories, legal liabilities and settlements, stock-based compensation expense, income taxes, and deferred tax valuation allowances. We base our estimates on historical experience and on various other assumptions that are believed by management to be reasonable under the circumstances. Actual results could materially differ from those estimates.

Segment Information

FASB ASC No. 280, "Segment Reporting" establishes standards for reporting information about reportable segments. Operating segments are defined as components of an enterprise about which separate financial information is available that is evaluated regularly by the chief operating decision maker, or decision-making group ("CODM"), in deciding how to allocate resources and in assessing performance. The CODM evaluates revenues and gross profits based on product lines and routes to market. Based on our integration and management strategies, we operate in a single reportable segment.

Recently Adopted Accounting Pronouncements

Effective January 1, 2018, we adopted the requirements of ASU No. 2014-09, "Revenue from Contracts with Customers (ASC Topic 606)," and all the related amendments ("new revenue standard"). The new revenue standard aims to achieve a consistent application of revenue recognition within the United States, resulting in a single revenue model to be applied by reporting companies under U.S. GAAP. Under the new model, recognition of revenue occurs when a customer obtains control of promised goods or services in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In addition, the new revenue standard requires that reporting companies disclose the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. We used the modified retrospective transition method for all contracts that were not completed as of the adoption date. In addition, we have applied the practical expedient to contract modifications, as allowed by the SEC, but did not have any material contract modifications to be included in the initial adoption of ASC Topic 606. The comparative information for 2017 presented below has not been restated and continues to be reported under ASC Topic 605, "Revenue Recognition." Our sales revenue from SUBSYS® continues to be recognized when product is delivered to wholesale pharmaceutical distributors and specialty retail pharmacies (collectively, our customers). In accordance with the new revenue standard, our sales revenue from SYNDROS® is now recognized when product is delivered to our customers, where revenue was previously deferred until the right of return no longer existed, which occurred at the earlier of the time SYNDROS®

units were sold to healthcare facilities or dispensed through patient prescriptions, or the expiration of the right of return. See Note 1, *Significant Accounting Policies - Revenue Recognition*, for additional discussion of our revenue recognition policy and variable consideration estimates. The impact of adopting the new revenue standard on our Consolidated Financial Statements is shown in the tables below.

The cumulative effect of the changes made to our January 1, 2018 Consolidated Balance Sheet for the adoption of the new revenue standard was as follows (in thousands):

	Balance at December 31, 2017 (As Revised)	Adjustments due to adoption of ASC Topic 606	Balance at January 1, 2018
Condensed Consolidated Balance Sheet:			
Inventories, net	$ 17,408	$ (59)	$ 17,349
Accrued sales allowances	16,290	320	16,610
Deferred revenue	1,109	(1,109)	—
Accumulated deficit	(212,424)	848	(211,576)

The impact of adopting the new revenue standard on our Consolidated Statements of Operations and Comprehensive Income (Loss) was as follows (in thousands):

	Year Ended December 31, 2018		
	Balances without Adopting ASC Topic 606	Impact of Adopting ASC Topic 606	As Reported
Consolidated Statements of Operations and Comprehensive Loss:			
Net revenue	$ 81,599	$ 481	$ 82,080
Cost of revenue	10,744	59	10,803
Gross profit	70,855	422	71,277
Operating loss	(128,145)	422	(127,723)
Loss before income taxes	(126,829)	422	(126,407)
Net loss	(124,929)	422	(124,507)

The impact of adopting the new revenue standard on our Consolidated Balance Sheet, excluding the cumulative effect of adoption on January 1, 2018 disclosed previously, was as follows (in thousands):

	As of December 31, 2018		
	Balances without Adopting ASC Topic 606	Impact of Adopting ASC Topic 606	As Reported
Consolidated Balance Sheet:			
Inventories, net	$ 8,490	118	$ 8,608
Total current assets	126,174	118	126,292
Total assets	192,409	118	192,527
Accrued sales allowances	7,897	265	8,162
Deferred revenue	1,856	(1,856)	—
Total liabilities	237,218	(1,591)	235,627
Accumulated deficit	(336,505)	422	(336,083)
Total liabilities and stockholders' (deficit) equity	192,409	118	192,527

Effective January 1, 2018, we adopted ASU No. 2016-01, “Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities,” and ASU No. 2018-03, “Technical Corrections and Improvements to Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities.” These standards amended the Financial Instruments topic of the ASC to address certain aspects of recognition, measurement, presentation, and disclosure of financial instruments. The standard requires that unrealized gains and losses on investments in equity securities to be recognized in net income (loss). In addition, the Company has elected to measure equity investments that do not have readily determinable fair values at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. The adoption of this guidance did not have a material impact on our Consolidated Financial Statements.

Effective January 1, 2018, we adopted ASU No. 2016-15, “Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments.” The guidance clarifies how certain cash flow transactions are classified in the statement of cash flows. The adoption of this guidance did not have a material impact on our Consolidated Financial Statements.

Effective January 1, 2018, we adopted ASU No. 2016-16, “Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory.” Prior to January 1, 2018, U.S. GAAP prohibited the recognition of current and deferred income taxes for an intra-entity asset transfer until the asset was sold to an outside party, which was an exception to the principle of comprehensive recognition of current and deferred income taxes in U.S. GAAP. This guidance eliminates the exception for an intra-entity transfer of an asset other than inventory. The adoption of this guidance did not have a material impact on our Consolidated Financial Statements.

Effective January 1, 2018, we adopted ASU No. 2017-09, “Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting.” The ASU requires modification accounting to a share-based payment award unless all of the following are the same immediately before and after the change: the award’s fair value; the award’s vesting conditions; and the award’s classification as an equity instrument or a liability instrument. The adoption of this guidance did not have a material impact on our Consolidated Financial Statements.

Effective January 1, 2018, we adopted ASU No. 2018-05, “Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118 (SEC Update).” The standard addresses any uncertainty or diversity of views in practice regarding the application of ASC Topic 740 in situations where a registrant did not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting under ASC Topic 740 for certain income tax effects of the 2017 Tax Cuts and Jobs Act (the “Act”) for the reporting period in which the Act was enacted. The Company recognized the provisional tax impacts of the Act in the fourth quarter of 2017. The Company completed its analysis of the Act in conjunction with the completion of its tax returns for 2017 and recorded a $1.0 million reduction of tax expense.

In June 2018, the FASB issued ASU No. 2018-07, “Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting.” The standard expands the scope of ASC Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees, and supersedes ASC Topic 505-50, “Equity – Equity Based Payments to Non-Employees.” Previously, the fair value of share-based payment awards to nonemployees was determined by the measurement date, which was the earlier of the date at which a commitment for performance by the counterparty is reached or the date at which the counterparty’s performance is complete. This concept caused significant differences in the accounting for share-based payment to nonemployees as compared to share-based payments to employees. Furthermore, the previous guidance required employers to revalue share-based payments to nonemployees at each reporting period if a measurement date could not be established, causing fluctuations in the resulting expense from period to period. The new standard eliminates the measurement date concept and requires the fair value of share-based payments to nonemployees to be measured on the grant date, consistent with share-based payments to employees. We early adopted the standard during the three months ended June 30, 2018. We remeasured the fair value of our equity-classified share-based payments to nonemployees for which a measurement date had not been established as of the adoption date of January 1, 2018. Because we had previously remeasured our share-based payments to nonemployees at each reporting period, the adoption did not result in a cumulative effect adjustment to opening retained earnings.

Recent Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, "Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement," to improve the effectiveness of disclosures. The amendments remove, modify, and add certain disclosure requirements in Topic 820, "Fair Value Measurement." The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. The amendments are effective for fiscal years beginning after December 15, 2019. Early adoption is permitted, including adoption in an interim period. Furthermore, an entity is permitted to early adopt any removed or modified disclosures upon issuance of the update and delay adoption of the additional disclosures until their effective date. We do not expect this amendment to have a material impact on our Consolidated Financial Statements.

In March 2017, the FASB issued ASU No. 2017-08, "Receivables—Nonrefundable Fees and Other Costs (Subtopic 310-20): Premium Amortization on Purchased Callable Debt Securities," to amend the amortization period for certain purchased callable debt securities held at a premium. The ASU shortens the amortization period for the premium to the earliest call date. Under current U.S. GAAP, entities generally amortize the premium as an adjustment of yield over the contractual life of the instrument. The amendments should be applied on a modified retrospective basis and are effective for fiscal years beginning after December 15, 2018. Early adoption is permitted, including adoption in an interim period. We do not expect this amendment to have a material impact on our Consolidated Financial Statements.

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments." The amendments effected by this ASU affect entities holding financial assets and net investment in leases that are not accounted for at fair value through net income and are effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years, and early adoption is permitted. ASU 2016-13 amends the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology, which will result in the timelier recognition of losses. We do not expect this amendment to have a material impact on our Consolidated Financial Statements.

In February 2016, the FASB issued ASU No. 2016-02, "Leases: (Topic 842)," to provide guidance on recognizing lease assets and lease liabilities on the balance sheet and disclosing key information about leasing arrangements, specifically differentiating between different types of leases. The core principle of Topic 842 is that a lessee should recognize the assets and liabilities that arise from all leases. The recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee have not significantly changed from previous U.S. GAAP guidance. There continues to be a differentiation between finance leases and operating leases. However, the principal difference from previous guidance is that the lease assets and lease liabilities arising from operating leases should be recognized in the balance sheet. The accounting applied by a lessor is largely unchanged from that applied under previous U.S. GAAP guidance. In July 2018, the FASB issued ASU No. 2018-11 "Leases: (Topic 842): Targeted Improvements," which provides entities with an additional optional transition method of recognizing the cumulative effect of applying the new standard as an adjustment to beginning retained earnings in the year of adoption while continuing to present all prior periods under previous lease accounting guidance. In July 2018, the FASB also issued ASU No. 2018-10, "Codification Improvements to Topic 842, Leases," which clarifies how to apply certain aspects of ASU 2016-02. We will adopt Topic 842 and related amendments on January 1, 2019. We currently expect that most of our operating lease commitments will be subject to the update and will be recognized as right-of-use assets and operating lease liabilities upon adoption. We estimate that the adoption of Topic 842 will result in the recognition of right-of-use assets and lease liabilities for operating leases of approximately $14.5 million on our Consolidated Balance Sheet, with no material impact to our Consolidated Statement of Comprehensive Income (Loss). The actual impact is subject to change prior to the filing of our 2019 first quarter results. Additional quantitative and qualitative presentations and disclosures will be required in accordance with the new standard. We have identified changes to our business processes and internal controls relating to review of leases, contracts and disclosures, that are needed upon the adoption of the new guidance.

3. Short-Term and Long-Term Investments

Cash, cash equivalents, and investments consisted of the following at December 31, 2018 (in thousands):

	December 31, 2018							
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Other-Than-Temporary Impairment Losses	Fair Value	Cash and Cash Equivalents	Short-term Investments	Long-term Investments
Cash and cash equivalents	$ 18,773	$ —	$ —	$ —	$ 18,773	$ 18,773	$ —	$ —
Money market securities	6,389	—	—	—	6,389	6,389	—	—
Marketable securities:								
Certificates of deposit	10,967	—	—	—	10,967	—	8,437	2,530
Commercial paper	11,468	—	—	—	11,468	5,890	5,578	—
Corporate securities	35,393	—	(89)	—	35,304	500	33,356	1,448
Federal agency securities	19,470	—	(124)	—	19,346	—	15,396	3,950
Municipal securities	1,365	—	(6)	—	1,359	—	1,359	—
Total marketable securities	78,663	—	(219)	—	78,444	6,390	64,126	7,928
Preferred stock	518	—	—	—	518	—	—	518
	$ 104,343	$ —	$ (219)	$ —	$ 104,124	$ 31,552	$ 64,126	$ 8,446

Cash, cash equivalents, and investments consisted of the following at December 31, 2017 (in thousands):

	December 31, 2017							
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Other-Than-Temporary Impairment Losses	Fair Value	Cash and Cash Equivalents	Short-term Investments	Long-term Investments
Cash and cash equivalents	$ 12,183	$ —	$ —	$ —	$ 12,183	$ 12,183	$ —	$ —
Money market securities	15,317	—	—	—	15,317	15,317	—	—
Marketable securities:								
Certificates of deposit	18,447	—	—	—	18,447	—	7,474	10,973
Commercial paper	10,560	—	—	—	10,560	1,499	9,061	—
Corporate securities	59,095	—	(206)	—	58,889	1,500	39,622	17,767
Federal agency securities	37,793	—	(203)	—	37,590	1,500	20,015	16,075
Municipal securities	10,446	—	(29)	—	10,417	—	9,017	1,400
Total marketable securities	136,341	—	(438)	—	135,903	4,499	85,189	46,215
Preferred stock	518	—	—	—	518	—	—	518
	$ 164,359	$ —	$ (438)	$ —	$ 163,921	$ 31,999	$ 85,189	$ 46,733

The amortized cost and estimated fair value of the marketable securities, by maturity, are shown below (in thousands):

	December 31, 2018		December 31, 2017	
	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Marketable securities:				
Due in one year or less	$ 70,667	$ 70,517	$ 90,071	$ 89,937
Due after one year through 5 years	7,996	7,927	46,270	45,966
Due after 5 years through 10 years	—	—	—	—
Due after 10 years	—	—	—	—
	$ 78,663	$ 78,444	$ 136,341	$ 135,903

The following table shows the gross unrealized losses and the fair value of our investments, with unrealized losses that are not deemed to be other-than-temporarily impaired aggregated by investment category and length of time that individual securities have been in a continuous unrealized loss position (in thousands):

	December 31, 2018				December 31, 2017			
	Less Than 12 Months		Greater Than 12 Months		Less Than 12 Months		Greater Than 12 Months	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Marketable securities:								
Corporate securities	$ 16,075	$ (16)	$ 17,985	$ (73)	$ 245	$ (153)	$ 7,839	$ (52)
Federal agency securities	3,727	(1)	14,625	(122)	26,244	(89)	11,346	(114)
Municipal securities	—	—	1,359	(7)	50,537	(18)	1,145	(12)
	$ 19,802	$ (17)	$ 33,969	$ (202)	$ 77,026	$ (260)	$ 20,330	$ (178)

As of December 31, 2018 and 2017, we have concluded that the unrealized losses on our marketable securities are temporary in nature. Marketable securities are reviewed quarterly for possible other-than-temporary impairment. This review includes an analysis of the facts and circumstances of each individual investment such as the severity of loss, the expectation for that security's performance and the creditworthiness of the issuer.

4. Fair Value Measurement

At December 31, 2018 and 2017, we held short-term and long-term investments, as described in Note 3, *Short-Term and Long-Term Investments,* that are required to be measured at fair value on a recurring basis. Except as discussed in Note 2, *Significant Accounting Policies - Property and Equipment, Net*, we had no assets or liabilities measured at fair value on a nonrecurring basis at December 31, 2018 and 2017. Substantially all available-for-sale investments held by us at December 31, 2018 and 2017, have been valued based on Level 2 inputs. Available-for-sale securities classified within Level 2 of the fair value hierarchy are valued utilizing reports from an independent third-party public quotation service based on closing prices on the last business day of the period presented. In addition, we use the public quotation service to perform price testing by comparing quoted prices listed in reports provided by the asset managers that hold our investments to quotes listed through the public quotation service. These asset managers utilize an independent pricing source to obtain quotes for most fixed income securities, and utilize internal procedures to validate the prices obtained.

Our assets and liabilities subject to the disclosure requirements of ASC 820 at December 31, 201 8 were as follows (in thousands):

	Fair Value Measurement at Reporting Date				
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total Gains (Losses)
Recurring fair value measurements					
Marketable securities:					
Certificates of deposit	$ 10,967	$ —	$ 10,967	$ —	$ —
Commercial paper	11,468	—	11,468	—	—
Corporate securities	35,304	—	35,304	—	—
Federal agency securities	19,346	—	19,346	—	—
Municipal securities	1,359	—	1,359	—	—
Total recurring fair value measurements	$ 78,444	$ —	$ 78,444	$ —	$ —
Nonrecurring fair value measurements					
Property and equipment (see Note 2)	$ —	$ —	$ —	$ —	$ (1,487)

Our assets and liabilities subject to the disclosure requirements of ASC 820 at December 31, 2017 were as follows (in thousands):

	Fair Value Measurement at Reporting Date			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Recurring fair value measurements				
Marketable securities:				
Certificates of deposit	$ 18,447	$ —	$ 18,447	$ —
Commercial paper	10,560	—	10,560	—
Corporate securities	58,889	—	58,889	—
Federal agency securities	37,590	—	37,590	—
Municipal securities	10,417	—	10,417	—
Total recurring fair value measurements	$ 135,903	$ —	$ 135,903	$ —

5. Inventories, Net

Inventories are stated at lower of cost or NRV. Cost, which includes amounts related to materials and costs incurred by our contract manufacturers, is determined on a first-in, first-out basis. Inventories are reviewed periodically for potential excess, dated or obsolete status. Management evaluates the carrying value of inventories on a regular basis, taking into account such factors as historical and anticipated future sales compared to quantities on hand, the price we expect to obtain for products in their respective markets compared with historical cost and the remaining shelf life of goods on hand.

The components of inventories, net of allowances, are as follows (in thousands):

	December 31, 2018	December 31, 2017
Finished goods	$ 2,489	$ 4,709
Work-in-process	3,542	5,752
Raw materials and supplies	2,577	6,947
Total inventories	8,608	17,408
Plus: non-current raw materials and finished goods	4,330	826
	$ 12,938	$ 18,234

As of December 31, 2018 and 2017, raw materials inventories consisted of raw materials used in the manufacture of the dronabinol API for SYNDROS® in our U.S.-based, state-of-the-art dronabinol manufacturing facility, the fentanyl API for SUBSYS®, and component parts and packaging materials used in the manufacture of both SUBSYS® and SYNDROS®. Work-in-process consists of actual production costs, including facility overhead and tooling costs of in-process dronabinol, SUBSYS® and SYNDROS® products. Finished goods inventories consisted of finished SUBSYS® and SYNDROS® products and deferred SYNDROS® cost of revenue of $0 and $59,000 as of December 31, 2018 and 2017, respectively. There was no deferred SYNDROS® cost of revenue as of December 31, 2018, due to the adoption of ASC Topic 606 on January 1, 2018. Non-current raw materials and finished goods represent those inventories not expected to be consumed or sold within 12 months of the balance sheet date and are included in other assets in our Consolidated Balance Sheets. As of December 31, 2018, all work-in-process inventory is expected to be used within 12 months of the balance sheet date and, therefore, is classified as current inventory. We maintain an allowance for excess and obsolete inventory, as well as inventory where its cost is in excess of its NRV. Inventories at December 31, 2018 and 2017 were reported net of these reserves of $2,938,000 and $13,664,000, respectively. During the year ended December 31, 2018, we decreased these reserves by $13,821,000 for the destruction of previously reserved product, partially offset by an increase to the reserves of $3,095,000. During the year ended December 31, 2017, we increased these reserves by $6,186,000, inclusive of an allowance of $2,100,000 resulting from a change in estimate as described in Note 2, *Significant Accounting Policies*. During the year ended December 31, 2016, we increased reserves by $7,397,000.

6. Property and Equipment

Property and equipment are comprised of the following (in thousands):

	Estimated Useful Life (in years)	As of December 31, 2018	2017
Computer equipment	3 — 7	$ 3,425	$ 3,523
Scientific equipment	3 — 10	13,560	14,962
Furniture	3 — 10	3,111	3,446
Manufacturing equipment	7 — 10	30,477	25,159
Leasehold improvements	*	36,327	35,595
Less: accumulated depreciation and amortization		(34,814)	(27,511)
Total fixed assets		$ 52,086	$ 55,174

* The estimated useful life of the leasehold improvements is the lesser of the lease term or the estimated useful life.

Total depreciation and amortization expense for the years ended December 31, 2018, 2017 and 2016 was $7,5 79,000, $7,337,000 and $6,249,000, respectively.

As of December 31, 2018 and 2017, respectively, there was $2,689,000 and $9,663,000 of construction in progress included in total fixed assets that had not been placed into service and was not subject to depreciation.

7. Commitments and Contingencies

Lease Commitments

We lease facilities under non-cancelable operating lease agreements. Future minimum commitments for these operating leases in place as of December 31, 2018, with a remaining non-cancelable lease term in excess of one year, are as follows (in thousands):

Years ending December 31,		
2019	$	3,044
2020		3,128
2021		2,340
2022		1,283
2023		1,295
Thereafter		11,851
Total	$	22,941

The terms of certain lease agreements provide for rental payments on a graduated basis. We recognize rent expense on the straight-line basis over the lease period and have accrued for rent expense incurred but not paid. Landlord incentives are recorded as deferred rent and amortized on a straight-line basis over the lease term. Deferred rent was approximately $3,080,000 as of December 31, 2018 and $3,237,000 as of December 31, 2017. Rent expense under operating leases for the years ended December 31, 2018, 2017 and 2016 was approximately $3,647,000, $3,335,000, and $2,757,000, respectively.

Letters of Credit

As of December 31, 2018, we had a $400,000 unused letter of credit related to the requirements of our facility lease agreement.

Material Agreements

Aptar

In October 2015, we entered into an amended and restated supply, development & exclusive licensing agreement with AptarGroup, Inc. (“Aptar”) which, among other things, extended our exclusive supply rights to the current sublingual device, currently utilized by SUBSYS®, as well as any new device(s) jointly developed by the two companies for a period of seven years. In addition to extending the term, this amendment added certain minimum purchase commitments and requires certain tiered royalties as a percentage of net revenue to be paid by us ranging from less than one percent to the low single digits, commencing in March 2016 through the term of this agreement, from our sales of SUBSYS® and future products that use the Aptar spray device technology.

In January 2016, we assigned our rights, title, duties and obligations of supply, development & exclusive licensing agreement with Aptar from our parent to our manufacturing subsidiary as part of a corporate restructuring.

In April 2017, we, through our manufacturing subsidiary, entered into a further amendment to our Aptar supply, development and exclusive licensing agreement. This amendment effectively eliminates any prior minimum purchase obligations that had been set forth in the amendment dated October 30, 2015, and beginning in 2019, replaces them with a new annual flat fee of up to $500,000 if the quantity of devices purchased in a calendar year is less than one million devices. As a result, the cumulative effect related to this amendment reduces our aggregated purchase commitment with Aptar from $20,790,000 to $9,000,000 through December 21, 2022. As of December 31, 2018, our remaining estimated annual contractual obligation under our agreement with Aptar was $6,000,000. All purchase commitments and fees required under our agreements with Aptar were met during the year ended December 31, 2018.

Renaissance

In April 2015, we entered into an amendment to our manufacturing and supply agreement with Renaissance, which extends our existing manufacturing and supply agreement to produce SUBSYS® until the end of 2020. In addition to extending the term, this amendment added certain minimum purchase commitments.

In January 2016, we assigned our rights, title, duties and obligations of our manufacturing and supply agreement with Renaissance from our parent to our manufacturing subsidiary as part of a corporate restructuring.

In April 2018, we, through our manufacturing subsidiary, entered into a further amendment to our Renaissance manufacturing and supply agreement. This amendment effectively eliminates any prior minimum purchase (and batch) obligations that had been set forth in the amendment dated July 2016 and replaces them with a new annual purchase commitment of $3,000,000 for the calendar year ended December 31, 2018, and $2,000,000 for the calendar years ending December 31, 2019 and 2020. As a result, the cumulative effect related to this amendment reduces our aggregated purchase commitment with Renaissance from $12,000,000 to $7,000,000 through December 31, 2020. As of December 31, 2018, our remaining estimated annual contractual obligation under our agreement with Renaissance was $4,000,000.

In February 2019, we, through our manufacturing subsidiary, entered into a further amendment to our Renaissance manufacturing and supply agreement. This amendment effectively eliminates any prior and future minimum purchase (and batch) obligations that had been set forth in the amendment dated April 2018. In addition, we entered into an Asset Purchase Agreement in which we agreed to sell, and Renaissance agreed to purchase, certain of our manufacturing equipment. In accordance with ASC 855, Subsequent Events, this amendment is not reflected in these Consolidated Financial Statements. The amendment will result in a loss on disposal of property and equipment of approximately $0.9 million and will be reflected in our Interim Unaudited Condensed Financial Statements for the three months ended March 31, 2019.

During the years ended December 31, 2018 and 2017, we recorded losses of $359,000 and $1,035,000, respectively, in cost of revenue in these Consolidated Statements of Comprehensive Income (Loss) for a portion of this commitment to Renaissance which represented firm, non-cancellable and unconditional purchase commitments for quantities in excess of our current forecasts for future demand.

The following table sets forth our aggregate minimum purchase commitments and exclusive supply rights with Renaissance and Aptar under these agreements as of December 31, 2018 (in thousands):

Years ending December 31,		
2019	$	4,000
2020		4,000
2021		2,000
2022		—
2023		—
Thereafter		—
Total	$	10,000

Defined Contribution Retirement Plans (401(k) Plan)

We sponsor a 401(k) plan covering all full-time employees. Participants may contribute up to the legal limit. The 401(k) plan provides for employee contributions, and beginning October 2014, our matching contribution is 50 percent of the first 6 percent of earnings contributed by each participant. During the years ended December 31, 2018, 2017, and 2016, matching contribution plan expenses totaled approximately $390,000, $647,000 and $730,000, respectively.

Legal Matters

Other than the matters that we have disclosed below, we from time to time become involved in various ordinary course legal and administrative proceedings, which include intellectual property, commercial, governmental and regulatory investigations, employee-related issues and private litigation, which we do not currently believe are either individually or collectively material.

We record accruals for contingencies when it is probable that a liability has been incurred and the amount can be reasonably estimated. These accruals are adjusted periodically as assessments change or additional information becomes available. If the reasonable estimate of a probable loss is a range, and no amount within the range is a better estimate, the minimum amount in the range is accrued. If a loss is not probable or a probable loss cannot be reasonably estimated, no liability is recorded. We have established reserves for certain of our legal matters. Our loss estimates are generally developed in consultation with outside counsel and outside accounting experts and are based on analyses of potential outcomes. As legal and governmental proceedings, disputes and investigations are inherently unpredictable and in part, beyond our control, unless otherwise indicated, we cannot reasonably predict the outcome of these legal proceedings, nor can we estimate the amount of loss, or range of loss, if any, that may result from these proceedings. While our liability in connection with certain claims cannot be currently estimated, the resolution in any reporting period of one or more of these matters could have a significant impact on our consolidated financial condition, results of operations, liquidity, and cash flows for that future period, and could ultimately have a material adverse effect on our consolidated financial position and could cause the market value of our common shares to decline. While we believe we have valid defenses in these matters, litigation and governmental and regulatory investigations are inherently uncertain, and we may in the future incur material judgments or enter into material settlements of claims.

Consistent with the practice of many publicly-traded companies, we have entered into, and continue to enter into, indemnity agreements with our executive officers and certain members of our board of directors. These indemnity agreements broadly provide for us to advance expenses (including attorneys' fees) incurred in connection with any legal proceeding, as well as indemnification for any and all expenses, actually and reasonably incurred, in connection with the investigation, defense, settlement or appeal of such a proceeding, in connection with matters related to their position. These indemnity agreements provide that the indemnitee shall repay all amounts so advanced if it shall ultimately be determined by final judicial decision from where there is no further right of appeal that the indemnitee is not entitled to be indemnified.

Government Proceedings

Like other companies in the pharmaceutical industry, we are subject to extensive regulation by national, state and local government agencies in the United States. As a result, interaction with government agencies occurs in the normal course of our operations. The following is a brief description of pending governmental investigations that we believe are potentially or actually material at this time. It is possible that criminal charges and substantial payments, fines and/or civil penalties or damages or exclusion from federal healthcare programs or other administrative actions, as well as a corporate integrity agreement, deferred prosecution or deferred exclusion agreement, or similar government mandated compliance document that institutes significant restrictions or obligations, could result for us from any government investigation or proceeding. In addition, even certain investigations that are not discussed below and which we do not deem to be material at this time could be determined to be material and could have a material adverse effect on our financial condition, results of operations and cash flows.

HHS Investigation. We received a subpoena, dated December 9, 2013, from the OIG in connection with an investigation of potential violations involving HHS programs. This subpoena was issued in connection with an investigation by the U.S. Attorney's Office for the Central District of California and requested documents regarding our business, including the commercialization of SUBSYS®. We continue to cooperate with this investigation and have produced substantial documents in response to the subpoena and have provided other requested information.

On April 13, 2018, the United States intervened in part and declined to intervene in part in five lawsuits: *United States ex rel. Guzman v. Insys Therapeutics, Inc.* (CV 13-5861 JLS (AJWx)), *United States ex rel Doe v. Insys Therapeutics, Inc.* (CV 14-3488 JLS (AJWx)), *United States ex rel. Andersson v. Insys Therapeutics, Inc.* (CV 14-9179 JLS (AJWx), *United States ex rel. Erickson v. Insys Therapeutics, Inc.* (CV 16-2956 JLS (AJWx), and *United States ex rel. Doe v. Insys Therapeutics, Inc.* (CV 16-7937 JLS (AJWx)). Qui tam lawsuits typically remain under seal (hence, usually unknown to the defendant) for some time while the government decides whether or not to intervene on behalf of a private qui tam plaintiff (known as a relator) and take the lead in the litigation. These lawsuits can involve significant monetary damages and penalties and award bounties to private plaintiffs who successfully bring the suits.

The States of California, Colorado, Indiana, Minnesota, New York, North Carolina, and Virginia (the "Plaintiff States") elected to intervene in part and declined to intervene in part in *United States ex rel. Guzman v. Insys Therapeutics, Inc.* (CV 13-5861 JLS (AJWx)) and *United States ex rel. Doe v. Insys Therapeutics, Inc.* (CV 16-7937 JLS (AJWx)). The States of Connecticut, Delaware, District of Columbia, Florida, Georgia, Illinois, Iowa, Louisiana, Maryland, Massachusetts, Michigan, Montana, Nevada, New Hampshire, New Jersey, New Mexico, Oklahoma, Rhode Island, Tennessee, Texas, Vermont, and Washington declined to intervene.

The United States' Complaint in Intervention, which was ordered unsealed on May 11, 2018, brings claims for False Claims Act: Presentation of False Claims pursuant to 31 U.S.C. § 3729(a)(1)(A), False Claims Act: Using False Statements to Get False Claims Paid pursuant to 31 U.S.C. § 3729(a)(1)(B), Payment by Mistake, and Unjust Enrichment. This case is currently stayed, and we continue to have ongoing discussion with respect to the DOJ Investigation (as discussed below). The *qui tam* plaintiffs may pursue the claims in which either the United States or the above-mentioned states declined to intervene.

HIPAA Investigation. On September 8, 2014, we received a subpoena issued pursuant to HIPAA from the U.S. Attorney's Office for the District of Massachusetts. The subpoena requested documents regarding SUBSYS®, including our sales and marketing practices related to this product. This investigation also relates to activities in our patient services hub. We continue to cooperate with this investigation and have produced a substantial number of documents in response to the subpoena and have provided other requested information.

DOJ Investigation and Agreement in Principle . We collectively refer to the HHS and HIPAA investigations discussed above as the "DOJ Investigation." In connection with our cooperation, we have been engaged in discussions with the DOJ about these matters, including a resolution of potential liability exposure.

Management accrued, as of September 30, 2017, an aggregate of $150,000,000, which represented our best estimate of the minimum liability exposure that we expected to be paid out over five years in connection with the DOJ Investigation. This estimate reflected a minimum exposure at which management had determined a willingness to settle these matters. The accrual was recorded in accrued litigation award and settlements on our Consolidated Balance Sheets and as an operating expense on our Consolidated Statements of Operations and Comprehensive Income (Loss).

On August 8, 2018, we announced that we reached an agreement in principle with the DOJ to settle the DOJ's civil and criminal investigation into inappropriate sales and commercial practices by some former company employees. Our initial estimate of the minimum liability exposure we previously accrued in connection with the DOJ Investigation of $150,000,000 expected to be paid over five years remains unchanged as of December 31, 2018, with the potential for contingency-based payments associated with certain events that, if they were to occur, management estimates would require additional payments ranging from $0 to $75,000,000. As of December 31, 2018, we have accrued interest expense in connection with the DOJ Investigation of approximately $1,700,000, which is recorded in charges related to litigation award and settlements in these Consolidated Statements of Operations and Comprehensive Income (Loss), and have reclassified $125,000,000 to noncurrent accrued litigation awards and settlements in these Consolidated Balance Sheets. This agreement in principle is subject to the negotiation of final settlement documents with the government. We expect that a final settlement, if completed, would include other material non-financial terms and conditions, including a fraud-based criminal felony plea by one of our subsidiaries and a deferred prosecution agreement with the Company related to the actions of our former employees. Additionally, we expect that a final settlement, if completed, will include a corporate integrity agreement and conditional exclusion release between the Company and OIG that will require the Company to exit the opioid business within 12 months of the effective date, in addition to other provisions. If executed, these agreements will require cooperation with the federal government's prosecutions, enhancements to our compliance program, fulfillment of reporting and monitoring obligations, and management certifications, among other requirements. In addition, compliance with the terms of these agreements will impose additional costs and burdens on us, including some form of employee training, third party reviews, compliance monitoring, reporting obligations and management attention. More importantly, if we fail to comply with the final agreement with DOJ and OIG, the DOJ or OIG may impose substantial monetary penalties or exclude us from federal healthcare programs, including Medicare, Medicaid or the VA, which would have a material adverse effect on our business, financial condition and results of operations.

Because other material, non-financial terms and conditions remain subject to the negotiation of final settlement documents, we cannot provide assurances as to the timing of the execution of final documentation and, like any pending negotiation, there is uncertainty as to the outcome. Moreover, any such final settlement is likely to involve entry into final agreements, which will impose significant costs and burdens and obligations on our business operations and could materially and adversely affect our results of operations and financial conditions as we implement and adhere to such requirements.

At this time, the aforementioned accrual does not currently meet the more likely than not standard to recognize a tax benefit; therefore, we have recognized no tax benefit for it in these Consolidated Financial Statements. It is possible that some or all of this accrual may meet the more likely than not standard in the future, at which time a tax benefit would be recognized.

***SEC Investigation*.** On January 11, 2018, the SEC's Los Angeles Regional office requested that the Company voluntarily provide information on the Company's: (1) restatement of the Company's interim Unaudited Condensed Consolidated Financial Statements as of and for the quarters ended September 30, June 30, and March 31, 2016 and 2015, filed on April 7, 2017; (2) sales and marketing practices; and (3) compliance program, internal controls and enhancements thereto. The Company provided such information and cooperated with the SEC's investigation, including responding to requests or demands for documents and other information. On October 4, 2018, the SEC notified the Company in writing that it had concluded its investigation and, based on information as of the date of the notification, it does not intend to recommend an SEC enforcement action against the Company.

Healthcare Professionals and Former Employees Related Investigations.

Investigations of Healthcare Professionals. A number of healthcare practitioners who formerly interacted with our Company are under investigation or have been charged in criminal proceedings. In addition to the below investigations that are specifically directed at us, we have received governmental agency requests for information, including subpoenas, from at least the following governmental bodies: the USAO and/or HHS OIG of California (Los Angeles), Central District of California, Colorado, Connecticut, Eastern District of Michigan, Eastern District of New York, Florida (Jacksonville), Kansas, Middle District of Florida, Middle District of Pennsylvania, New Hampshire, New Jersey, Northern District of California, Northern District of Georgia, Northern District of Texas, Rhode Island, Southern District of Alabama, Southern District of New York, Southern District of Ohio, Western District of New York, and the states of Arizona, Delaware, Maryland and New York, regarding specific healthcare professionals with which we have interacted with in those states. In addition, at least the following healthcare practitioners formerly interacting with our Company have been charged as follows:

On or about June 23, 2015, a nurse practitioner located in Connecticut, who served on our speaker bureau in connection with our speaker programs designed to educate and promote product awareness and safety for external healthcare providers, pled guilty to violating the federal Anti-Kickback Statute in connection with payments of approximately $83,000 from us.

On or about November 7, 2016, a healthcare professional located in Michigan who served on our speaker bureau pled guilty to healthcare fraud in connection, in part, with receiving payments from us.

On February 23, 2017, two Alabama healthcare professionals who served on our speaker bureau were convicted on 19 of 20 counts brought against them, which included charges related to distribution of a controlled substance, drug conspiracy, healthcare fraud conspiracy and money laundering.

On or about March 22, 2017, the U.S. Attorney's Office for the District of New Hampshire filed an indictment against a physician assistant, who served on our speaker bureau, charging him with violating the federal Anti-Kickback Statute and conspiring to violate the federal Anti-Kickback Statute in connection with payments received for serving as an Insys promotional speaker. On December 18, 2018, a jury convicted the physician assistant on all seven counts.

On or about October 20, 2017, a healthcare professional in Rhode Island, who served on our speaker bureau pled guilty to healthcare fraud and conspiracy to receive kickbacks in connection with payments of approximately $188,000 from us.

On or about March 14, 2018, the U.S. Attorney's Office for the Southern District of New York filed an indictment against five healthcare professionals who served on our speaker bureau, charging them with conspiracy to violate the federal Anti-Kickback Statute, violation of the federal Anti-Kickback Statute, and conspiracy to commit honest services fraud, and charged certain of them with aggravated identity theft, false statements, and wrongful disclosure of individually identifiable health information.

On or about June 4, 2018, a Florida healthcare professional who served on our speaker bureau pled guilty to conspiracy to receive healthcare kickbacks in connection, in part, with receiving payments from us.

On or about June 28, 2018, an Ohio healthcare professional who served on our speaker bureau was indicted for violating the federal Anti-Kickback Statute in connection with receiving payments of more than $103,000 from us.

Investigations of Former Employees. A number of our former employees have been charged in criminal proceedings related to our federal investigations and the following is certain information related thereto.

On or about February 18, 2016, one of our former sales employees located in Alabama pled guilty to a conspiracy to violate the federal Anti-Kickback Statute in connection with two convicted Alabama healthcare professionals mentioned above. On or about April 23, 2018, the former sales employee was sentenced to six months' home confinement.

On or about June 8, 2016, a former district sales manager in New York and a former sales representative in New Jersey were charged in a federal court in Manhattan, New York, with violating the federal Anti-Kickback Statute in connection with interacting with healthcare professionals who prescribed our product and served on our speaker bureau. On June 1, 2017, the former district sales manager was charged in a superseding indictment with additional charges of honest services wire fraud and aggravated identity theft in connection with falsifying sign-in sheets for our speaker programs. On or about March 16, 2018, records were unsealed indicating that the two former employees each pled guilty to the following counts contained in a superseding indictment: conspiracy to violate the Anti-Kickback Statue, violation of the Anti-Kickback Statue, violation of HIPAA, conspiracy to commit honest services wire fraud, and aggravated identity theft, and that the former sales representative also pled guilty to healthcare fraud.

On or about December 8, 2016, the U.S. Attorney's Office for the District of Massachusetts issued an indictment against six former employees, including Michael L. Babich, our former President, CEO and director, on charges including racketeering conspiracy, conspiracy to commit mail fraud, conspiracy to commit wire fraud, conspiracy to violate the Anti-Kickback Statute and forfeiture (the "Original Indictment"). On or about October 26, 2017, the U.S. Attorney's Office for the District of Massachusetts issued a superseding indictment in connection with the Original Indictment and added charges against our former President, CEO and director, Dr. John N. Kapoor. After Dr. Kapoor's indictment, he agreed to put his ownership of our common stock in a trust to be controlled independently, which was effective as of February 27, 2018. The related voting trust agreement was filed with the SEC on a Current Report on Form 8-K on March 1, 2018. On September 11, 2018, the U.S. Attorney's Office for the District of Massachusetts filed a second superseding indictment which contained one count of racketeering conspiracy for all the defendants. This superseding indictment includes a request for forfeiture upon conviction of any interest or property acquired or maintained in violation of such charges, which expressly includes any and all shares of the Company's common stock or options to purchase such stock, salaries, bonuses and other benefits. On or around November 28, 2018, Alec Burlakoff pleaded guilty to the racketeering conspiracy count in the second superseding indictment. On or around January 9, 2019, Michael L. Babich pleaded guilty to one count of conspiracy to commit violations of (a) 18 U.S.C. § 1341 (mail fraud) and (b) 18 U.S.C. § 1343 (wire fraud) and one count of mail fraud; aiding and abetting (18 U.S.C. §§ 1341 and 1342).

As prescribed by the indemnity agreements we entered into with these former executives, we are responsible for any and all expenses, actually and reasonably incurred in their defense, subject to certain limitations set forth in the indemnity agreements. We have recognized expenses associated with the criminal and civil defense of Dr. Kapoor of approximately $25,700,000 for the year ended December 31, 2018, of which $21,900,000 are reported in accrued legal expense in the accompanying Consolidated Balance Sheet as of December 31, 2018. The Company is disputing the reasonableness of a portion of these expenses as they relate to the criminal defense and is analyzing the reasonableness of the civil defense expenses. We continue to accrue all of these costs in our Consolidated Statements of Operations and Comprehensive Income (Loss). As of December 31, 2018, the Company has made cash payments of $5,600,000 related to these legal expenses incurred as part of Dr. Kapoor's criminal defense. If such disputed amounts are subsequently determined not to be due and payable, we would recognize a reversal of these expenses in a future period. The reversal of these expenses could have a material impact on our Consolidated Statements of Operations and Comprehensive Income (Loss). If it is subsequently determined that all of these costs are reasonable, and the Company is required to pay the remaining balance, this could have a material adverse impact on our cash position and liquidity.

On or about February 8, 2017, a former district sales manager in the Northeast was charged in federal court in New Haven, Connecticut, with violating the federal Anti-Kickback Statute in connection with interacting with healthcare professionals who prescribed our product and served on our speaker bureau. On August 8, 2018, the former district sales manager pleaded guilty to engaging in a kickback scheme that defrauded federal healthcare programs.

On April 5, 2017, the U.S. Attorney's Office for the District of Massachusetts filed an information charging a former prior authorization specialist and manager of our patient services hub with one count of wire fraud conspiracy; the former employee pled guilty to that information on June 19, 2017.

On or about July 11, 2017, a former district sales manager pled guilty to conspiring to violate the federal Anti-Kickback Statute related to her activities in the Southern District of Alabama, as well as the Middle and Southern Districts of Florida, including in connection with the two convicted Alabama healthcare professionals mentioned above.

On or about May 30, 2018, a former specialty sales professional pled guilty to a second-degree charge of conspiracy to commit commercial bribery related to her activities in New Jersey.

Except as otherwise indicated, we understand that each of these indicted individuals have entered pleas of not guilty to the charges against them.

Given the ongoing investigations related to our Company and former employees, as well as other individuals associated with our Company, including healthcare professionals, it is possible that additional individual or company criminal charges and convictions and pleas could result from our ongoing federal and state government investigations and related proceedings and the foregoing disclosure and the disclosure below is merely intended to provide general insight into the comprehensive nature of the scope and breadth of investigations that are being conducted related to our Company and is not, nor is it intended to be, an exhaustive listing of every charge, conviction or pleading in connection with our Company.

Ongoing State-Related Investigations. We have received CIDs or subpoenas, as the case may be, from at least each of the following state's Office of the Attorney General (or similarly named and authorized office) which have ongoing investigations directed at our Company: Arizona, Colorado, Florida, Kansas, Kentucky, Maryland, Minnesota, Missouri, New Jersey, New York, North Carolina, Pennsylvania, Rhode Island, Virginia and Washington. Moreover, we have received an administrative subpoena from the California Insurance Commissioner. In addition, we understand that numerous physicians practicing within several of the aforementioned states have received subpoenas from certain state Attorney General or Department of Justice offices in connection with interactions with us. Generally, these CIDs and subpoenas request documents regarding SUBSYS®, including our sales and marketing practices related to SUBSYS® in the applicable state, as well as our patient services hub. We are cooperating with each of these investigations and have produced, or anticipate producing, documents in response to these CIDs, subpoenas and related requests for information from each office.

Resolved State-Related Investigations. Our Company has resolved investigations conducted by certain states' Office of the Attorney General (or similarly named and authorized office) as follows:

In connection with the investigation by the ODOJ, we entered into a settlement agreement with the ODOJ, referred to as an AVC, and made monetary payments totaling approximately $1,100,000. The AVC requires us to maintain certain controls and processes around our promotional and sales activity related to SUBSYS® in Oregon. This AVC expressly provides that we do not admit any violation of law or regulation. This settlement was reached as a result of our cooperation with the ODOJ's investigation and after producing documents in response to certain CIDs and related requests for information from the ODOJ. All monetary payments in connection with this settlement were made prior to December 31, 2015.

In connection with the investigation by the Illinois Office of the Attorney General, such office filed a complaint against us on behalf of the State of Illinois on August 25, 2016, in the Circuit Court of Cook County, Illinois, Chancery Division, asserting a claim for violation of the Illinois Consumer Fraud and Deceptive Business Practices Act in connection with the sales and marketing of SUBSYS®. On August 18, 2017, the Circuit Court of Cook County entered a Final Judgment and Consent Decree, which, among other things, provided for a monetary payment of $4,450,000 by Insys and requires us to maintain certain controls and processes around our promotional and sales activity related to SUBSYS® in Illinois. The Final Judgment and Consent Decree expressly provides that we do not admit any violation of law or regulation. All monetary payments in connection with this Final Judgment and Consent Decree were accrued in the Consolidated Balance Sheets as of June 30, 2017 and the payments in connection with this settlement were made prior to September 30, 2017.

In connection with the investigation by the State of New Hampshire, we entered into a settlement agreement with the State of New Hampshire referred to as an assurance of discontinuance, and made monetary payments totaling approximately $2,900,000 to the State of New Hampshire and a charitable contribution of $500,000 to be used by a New Hampshire charitable foundation in preventing or remediating problems related to abuse, misuse or misprescribing of opioid drugs. The assurance of discontinuance expressly provides that we do not admit any violation of law or regulation and requires us to maintain certain controls and processes around our promotional and sales activity related to SUBSYS® in New Hampshire. This settlement was reached as a result of our cooperation with the State of New Hampshire investigation and after producing documents in response to certain requests for information by the State of New Hampshire. These amounts were accrued in the Consolidated Balance Sheet as of December 31, 2016 and the payments in connection with this settlement were made during the three months ended March 31, 2017.

In connection with the investigation by the State of Massachusetts, we entered into a settlement with the State of Massachusetts, which was entered by the Superior Court of the Commonwealth of Massachusetts in a Final Judgment by Consent on October 5, 2017. The Final Judgment by Consent provided for a monetary payment of $500,000 and requires us to maintain certain controls and processes around our promotional and sales activity related to Massachusetts. The Final Judgment by Consent expressly provides that we do not admit any liability or wrongdoing. The amount of the monetary payment was accrued in the Consolidated Balance Sheet as of September 30, 2017 and the payments in connection with this settlement were made during the three months ended December 31, 2017.

Ongoing Complaints filed in connection with State Related Investigations . Our Company has a number of ongoing legal proceedings related to complaints filed in connection with investigations conducted by certain states' Office of the Attorney General (or similarly named and authorized office) as follows:

In connection with the investigation by the State of Arizona, on August 30, 2017, the Arizona Attorney General filed a complaint on behalf of the State of Arizona against us in the Maricopa County, Arizona Superior Court. The complaint asserts claims for violations of the Arizona Consumer Fraud Act in connection with the sales and marketing of SUBSYS® in Arizona and in connection with our patient services hub. The complaint seeks a permanent injunction preventing us from engaging in practices in violation of the Arizona Consumer Fraud Act, restitution to consumers and other persons, disgorgement of profits, civil penalties, and investigative costs. On or about November 10, 2017, we filed a motion to dismiss. On January 17, 2018, the Court dismissed, based upon preemption by the federal Sunshine Act, the State's claim to the extent related to remedies that are based upon the payment and disclosure of speaker fees, but did not dismiss the rest of the complaint. The State filed a motion for leave to amend its complaint, which the Court granted. We filed our answer to the amended complaint on April 5, 2018.

In connection with the investigation by the State of New Jersey, on October 5, 2017, the New Jersey Attorney General, on behalf of the State of New Jersey, and the Acting Director of the New Jersey Division of Consumer Affairs filed a complaint against us in the Superior Court of New Jersey, Chancery Division, Middlesex Vicinage. The complaint asserts claims for violations of the New Jersey Consumer Fraud Act and for violations of the New Jersey False Claims Act in connection with the sales and marketing of SUBSYS® in New Jersey and in connection with our patient services hub. The complaint seeks a permanent injunction preventing us from engaging in practices in violation of the New Jersey Consumer Fraud Act, disgorgement of profits, civil penalties, treble damages for alleged violations of the New Jersey False Claims Act, and costs and attorneys' fees. On November 16, 2017, the New Jersey Attorney General filed an Amended Complaint, which we moved to dismiss on January 8, 2018. The New Jersey Attorney General opposed our motion on March 28, 2018, and we replied. On December 19, 2018, the Court denied our motion to dismiss.

On December 21, 2017, Attorney General of the State of North Carolina filed a complaint in Wake County, North Carolina Superior Court against us. The complaint asserts claims related to alleged violations of the North Carolina Consumer Protection Act. On or about September 25, 2018, we moved to dismiss the complaint. The motion remains pending.

On February 1, 2018, the Attorney General of the State of New York, filed a complaint against us in the Supreme Court of the State of New York, County of New York. The complaint asserts claims related to alleged deceptive acts and practices. We moved to dismiss the complaint on April 18, 2018. In response, on May 25, 2018, the New York Attorney General opposed our motion to dismiss and filed a cross-motion for partial summary judgment related to the State's commercial bribery claim. On June 29, 2018, we filed a reply in support of our motion to dismiss and opposed the State's motion for partial summary judgment. The Court conducted oral argument on the motions to dismiss and the cross-motion for summary judgement on October 4, 2018. The motion remains pending.

On February 5, 2018, the Consumer Protection Division, Office of the Attorney General of Maryland, filed a petition to enforce an administrative subpoena against us. The State voluntarily dismissed the action on September 5, 2018. On September 6, 2018, however, the Consumer Protection Division, Office of the Attorney General of Maryland, filed a Statement of Charges against us with the Consumer Protection Division, Office of the Attorney General. Insys filed its response to the Statement of Charges on October 17, 2018. On November 21, 2018, Insys filed a Motion to Dismiss the Statement of Charges. On January 31, 2019, the Administrative Law Judge issued a Proposed Ruling on Motion to Dismiss Statement of Charges in which he recommended that the Consumer Protection Division deny the Motion to Dismiss. The merits hearing is scheduled to begin on April 8, 2019.

On May 30, 2018, the Attorney General of the State of Minnesota and the Minnesota Board of Pharmacy filed a complaint against us in the Hennepin County District Court, State of Minnesota. The complaint asserts claims related to alleged deceptive acts and practices and consumer fraud, as well as claims under the Minnesota Wholesale Drug Distribution Licensing Act (Minn. Stat. § 151.461). On August 28, 2018, Insys moved to dismiss the complaint. On the same day, the Attorney General and the Board of Pharmacy filed a motion for temporary injunction. The Court held oral argument on both the motion to dismiss and the motion for temporary injunction, and the Court denied both motions on January 15, 2019. Also, on May 30, 2018, the Minnesota Board of Pharmacy filed an administrative action against us before the State of Minnesota Office of Administrative Hearings for the Board of Pharmacy, which seeks a determination regarding whether certain alleged conduct by Insys constitutes grounds for disciplinary action. The Office of Administrative Hearings has indicated that it will set a hearing in this matter for March or April 2019.

On November 19, 2018, the Attorney General of the Commonwealth of Kentucky filed a complaint against us in the Hardin County Circuit Court, Commonwealth of Kentucky. The complaint asserts claims related to alleged violations of the Kentucky Consumer Protection Act, as well as Medicaid and Kentucky Assistance Program Fraud, public nuisance, fraud, unjust enrichment, negligence, negligence per se, and punitive damages. On January 16, 2019, Insys moved to dismiss the complaint. The motion remains pending.

Multi-District Prescription Opioid Litigation. We have been named along with various other opioid manufacturers, opioid distributors, prescribers, pharmacies, and others in complaints focused on the national opioid epidemic filed by various cities, counties, states, Native American tribes, and third-party payers in many state and federal courts in Alabama, Arizona, Arkansas, California, Connecticut, Florida, Georgia, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Nebraska, New Hampshire, New Jersey, New Mexico, New York, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah and West Virginia. We are involved in more than 800 of these cases, the majority of which have been consolidated into multi-district litigation (MDL No. 2804) in the Northern District of Ohio. Most of the cases in the multi-district litigation are presently stayed while the Court seeks to facilitate a resolution. On April 2, 2018, the United States filed a motion to participate in settlement discussions and as a friend of the court. Additionally, the Court set certain cases for a litigation track, and those cases will move forward toward trial, which is scheduled to commence on October 21, 2019. Additionally, the Court recently set another set of cases for a subsequent litigation track.

We have also been named, along with various other opioid manufacturers and distributors, in putative class action complaints that seek to assert claims allegedly related to the national opioid epidemic on behalf of (1) purchasers of health insurance between 1996 and the present, and (2) children born addicted to opioids. Most of these cases have been consolidated into MDL No. 2804. Finally, Insys has been named in at least one lawsuit in which a personal injury plaintiff sued Insys and other opioid manufacturers for harm allegedly caused by a tortfeasor who was addicted to opioids.

Congressional and Other Inquiries. Many federal agencies and branches are focused on the abuse of opioids in the United States and agencies such as the HHS have expressed their belief that the United States is in the midst of a prescription opioid abuse epidemic. Moreover, President Trump has declared the opioid crisis to be a public health emergency and has made it a priority to address this crisis.

Members of our U.S. Congress have been conducting hearings and other inquiries into causes and solutions to the national opioid epidemic that have involved inquiries into our Company's practices. For example, on March 28, 2017, the Ranking Member of the Committee on Homeland Security and Governmental Affairs of the United States Senate distributed a letter to five manufacturers of opioid products, including us, requesting documents and information intended to aid such committee in understanding the challenges industry practices pose to efforts to curb opioid addiction and stem rising prescription drug costs for the federal government. This letter requested documents regarding our business, including the commercialization of SUBSYS®. This inquiry continues and has resulted in at least four reports that mention or address our Company. We continue to cooperate with this inquiry.

Similarly, on August 2, 2018, bipartisan leaders of the House of Representatives Committee on Energy and Commerce sent letters to three manufacturers of opioid products, including us, requesting documents and information intended to aid such committee in investigating potential breakdowns in the controlled substances supply chain which may have contributed to the nation's opioid epidemic. This letter requested documents regarding our business, sales practices, and speaker programs. We continue to cooperate with this inquiry.

The Company also received a letter from Senator Dianne Feinstein dated January 25, 2019, requesting that the Company voluntarily end its promotion of SUBSYS® to physicians. The Company replied to that letter on February 21, 2019.

With the exception of the investigations by the ODOJ, the State of New Hampshire, the State of Illinois, the State of Massachusetts, and the DOJ, which we have quantified above, we believe a loss from an unfavorable outcome of these federal and state governmental proceedings is reasonably possible and an estimate of the amount or range of loss from an unfavorable outcome is not determinable at these stages. We believe we have meritorious legal positions and will continue to represent our interests vigorously in these matters. However, responding to government investigations has and could continue to burden us with substantial legal costs in connection with defending any claims raised. Any potential resulting fines, restitution, damages and penalties, settlement payments, pleas or exclusion from federal healthcare programs or other administrative actions, as well as any related actions brought by stockholders or other third parties, could have a material adverse effect on our financial position, results of operations or cash flows. Additionally, these matters could also have a negative impact on our reputation and divert the attention of our management from operating our business.

Federal Securities Litigation and Derivative Complaints

Federal Securities Litigation. On or about February 2, 2016, a complaint (captioned Richard Di Donato v. Insys Therapeutics, Inc., et al., Case 2:16-cv-00302-NVW) was filed in the United States District Court for the District of Arizona against us and certain of our current and former officers. The complaint was brought as a purported class action on behalf of purchasers of our common stock between March 3, 2015 and January 25, 2016. In general, the plaintiffs allege that the defendants violated the anti-fraud provisions of the federal securities laws by making materially false and misleading statements regarding our business, operations and compliance with laws during the class period, thereby artificially inflating the price of our common stock. On June 3, 2016, the Court appointed Clark Miller to serve as lead plaintiff. On June 24, 2016, the plaintiff filed a first amended complaint naming a former employee of Insys Therapeutics, Inc. as an additional defendant and extending the class period. On December 22, 2016, the plaintiff filed a second amended complaint, primarily to add allegations relating to an indictment of Michael L. Babich and certain of our former employees announced on December 8, 2016, and to extend the class period from August 12, 2014 through December 8, 2016. On January 12, 2017, the defendants moved to dismiss the second amended complaint. Oral arguments were heard by the Court on July 28, 2017, and the Court granted the motion in part and denied it in part. The plaintiff subsequently moved for leave to further amend the complaint, which we opposed. The Court denied plaintiff's motion on March 31, 2018, and Insys filed its answer on April 15, 2018. Plaintiff subsequently filed a motion to certify class, which we opposed. The plaintiff seeks unspecified monetary damages and other relief. We continue to vigorously defend this matter.

On or about March 17, 2017, a complaint (captioned Kayd Currier v. Insys Therapeutics, Inc., et al., Case 1:17-cv-01954-PAC) was filed in the United States District Court for the Southern District of New York against us and certain of our current and former officers. The complaint was brought as a purported class action on behalf of purchasers of our securities between February 23, 2016, and March 15, 2017. In general, the plaintiffs allege that the defendants violated the anti-fraud provisions of the federal securities laws by making materially false and misleading statements regarding our business and financial results during the class period, thereby artificially inflating the price of our securities. On or about March 28, 2017, a second complaint making similar allegations (captioned Hans E. Erdmann v. Insys Therapeutics, Inc., et al., Case 1:17-cv-02225-PAC) was filed in the same Court. On May 31, 2017, the Court consolidated the first and second complaint and appointed lead counsel in the consolidated action. On July 31, 2017, the lead counsel filed a consolidated complaint. On October 11, 2017, the Court held a pre-motion conference, at which the Court granted leave to plaintiffs to again amend the complaint. The amendment was filed on October 27, 2017, and we moved to dismiss. The Court subsequently dismissed the complaint as to Santosh Vetticaden, our former Interim CEO and Chief Medical Officer, and otherwise denied our motion to dismiss. Insys filed its answer on June 26, 2018. The plaintiffs in both actions seek unspecified monetary damages and other relief. We continue to vigorously defend this matter.

Derivative Litigation. On or about August 26, 2016, Gary Hirt and Precieux Art Jewelers Inc. filed a derivative complaint in the Court of Chancery of Delaware against members of our Board of Directors and Michael L. Babich. The plaintiffs allege, among other things, that the defendants breached their fiduciary duties by (a) knowingly overseeing the implementation of an illegal sales and marketing program, (b) consciously disregarding their duty of oversight of our compliance with laws and (c) trading on the basis of material non-public information. On November 8, 2016, the plaintiffs filed an amended derivative complaint, and on January 26, 2017, the plaintiffs supplemented the amended derivative complaint, primarily to add allegations relating to the indictment of Michael L. Babich and certain of our former employees announced on December 8, 2016. On November 22, 2016, the defendants moved to dismiss the action.

On or about February 2, 2017, Michael Bourque filed a derivative complaint in the Court of Chancery against members of our Board of Directors; Michael L. Babich; Franc Del Fosse, our General Counsel; and Sanga Emmanuel, our Vice President and Chief Compliance Officer. The Bourque derivative complaint contains similar claims as the other derivative complaint. All parties stipulated to consolidate the two actions, and the consolidated action is captioned In re Insys Therapeutics, Inc. Derivative Litigation, C.A. No. 12696-VCMR. Following the submission of motions for appointment as lead counsel, the Court held a hearing on March 23, 2017, and appointed counsel for Gary Hirt and Precieux Art Jewelers Inc. as lead counsel. Lead counsel is required to designate an operative complaint or file a consolidated complaint. The plaintiffs seek unspecified monetary damages and other relief derivatively on behalf of Insys Therapeutics, Inc.

On or about April 28, 2017, lead counsel filed a consolidated and amended complaint which maintained the original defendants this lead counsel had included in its original complaint and did not include any additional defendants included in the Bourque complaint. On May 31, 2017, we subsequently moved to stay or to dismiss the

complaint and, on or about July 28, 2017, lead counsel filed an answering brief in opposition to our motion to stay or dismiss. On November 30, 2017, the Court granted our motion to stay but has required us to provide certain discovery to the plaintiffs. On February 8, 2018, in response to the plaintiffs' motion to alter or clarify judgment, the Court ordered us to provide additional discovery to the plaintiffs. On March 16, 2018, the Court entered the parties' stipulated proposed order implementing the Court's ruling of February 8, 2018. On January 15, 2019, the plaintiffs filed a motion to lift the stay. We continue to vigorously defend this matter.

On or about June 5, 2018, Jim Soltau filed a derivative complaint ("the Soltau complaint") in the United States District Court, District of Arizona (18-cv-01720-SPL), against members of our Board of Directors, former directors and officers, as applicable, John Kapoor, Michael Babich, Patrick Forteau, Brian Tambi, the Estate of Dr. Theodore Stanley, and former officers Darryl Baker and Santosh Vetticaden. The plaintiff alleged, among other things, that these individuals breached their fiduciary duties as our officers and/or directors and are liable for unjust enrichment, waste of corporate assets, abuse of control, gross mismanagement, and violations of Sections 14(a), 10(b) and 20(a) of the Securities Exchange Act of 1934. On July 20, 2018, Insys filed its answer to the complaint. On September 12, 2018, the Court granted a motion to stay the case. We continue to vigorously defend this matter.

On or about June 10, 2018, David Bennett filed a derivative complaint in the United States District Court, District of Arizona (18-cv-02170), against members of our Board of Directors, former directors and officers, as applicable, John Kapoor, Michael Babich, Patrick Forteau, Brian Tambi, the Estate of Dr. Theodore Stanley, and former officers Darryl Baker and Santosh Vetticaden. This complaint contains similar claims as the Soltau complaint. On August 10, 2018, the Soltau and Bennett cases were consolidated, and on September 12, 2018, the Court granted a motion to stay the case. We intend to vigorously defend this matter.

On August 6, 2018, Hamid Ravansari filed a derivative complaint in the United District Court, Southern District of New York (18-CV-07026) against members of our Board of Directors, former directors and officers, as applicable, John Kapoor, Michael Babich, Patrick Fourteau, Pierre Lapalme, Steven Meyer, Brian Tambi, the Estate of Dr. Theodore Stanley, and former officers Darryl Baker and Santosh Vetticaden. The plaintiffs allege, among other things, that these individuals breached their fiduciary duties as our officers and/or directors and are liable for unjust enrichment, abuse of control, gross mismanagement and waste of corporate assets. On October 29, 2018, Insys filed its answer to the complaint. On December 3, 2018, the Court granted a motion to stay the case. We intend to vigorously defend this matter.

Shareholder Demands. On or about April 18, 2018, putative shareholder Kyle Stefurak demanded that the Company's Board of Directors take action to remedy breaches of fiduciary duties by certain of our current and/or former directors and executive officers. The Board of Directors referred this demand to the Special Litigation Committee of the Board of Directors ("SLC").

On or about November 20, 2018, putative shareholder Cora Foxx Greenwald demanded that the Company's Board of Directors take action against present or former Board members and former executives who are allegedly responsible for violations of law and damages sustained by the Company as a result of certain misconduct. The Board of Directors referred this demand to the SLC.

Paragraph IV Challenges

On or about August 2, 2017, we received a Paragraph IV Notice Letter from counsel for TEVA Pharmaceuticals USA ("TEVA USA") related to SUBSYS® 0.4mg dose. The letter asserts that (i) the FDA received an ANDA from TEVA USA and (ii) that TEVA USA's formulation does not infringe SUBSYS® patents and/or that our patents for SUBSYS® are invalid. On September 13, 2017, we filed suit in United States District Court for the District of Delaware, in which we allege patent infringement. On January 15, 2018, TEVA USA filed an answer and counterclaims, to which we have replied. Additionally, on December 3, 2018, TEVA USA filed a claim construction brief, to which we replied. A Markman claim construction hearing occurred on February 12, 2019. The Court ruled in favor of Insys and has upheld the patent claims as originally issued. We intend to represent our interests vigorously in this matter.

On or about January 31, 2018, we received a Paragraph IV Notice Letter from counsel for TEVA USA related to SUBSYS® 0.1mg, 0.2mg, 0.6mg, 1.2mg and 1.6mg doses. The letter asserts that (i) the FDA received an ANDA from TEVA USA and (ii) that TEVA USA's formulation does not infringe SUBSYS® patents and/or that our patents for SUBSYS® are invalid. We filed a patent infringement lawsuit against TEVA USA on March 16, 2018.

TEVA USA filed its answer to our complaint and counterclaims, to which we have replied. We intend to represent our interests vigorously in this matter.

On or about July 10, 2018, we received a Paragraph IV Notice Letter from counsel for TEVA USA related to SUBSYS® 0.8mg dose. The letter asserts that (i) the FDA received an ANDA from TEVA USA and (ii) that TEVA USA's formulation does not infringe SUBSYS® patents and/or that our patents for SUBSYS® are invalid. We filed a patent infringement lawsuit against TEVA USA on August 23, 2018. TEVA USA filed its answer to our complaint and counterclaims, to which we have replied. We intend to represent our interests vigorously in this matter.

On September 26, 2018, we received two Paragraph IV Notice Letters from counsel for TEVA USA related to SUBSYS® 0.1mg, 0.2mg, 0.4mg, 0.6mg, 0.8mg, 1.2mg and 1.6mg doses. The letter asserts that (i) the FDA received an ANDA from TEVA USA and (ii) that TEVA USA's formulation does not infringe SUBSYS® patents and/or that our patents for SUBSYS® are invalid. We filed a patent infringement lawsuit on November 9, 2018. We intend to represent our interests vigorously in this matter.

The Court has consolidated the aforementioned TEVA USA patent infringement lawsuits in case C.A. No. 17-1303 (CFC).

General Litigation and Disputes

Kottayil vs. Insys Pharma, Inc. On September 29, 2009, Insys Pharma, Inc., our wholly owned subsidiary, and certain of our officers and the five directors who comprised the Insys Pharma board of directors as of June 2009, as well as their spouses, were named as defendants in a lawsuit in the Superior Court of the State of Arizona, Maricopa County, or the Arizona Superior Court, brought by Santosh Kottayil, Ph.D., certain of his family members and a trust of which Dr. Kottayil is the trustee. Dr. Kottayil formerly served as President, Chief Scientific Officer and a director of Insys Pharma, among other positions.

In February 2010, Insys Pharma and the other defendants answered and filed counter-claims to Dr. Kottayil's amended complaint. The counter-claims include actions for breach of fiduciary duty, fraud and negligent misrepresentations and omissions with respect to the time during which Dr. Kottayil was employed at Insys Pharma. The counter-claims, among other relief, sought compensatory and punitive damages.

The trial commenced on December 1, 2014, with the evidence phase of the trial completed on January 29, 2015.

On June 8, 2015, the Court issued findings of fact and conclusions of law in its final trial ruling, which included a finding in favor of Kottayil and against Insys Pharma on Insys Pharma's counterclaims of breach of fiduciary duty, fraud, and negligent misrepresentation.

On October 2, 2015, the Court denied Kottayil's request to submit an application for attorneys' fees for his defense of the Insys Pharma counterclaims, finding that the request was premature.

On or around November 1, 2015, we received a notice from Dr. Kottayil's attorneys demanding indemnification for legal and other defense costs alleged to have been incurred in connection with Dr. Kottayil's defense of the Insys Pharma counterclaims in the amount of $3,630,000. We responded to these demands by, among other things, requesting supporting documents and information from the plaintiffs' counsel, which we have not received. On June 1, 2018, Dr. Kottayil filed a complaint in Superior Court in the State of Arizona in and for the County of Maricopa against Insys Pharma, Inc., our wholly owned subsidiary. The complaint seeks indemnification in the amount of $3,630,000, plus interest. On July 26, 2018, Insys moved to dismiss the complaint, which the Court granted. Dr. Kottayil subsequently moved for reconsideration of the Court's dismissal ruling, which the Court granted. Because of the uncertainty surrounding the ultimate outcome, we have not accrued for this claim at this time; however, we believe that that it is reasonably possible that there may be a material loss associated with this claim and we currently estimate the range of the reasonably possible loss to be between $0 and the $3,630,000 claimed, plus interest. The legal rate of interest is 5% over the Federal Reserve discount rate.

Insurance Litigation. On June 23, 2017, Aetna, Inc. and a subsidiary filed an action against us and a number of former employees in the Pennsylvania Court of Common Pleas, Philadelphia County (captioned Aetna Inc. v. Insys Therapeutics, Inc., Case No. 170602779). Plaintiffs bring claims against us for: (1) insurance fraud; (2) civil conspiracy; (3) common law fraud; (4) unjust enrichment; (5) negligent misrepresentation; and (6) negligence. Through all of the claims, Aetna seeks recovery of millions of dollars paid for SUBSYS® prescriptions that, allegedly, were not properly covered. It also seeks punitive damages, investigative expenses and costs of suit, reasonable attorneys' fees and expenses, and prejudgment and post-judgment interest. Plaintiffs served their complaint on September 25, 2017. On October 25, 2017, we removed this matter to federal court. Aetna subsequently moved to remand the case to state court. On January 6, 2018, the district court denied Aetna's motion to remand. We moved to dismiss Aetna's claims. On August 24, 2018, the Court dismissed Aetna's negligent misrepresentation and negligence claims and otherwise denied the motion to dismiss. We intend to vigorously defend this matter.

On July 12, 2017, numerous subsidiaries of Anthem, Inc. filed a complaint in the U.S. District Court for the District Court for the District Court for the District of Arizona against us (captioned Blue Cross of California, Inc. d/b/a Anthem Blue Cross of California v. Insys Therapeutics, Inc., Case No. 2:17-cv-02286-DLR). Plaintiffs brought claims against us for: (1) violation of various state laws prohibiting deceptive, unfair, and unlawful business practices (i.e., consumer fraud); (2) fraud; (3) negligent misrepresentation; (4) unjust enrichment; and (5) civil conspiracy to commit fraud and unfair business practices. Through all of the claims, Anthem seeks recovery of more than $19,000,000 paid for SUBSYS® prescriptions that, allegedly, were not properly covered. It also seeks punitive damages and an injunction to prevent Insys from continuing to engage in the conduct underlying its claims. Plaintiffs served their complaint on July 14, 2017. On August 4, 2017, we filed an answer to such complaint. On February 2, 2018, Plaintiffs filed a motion for leave to file a second amended complaint and on February 16, 2018, we filed (i) an opposition to Plaintiff's motion to file a second amended complaint and (ii) a motion to stay the case. On or about July 23, 2018, the Court granted Plaintiff's motion to file a second amended complaint. On August 8, 2018, the Court denied our motion to stay. On September 14, 2018, we moved to dismiss Anthem's second amended complaint. Discovery in this case is ongoing. We intend to vigorously defend this matter.

On May 21, 2018, MSPA Claims I, LLC, MAO-MSO Recovery II, LLC, and MSP Recovery Claims, Series LLC filed a complaint in the United States District Court, Northern District of Ohio, against Insys Therapeutics, Inc. Plaintiffs bring claims for violations of the Racketeer Influenced and Corrupt Organizations Act ("RICO"), common law fraud, and unjust enrichment. Plaintiffs subsequently amended their complaint on August 22, 2018, and we moved to dismiss the complaint on September 25, 2018. We intend to vigorously defend this matter.

On December 10, 2018, Blue Cross and Blue Shield of Louisiana and HMO Louisiana, Inc., on behalf of themselves and all others similarly situated, filed a putative class action complaint in the United States District Court, District of Massachusetts, against Insys Therapeutics, Inc. Plaintiffs bring claims for violation of 18 U.S.C. § 1962(c) (RICO), violation of 18 U.S.C. § 1962(d) (RICO conspiracy), civil conspiracy, unjust enrichment, and violation of the Alaska Unfair Trade Practices and Consumer Protection Act, the Arizona Consumer Fraud Act, the California Consumers Legal Remedies Act, the California Unfair Competition Law, the Colorado Consumer Protection Act, the Connecticut Unfair Trade Practices Act, the Delaware Consumer Fraud Act, the District of Columbia Consumer Protection Procedures Act, the Florida Deceptive and Unfair Trade Practices Act, the Idaho Consumer Protection Act, the Illinois Consumer Fraud and Deceptive Business Practices Act, the Indiana Deceptive Consumer Sales Act, the Kentucky Consumer Protection Act, the Maine Unfair Trade Practices Act, the Maryland Consumer Protection Act, the Michigan Consumer Protection Act, the Minnesota Prevention of Consumer Fraud Act, the Missouri Merchandising Practices Act, the Nebraska Consumer Protection Act, the Nevada Deceptive Trade Practices Act, the New Hampshire Consumer Protection Act, the New Jersey Consumer Fraud Act, the New Mexico Unfair Trade Practices Act, New York General Business Law § 349, the North Carolina Unfair and Deceptive Trade Practices Act, the North Dakota Unlawful Sales or Advertising Practices Act, the Ohio Deceptive Trade Practices Act, the Oklahoma Consumer Protection Act, the Pennsylvania Unfair Trade Practices and Consumer Protection Law, the Rhode Island Unfair Trade Practices and Consumer Protection Act, the South Dakota Deceptive Trade Practices and Consumer Protection Law, the Virginia Consumer Protection Act, the Washington Consumer Protection Act, the West Virginia Consumer Credit and Protection Act, and the Wisconsin Deceptive Trade Practices Act. We intend to vigorously defend this matter.

On February 19, 2019, United Healthcare Services, Inc. (“United”) filed a complaint in the Superior Court of the State of California, for the County of Orange, against Insys Therapeutics, Inc. Plaintiff brings claims for common law fraud, negligent misrepresentation, unjust enrichment, and unlawful and fraudulent business practices. Through all of its claims, United alleges that it paid over $50 million for SUBSYS® prescriptions that did not qualify for coverage under United’s criteria and for unnecessarily high doses. We intend to vigorously defend this matter.

On February 22, 2019, Horizon Blue Cross Blue Shield of New Jersey filed a complaint in the Superior Court of New Jersey, Essex County, against Insys Therapeutics, Inc., a number of our former employees, and a former member of our speaker bureau. Plaintiff brings claims for violation of New Jersey RICO (N.J.S.A. 2C:41-2(c)), conspiracy to violate New Jersey RICO (N.J.S.A. 2C:41-2(d)), insurance fraud – violation of New Jersey Insurance Fraud Prevention Act (N.J.S.A. 17:33A-4), common law fraud, unjust enrichment, and misrepresentation. Plaintiff asserts that it paid over $4,000,000 for off-label prescriptions of SUBSYS®, over $2,000,000 of which was allegedly paid for plan members with no history of cancer. We intend to vigorously defend this matter.

Management accrued, as of December 31, 2018, an aggregate of $14,000,000, which represents our best estimate of the minimum liability exposure that we expect to be paid out in connection with the potential settlement of insurance litigation discussed above. The accrual was recorded in accrued litigation award and settlements in these Consolidated Balance Sheets and as an operating expense on these Consolidated Statements of Operations and Comprehensive Income (Loss).

Goodell, Devries, Leech & Dann, LLP . On or around February 19, 2019, Goodell, Devries, Leech & Dann, LLP filed a complaint in Baltimore City Circuit Court, Maryland, against Insys Therapeutics, Inc. Plaintiff brings a claim for breach of contract. We intend to vigorously defend this matter.

Markland. On July 1, 2016, Robert N. Markland, as the Personal Representative of the Estate of Carolyn S. Markland filed a complaint in the Circuit Court, Fourth Judicial Circuit, in and for Duval County, Florida, against Insys Therapeutics, Inc. The complaint states that it is a wrongful death products liability action brought pursuant to Section 768.16, et seq. under Florida law in connection with a death occurring in July 2014 and includes a claim of negligent marketing. The lawsuit seeks unspecified damages for past expenses and costs, pain and suffering and loss of consortium and earnings. On August 4, 2016, we removed this case to U.S. District Court in the Middle District of Florida. On September 2, 2016, we filed a motion to dismiss. The Court granted our motion on September 15, 2017. The plaintiff subsequently filed a notice of appeal, and the opening brief on appeal was filed on March 9, 2018. We filed our answering brief on May 24, 2018, and the reply brief was filed on July 9, 2018. On December 19, 2018, the Eleventh Circuit Court of Appeals affirmed the District Court’s dismissal of plaintiff’s claim.

Buchalter. On September 9, 2016, Jeffrey Buchalter filed a complaint in the Circuit Court for Anne Arundel County, Maryland, Case No. C-02-cv-16-002718, against Dr. William Tham, Physical Medicine & Pain Management Associates, Maryland Neurological Institute, various physician assistants, and Insys Therapeutics, Inc. Plaintiff's complaint states it is a personal injury action against Insys related to negligent misrepresentation, failure to warn and fraud under state laws. The lawsuit seeks unspecified compensatory and punitive damages. We filed a motion to dismiss and on or about May 6, 2017, the Court denied the motion to dismiss. On March 22, 2018, Plaintiff filed a motion to file a second amended complaint, which, among other things, sought to add as defendants certain former Insys officers and employees. The motion to file a second amended complaint was subsequently granted. Insys filed its answer to the second amended complaint on June 20, 2018. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Fuller. On or about March 23, 2017, Deborah Fuller & David Fuller, as Administrators Ad Prosequendum for the Estate of Sarah A. Fuller, deceased, and Deborah Fuller and David Fuller, individually, filed a complaint in the Superior Court of New Jersey Law Division, Middlesex County, Case No. L1859-17, against Vivienne Matalon, M.D., TLC Healthcare 2, LLC, Linden Care and Insys Therapeutics, Inc. The plaintiff's complaint alleges negligence violations under the Wrongful Death Act pursuant to N.J.S.A 2A:31, *et seq.* and also brings claims for fraud and negligent misrepresentation. We filed a motion to dismiss the complaint on May 19, 2017, and the Court held oral argument on the motion on June 29, 2017. On July 27, 2017, the Court issued a ruling on the multi-party motion to dismiss. The Court dismissed some claims but denied the motion to dismiss on certain of plaintiffs' claims. We answered the complaint, and, after plaintiffs dismissed the treating physician, on October 4, 2017, we removed the case to U.S. District Court for the District of New Jersey. Plaintiffs subsequently filed a motion to remand the case to state court on October 11, 2017. On January 19, 2018, the Magistrate Judge issued a Report and Recommendation, recommending that the District Court deny plaintiffs' motion to remand. On February 5, 2018, the District Court adopted the Report and Recommendation. On February 6, 2018, plaintiffs filed a motion for leave to amend, seeking to add as defendants certain former Insys officers and a former employee. Insys filed its opposition to the motion for leave to amend on February 21, 2018. Consistent with our opposition, the Court denied plaintiffs' motion as to the former employee and granted the motion as to the former officers. Plaintiffs filed their first amended complaint on June 12, 2018. On June 26, 2018, Insys moved to dismiss, in part, plaintiffs' first amended complaint. Plaintiffs filed a response in opposition to the motion on July 18, 2018, and the Court set a return date of August 6, 2018. Plaintiffs subsequently stipulated to dismiss certain allegations and claims against Insys, and the motion to dismiss was withdrawn. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Cantone. On or about June 15, 2017, we received service of a complaint filed by Angela Mistrulli Cantone and Philip L. Cantone in the State Court of South Carolina, County of Greenville, C.A. No.: 2017-CP-23 against Insys Therapeutics, Inc., Linden Care, LLC, Aathirayen Thiyagarajah, M.D. and Spine and Pain, LLC. The plaintiffs' complaint alleges medical negligence, negligence, negligent misrepresentation, unjust enrichment, common law fraud, unfair and deceptive trade practices, aiding and abetting and loss of consortium. We filed a motion to dismiss, which the Court denied. We filed our answer on November 14, 2017. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Ballou. On or about September 1, 2017, Carey Ballou filed a complaint in the circuit Court of Johnson County, Kansas, Case No. 17CV05004, against Insys Therapeutics, Inc., Insys Pharma, Inc., Torgny Andersson, Mid-America Physiatrist, P.A., Steven Simon M.D., Donna Ruck, Pharma Consultants KC, LLC, AmerisourceBergen Corporation, and Morris & Dickson Co., LLC. The plaintiffs bring claims against Insys for negligence, common law fraud, negligent misrepresentation, unfair and deceptive trade practices, unjust enrichment, conspiracy, and aiding and abetting. On December 26, 2017, Plaintiff filed a second amended complaint, which added as defendants certain former officers and employees. Insys moved to dismiss the second amended complaint on February 26, 2018. On August 22, 2018, the Court held oral argument on the motion to dismiss. The motion remains pending. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Whitham. On or about September 1, 2017, James "Mike" Whitham and Ashley Whitham filed a complaint in the Circuit Court of Johnson County, Kansas, Case No. 17CV05005, against Insys Therapeutics, Inc., Insys Pharma,

Inc., Torgny Andersson, Mid-America Physiatrist, P.A., Steven Simon M.D., Donna Ruck, Pharma Consultants KC, LLC, AmerisourceBergen Corporation, and Morris & Dickson Co., LLC. The plaintiff brings claims against Insys for negligence, common law fraud, negligent misrepresentation, unfair and deceptive trade practices, unjust enrichment, loss of consortium, conspiracy, and aiding and abetting. On December 26, 2017, Plaintiff filed a second amended complaint, which added as defendants certain former officers and employees. Insys moved to dismiss the second amended complaint on February 26, 2018. On August 22, 2018, the Court held oral argument on the motion to dismiss. The motion remains pending. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Hartsfield. On or about October 4, 2017, Cheryl Hartsfield filed a complaint in the Circuit Court of Pulaski County, Arkansas, Case No. 60CV-17-5581, against Insys Therapeutics, Inc., Linden Care, LLC, Mahmood Ahmad, and United Pain Care, Ltd. The plaintiff brings claims against Insys for common law fraud and deceit, breach of fiduciary duty, violations of the Arkansas deceptive trade practices act, civil conspiracy, acting in concert, and negligence. Insys filed its answer to the complaint on November 27, 2017. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Jordan. On January 5, 2018, Bobby Ray Jordan, individually and as Special Administrator of the Estate of Doris L. Jordan, deceased, filed a complaint in the District Court of Leavensworth County, Kansas against Insys Therapeutics, Inc., Insys Pharma, Inc., Torgny Andersson, Mid-America Physiatrist, P.A., Steven Simon, M.D., Donna Ruck, Pharma Consultants KC, LLC, John N. Kapoor, Michael L. Babich, and Alec Burlakoff. The plaintiff brings claims against Insys for negligence, conspiracy to commit fraud and breach of fiduciary duty, negligent misrepresentation, unfair and deceptive trade practices, unjust enrichment, survival action, and wrongful death action. On January 31, 2018, Insys moved to consolidate this case with the Ballou and Witham actions, which the Court denied. On April 16, 2018, we moved to transfer venue to Johnson County, Kansas, and on May 14, 2018, we moved to dismiss the case. The Court denied both motions. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Mencucci. On February 23, 2018, Lisa Mencucci and Angelo Mencucci filed a complaint in the Superior Court of Providence, Rhode Island against Insys Therapeutics, Inc. and Jerrold Rosenberg, M.D. Plaintiffs bring claims against Insys for common law fraud, common law fraud and misrepresentation – punitive damages, conscious misrepresentation involving risk of physical harm, conscious misrepresentation involving risk of physical harm – punitive damages, Rhode Island General Law 9-1-2, Rhode Island General Law 9-1-2 – punitive damages, negligent misrepresentation, negligent misrepresentation involving risk of physical harm, negligence, and violation of the Rhode Island Deceptive trade practices act. Our answer to the Complaint was filed on April 26, 2018. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Hemmings. On March 21, 2018, William Hemmings filed a complaint in the United States District Court for the Northern District of Illinois against Insys Therapeutics, Inc. Plaintiff brings claims against Insys for negligence, fraud, and consumer fraud. On May 16, 2018, we filed an answer and a motion to dismiss. On January 23, 2019, the Court denied our motion to dismiss. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Hampton. On March 8, 2018, Scott Hampton, as Heir, Executor and Personal Representative of the Estate of Diana Hampton, individually and on behalf of his minor children I.S. and S.M., filed a complaint in Clark County, Nevada District Court against Steven A. Holper and Insys Therapeutics, Inc. Plaintiffs bring claims against Insys for wrongful death: negligence, survivor action: negligence, wrongful death: intentional/reckless conduct, survivor's action: intentional/reckless conduct, negligence, strict liability – defect in design – product liability, strict liability – failure to warn, and punitive damages. On April 16, 2018, Insys removed this case to the United States District Court for the District of Nevada. On April 17, 2018, the District Judge entered an Order to Show Cause why the case should not be remanded to state court, and subsequently remanded the case to state court. On June 26, 2018, Insys moved to dismiss the case. On June 29, 2018, plaintiffs sought leave to amend the complaint, which the court granted. Oral argument on the motion occurred on July 30, 2018, and the Court denied the motion. Plaintiffs filed a second amended complaint on September 7, 2018 and Insys subsequently moved to dismiss the second amended

complaint. On November 13, 2018, the Court granted in part and denied in part our motion to dismiss. Plaintiffs subsequently filed a third amended complaint and we filed our answer on January 18, 2019. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Munson. On April 4, 2018, Morgan Michelle Munson and Christopher Edward Munson filed a complaint in Duval County, Florida Circuit Court against Insys Therapeutics, Inc. and Linden Care, LLC. Plaintiffs bring claims against Insys for civil conspiracy, negligence, and aiding and abetting. On May 21, 2018, Insys removed the case to the United States District Court for the Middle District of Florida. On June 12, 2018, plaintiffs filed a motion for leave to file amended complaint and to remand. We filed our response in opposition on July 10, 2018. On November 6, 2018, the Court denied plaintiffs' motion for leave to file amended complaint and to remand. It also dismissed plaintiffs' complaint without prejudice as a "shotgun" pleading. Plaintiffs subsequently filed an amended complaint and we moved to dismiss the amended complaint on January 22, 2019. We intend to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Tisher/Starling. On May 4, 2018, Herbert Tisher and Jane Tisher filed a complaint in the Superior Court of the State of Delaware against Insys Therapeutics, Inc., Compassionate Pain Management, LLC, Compassionate Diagnostics, LLC d/b/a Cutting Edge Treatment Center, and Eva C. Dickinson, M.D. On July 3, 2018, the Complaint was amended to add as Plaintiffs James Starling, Jr. and Pamela Starling, and to remove as a Plaintiff Jane Tisher. The Amended Complaint also added as defendants Michael J. Babich, Alec Burlakoff, Michael J. Gurry, Richard Simon, Sunrise Lee, Joseph A. Rowan, John N. Kapoor, Rodney Village Pharmacy LLC, Hometown Drug LLC, and Sanjana Company, LLC. Plaintiffs bring claims against Insys for general negligence, negligent misrepresentation, common law fraud, aiding and abetting, unjust enrichment, and civil conspiracy. We filed an answer to the amended complaint on August 31, 2018. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Kyle. On May 10, 2018, Jeffrey A. Kyle and Polly Kyle filed a complaint in the State of New Hampshire Superior Court, Stratford, SS, against Christopher Clough, PA, Dr. John J. Schermerhorn, Dr. O'Connell's Pain Care Centers, Inc., and Insys Therapeutics, Inc. Plaintiffs bring claims against Insys for negligence and loss of consortium. Insys filed its answer to the complaint on July 13, 2018. On September 20, 2018, the Court issued an order that appears to dismiss the complaint against all the defendants. As Insys had not previously sought dismissal, however, Insys filed a motion for clarification of the Court's dismissal order and a motion for summary judgment. The Court denied the motion for clarification and granted the motion for summary judgment, but granted leave for plaintiff to amend the complaint to add a fraud claim. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Gruenspecht. On June 14, 2018, Mark Gruenspecht filed a complaint in the Supreme Court of the State of New York, County of New York, against Upper East Side Pain Medicine, P.C., Gordon Freedman, M.D., and Insys Therapeutics, Inc. Plaintiff brings a single untitled claim against Insys, asserting, among other things, that Insys's conduct constituted fraud, deception, misrepresentation, wantonness, negligence, and gross negligence. The complaint was served on June 27, 2018. We filed a motion to dismiss the complaint on October 5, 2018. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Hanson. On July 10, 2018, Cynthia L. Hanson filed a complaint in the Circuit Court of Johnson County, Kansas against Insys Therapeutics, Inc., Insys Pharma, Inc., Torgny Andersson, Mid-America Physiatrist, P.A., Steven Simon, M.D., Donna Ruck, Pharma Consultants KC, LLC, AmerisourceBergen Corporation, and Morris & Dickson Co., LLC. Plaintiff brings bring claims against Insys for negligence, conspiracy to commit fraud and breach of fiduciary duty, negligent misrepresentation, unfair and deceptive trade practices, unjust enrichment, survival action, and wrongful death action. On July 23, 2018, we accepted service and we filed a motion to dismiss the complaint on September 21, 2018. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Kelley. On July 18, 2018, Michael and Julie Kelley filed a complaint in the Common Pleas Court of Erie County, Ohio against Insys Therapeutics, Inc., Insys Pharma, Inc., and Insys Manufacturing, LLC. Plaintiffs bring claims against Insys for negligence, negligent misrepresentation, strict products liability due to inadequate warning, strict products liability defective due to inadequate warning pursuant to Ohio Revised Code Section 2307.76, strict products liability defect due to design defect, strict products liability defective pursuant to Ohio Revised Code Section 2307.75, fraud, Ohio Consume Sales Practices Act pursuant to Ohio Revised Code Chapter 1345, false advertising, unjust enrichment, loss of consortium, negligent infliction of emotional distress, and punitive damages. We were served with the complaint on July 30, 2018. On July 31, 2018, we removed the case to the United States District Court for the Northern District of Ohio. On September 21, 2018, we moved to dismiss the complaint. On January 25, 2019, the Court granted in part and denied in part our motion to dismiss. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Mascio. On July 31, 2018, Robin Mascio filed a complaint in the Supreme Court of the State of New York, County of New York, against Todd R. Schlifstein D.O., Jeffrey Goldstein M.D., Kathryn E. Moran P.A., Aja Snow P.A., Fountain Medical Group Holdings Inc., Fountain Medical Holdings Inc., EGA medical Management LLC, NACSIP Inc., NACSIP Inc. d/b/a Lake Mahopac Pharmacy & Surgical, Nagi Wissa, Dorvit Pharmacy Inc. d/b/a The Cure Pharmacy, Third Avenue Lerman Pharmaceutics, Inc., Vishi Pharmacy Corp. d/b/a The Cure Pharmacy, David Lerman, and Insys Therapeutics, Inc. Plaintiff brings claims against Insys for fraud, negligent representation, lack of informed consent, and an unspecified claim that may be a claim for negligence and/or gross negligence. Insys was served with the complaint on October 12, 2018. On January 14, 2019, we filed a motion to dismiss. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Wagner**.** On August 21, 2018, Dorrie Wagner filed a complaint in the County of Greenville, South Carolina Court of Common Pleas against Insys Therapeutics, Inc., John N. Kapoor, Michael L. Babich, Alec Burlakoff, Linden Care, LLLC, Aathirayen Thiyagarajah, M.D., Pain and Spine Consultants, PA and Spine and Pain, LLC. Plaintiff brings claims against Insys for general negligence, aiding and abetting, unjust enrichment, and for violations of the unfair and deceptive trade practices act. On September 10, 2018, plaintiffs filed a second complaint against the same defendants, which includes the same claims. Insys filed its answer to the complaint on October 17, 2018. We continue to vigorously defend this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Crownover. On October 8, 2018, Michelle Crownover, Brandon Crownover, and Bailee, Makena, and Payton Crownover filed a complaint in the Franklin County, Ohio, Court of Common Pleas against Jimmy M. Henry, M.D., Midwest Pain Spine and Pain Consultants, LLC, Thomas Tadsen, Shaffer Pharmacy, Inc., Christopher Dinoffria, Avella of Columbus, Inc., and Insys Therapeutics, Inc. Plaintiffs also included Aetna, Inc. and Anthem Blue Cross/Blue Shield as involuntary plaintiffs. Plaintiffs bring claims against Insys for civil conspiracy, fraud, civil liability for criminal conduct, negligence, and loss of consortium. Insys filed an answer to the complaint. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Tudhope. On October 17, 2018, Carole Tudhope and John Tudhope filed a complaint in the Circuit Court of Jackson County, Missouri at Independence, against Insys Therapeutics, Inc., Insys Pharma, Inc., John N. Kapoor, Michael L. Babich, Alec Burlakoff, , Mid-America Physiatrist, P.A., Steven Simon, M.D., Gregory Buhler, D.O., Kathryn McConnaughey, Pharma Consultants KC, LLC, University of Kansas Hospital Authority d/b/a Cancer Center Pharmacy East, Amerisourcebergen Drug Corporation, and Morris & Dickson Co., LLC. Plaintiffs bring claims against Insys for negligence, conspiracy to commit fraud and breach of fiduciary duty, negligent misrepresentation, unfair and deceptive trade practices, unjust enrichment, and loss of consortium. On November 21, 2018, a co-defendant removed this case to the United States District Court for the Western District of Missouri. The co-defendant also requested that the case be transferred to MDL No. 2804, currently pending in the Northern District of Ohio. The case is stayed pending the Joint Panel on Multidistrict Litigation's decision on that request. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Perry. On October 25, 2018, Colleen Perry filed a complaint in the State of New Hampshire Superior Court, Strafford, against Insys Therapeutics, Inc. Plaintiff brings a claim for fraud, consumer protection, and negligence. On December 19, 2018, Insys removed this case to the United States District Court for the District of New Hampshire. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Farquhar. On November 5, 2018, Timothy and Kelley Farquhar filed a complaint in the Circuit Court of Johnson County, Kansas against Insys Therapeutics, Inc., Insys Pharma, Inc., Torgny Andersson, Mid-America Physiatrists, P.A., Steven Simon, M.D., Donna Ruck, Pharma Consultants KC, LLC, AmerisourceBergen Drug Corp., Morris & Dickson Co., LLC, John N. Kapoor, Michael L. Babich, and Alex Burlakoff. Plaintiff brings bring claims against Insys for negligence, conspiracy to commit fraud and breach a fiduciary duty, negligent misrepresentation, unfair and deceptive trade practices (Kansas Consumer Protection Act), unjust enrichment, and loss of consortium. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Cordes. On December 18, 2018, Eleanor Cordes filed a complaint in the Superior Court of New Jersey, Warren County, against Dr. Kenneth Sun, New Jersey Progressive Pain Solutions LLC, Insys Therapeutics, Inc., Linden Care LLC, Michelle Breitenbach, and Jeffrey Pearlman. Plaintiff brings claims against Insys for negligence and fraud. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Haddock. On December 21, 2018, Iliana Haddock filed a complaint in the Circuit Court, in and for the Fifteenth Judicial Circuit of Palm Beach County, against Insys Therapeutics, Inc. and My Community Pharmacy of Boynton, Inc. d/b/a My Best Pharmacy. Plaintiff brings claims against Insys for negligence and strict products liability design defect. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

***Sorrentino*.** On December 21, 2018, Paula Sorrentino sent a letter to Insys Therapeutics, Inc. alleging that she sustained injuries by reason of Insys's negligence and improper marketing and promotion and distribution of SUBSYS®. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Langlois. On January 2, 2019, Pamela Langlois filed a complaint in the State of New Hampshire Superior Court, Stratford, against Insys Therapeutics, Inc. Plaintiff brings claims for fraud, consumer protection, and negligence and civil conspiracy. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Nicholson. On January 16, 2019, Peter Nicholson filed a complaint in the Superior Court of Providence, Rhode Island, against Insys Therapeutics, Inc. and Jerrold Rosenberg, M.D. Plaintiff brings claims against Insys for common law fraud and misrepresentation, conscious misrepresentation involving risk of physical harm, violation of R.I.G.L. 9-1-2, negligent misrepresentation, negligent misrepresentation involving risk of physical harm, negligence, violation of R.I.G.L. 6- 13.1-1 et seq. – Rhode Island Deceptive Trade Practices Act, and punitive damages relating to certain claims. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

DeRuiter/Medina/Santiago/Mitchell. On January 17, 2019, Frances DeRuiter, Daisey Medina, Marysol Santiago, Jennifer Mitchell, and Douglas Mitchell filed a complaint in the Superior Court of Providence, Rhode Island against Insys Therapeutics, Inc. and Jerrold Rosenberg, M.D. Plaintiffs bring claims against Insys for common law fraud and misrepresentation, conscious misrepresentation involving risk of physical harm, violation of R.I.G.L. 9-1-2, negligent misrepresentation, negligent misrepresentation involving risk of physical harm, negligence, violation of R.I.G.L. 6- 13.1-1 et seq. – Rhode Island Deceptive Trade Practices Act, and punitive damages relating to certain claims. We anticipate vigorously defending this matter and based on currently available information, we do not believe any resolution of this matter, when taken individually, will have a material adverse effect on our business, financial position, or future results of operations.

Except as it pertains to (i) the final settlements addressed above, (ii) the accrual of $150,000,000 related to the DOJ Investigation, (iii) the accrual of $14,000,000 related to the potential settlement of insurance litigation, and (iv) the potential for damages in the federal securities litigation and derivative action that we believe could be covered by in whole or part our director and officers insurance policies (once we have met any applicable retainage requirement under the applicable policy), we believe that the probability of unfavorable outcome or loss related to all of the above litigation matters and an estimate of the amount or range of loss, if any, from an unfavorable outcome are not determinable at this time. We believe we have meritorious legal positions and will continue to represent our interests vigorously in these matters but the range of possible outcomes on these matters is very broad and, unless otherwise provided above, we are not able to provide a reasonable estimate of our potential liability, if any, nor are we able to predict the outcome of each litigation matter.

The expense and time required to respond to each of these litigation matters and legal proceedings and related actions, defending any claims raised, and any resulting fines, restitution, damages and penalties, or settlement payments, as well as any related actions brought by shareholders or other third parties, could have a material impact on our reputation, business and financial condition and divert the attention of our management from operating our business.

8. Equity

Preferred Stock

In August 2014, we entered into a Rights Agreement with respect to a newly-designated Series A Junior Participating Preferred Stock. In connection with the Rights Agreement, our Board of Directors declared a dividend distribution of the right to purchase one one-hundredth of one share of our Series A Junior Participating Preferred Stock, par value $0.001 per share (a “Right”), for each outstanding share of common stock, par value $0.01 per share, held by the stockholders of the Company at the close of business on September 1, 2014 (the “Record Date”).

Each Right entitles the registered holder to purchase from us one one-hundredth of a share of preferred stock (each, a "Preferred Share" and collectively, the "Preferred Shares") at a price of $160 per one one-hundredth of a Preferred Share (the "Purchase Price"), subject to adjustment. Each one one-hundredth of a Preferred Share has the designations, powers, privileges, preferences, rights, qualifications, limitations and restrictions that are designed to make it the economic equivalent of one share of common stock.

The Rights will not become exercisable until the earlier to occur of the close of business on (i) the tenth calendar day following acquisition by any person, entity or group of affiliated or associated persons of beneficial ownership of 15% or more of our outstanding shares of common stock (an "Acquiring Person") or (ii) the tenth business day (or such later date as may be determined by action of the Board prior to such time as any person or entity becomes an Acquiring Person) following the date of commencement of, or the first announcement of, an intention to commence, a tender offer or exchange offer, the consummation of which would result in any person or entity or group of persons or entities acting in concert becoming an Acquiring Person (the earlier of such dates being called the "Distribution Date"). Until the Distribution Date, the Rights will be transferable with and only with our Common Shares. The Rights will expire ten years after the execution of the Rights Agreement unless the Rights are earlier redeemed or exchanged by us.

Each Preferred Share is entitled to a minimum preferential quarterly dividend payment equal to the greater of $1.00 per share or 100 times the aggregate per share price of all cash and non-cash dividends declared per share of common stock. In the event of liquidation, the holders of the Preferred Shares would be entitled to a minimum preferential liquidation payment of $100 per share plus an amount equal to accrued and unpaid dividends and distributions thereon, provided that the Preferred Shares would be entitled to receive an aggregate amount per share equal to 100 times the aggregate amount to be distributed per share to holders of common stock. Each Preferred Share has 100 votes, voting together with the common stock.

Common Stock

The holders of each share of common stock shall be entitled to one vote per share on all matters to be voted upon by the Company's stockholders.

Stock Repurchase Program

On November 5, 2015, we announced a stock repurchase program. The stock repurchase program authorizes up to $50 million in repurchases of common stock, and any shares acquired will be retired as repurchased. This program was effective immediately and has no planned expiration date. The following table summarizes our share repurchase activity for our share repurchase program:

	Number of Shares Purchased	Cost of Share Purchases
Shares purchased at December 31, 2016	1,403,275	$ 32,558,000
Shares purchased during 2017	—	—
Shares purchased at December 31, 2017	1,403,275	$ 32,558,000
Shares purchased during 2018	—	—
Shares purchased at December 31, 2018	1,403,275	$ 32,558,000

As of December 31, 2018, we had $17,442,000 remaining under this program.

9. Stock-based Compensation

We currently have the following stock-based incentive plans:

2013 Employee Stock Purchase Plan

The 2013 Employee Stock Purchase Plan (the "ESPP") was adopted by our Board of Directors and approved by our stockholders, and became effective in connection with our initial public offering in May 2013. Under the terms of the ESPP, eligible employees are granted a purchase right to purchase shares of our common stock that cannot exceed 15% of their earnings, nor exceed the Board of Director defined limits on the number of our common

shares that can be offered under the ESPP. The purchase right entitles the eligible employee to purchase shares at the lesser of an amount equal to 85% of the fair market value of the shares on the offering date or 85% of the fair market value of the shares on the purchase date. The ESPP authorized the issuance of 530,400 shares of common stock pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2014 through January 1, 2023, by the least of (a) 1% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year, (b) 600,000 shares (200,000 on a pre-split basis), or (c) a number determined by our Board of Directors that is less than (a) and (b). The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Internal Revenue Code of 1986, as amended (the "Code"). As of December 31, 2018, 1,888,631 shares of common stock have been purchased under the ESPP.

2013 Equity Incentive Plan

The 2013 Equity Incentive Plan (the "2013 Plan") is the successor to and continuation of the 2006 Equity Incentive Plan and the Insys Pharma, Inc., Amended and Restated Equity Incentive Plan. The 2013 Plan was adopted by our Board of Directors and approved by our stockholders, and became effective in connection with our initial public offering in May 2013. The 2013 Plan provides for the grant of stock awards, including stock options, restricted stock, stock appreciation rights, performance units, performance shares and other stock awards, to our employees, directors and consultants. The number of shares of common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2014 through January 1, 2023, by the lesser of (a) 4% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year; or (b) a number of shares of common stock that may be determined each year by our Board of Directors that is less than the preceding clause (a). As of December 31, 2018, options to purchase 6,127,202 shares of common stock were outstanding and 8,680,179 shares remained available for future grant.

Amounts recognized in the Consolidated Statements of Comprehensive Income (Loss) with respect to our stock-based compensation plans were as follows (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Research and development	$ 2,962	$ 3,217	$ 3,931
General and administrative	9,054	12,798	17,658
Total cost of stock-based compensation	$ 12,016	$ 16,015	$ 21,589

Included in stock-based compensation for the years ended December 31, 2018, 2017 and 2016 was approximately $0, $1,450,000 and $3,878,000, respectively, of expense associated with the accelerated vesting of option awards related to terminated employees.

The following table summarizes stock option activity during the year ended December 31, 201 8:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in millions)
Outstanding as of December 31, 2015	7,138,089	$ 7.57		
Granted	2,337,043	$ 14.86		
Cancelled	(1,536,538)	$ 18.67		
Exercised	(637,721)	$ 5.96		$ 7.0
Outstanding as of December 31, 2016	7,300,873	$ 12.36		
Granted	2,577,650	$ 10.73		
Cancelled	(2,059,826)	$ 17.76		
Expired	(9,834)	$ 20.13		
Exercised	(1,476,448)	$ 3.08		$ 10.6
Outstanding as of December 31, 2017	6,332,415	$ 12.10		
Granted	1,456,700	$ 7.88		
Cancelled	(1,214,810)	$ 13.29		
Expired	(4,912)	$ 8.54		
Exercised	(442,191)	$ 2.53		$ 2.3
Outstanding as of December 31, 2018	6,127,202	$ 11.55	7.1	$ 1.2
Vested and exercisable as of December 31, 2018	3,798,636	$ 12.33	6.1	$ 1.2

The aggregate intrinsic value for stock options outstanding and exercisable is defined as the positive difference between the fair market value of our common stock and the exercise price of the stock options. As of December 31, 2018, we expect to recognize $13,852,000 of stock-based compensation for our outstanding options over a weighted-average period of 2.2 years.

The total fair value of shares vested for the years ended December 31, 2018, 2017, and 2016 was $9,488,000, $14,511,000 and $19,970,000, respectively.

Cash received from option exercises under all share-based payment arrangements for the years ended December 31, 2018, 2017, and 2016 was $1,096,000, $4,545,000 and $3,803,000, respectively. For the year ended December 31, 2016, we recorded net reductions of $122,000 respectively, of our federal and state income tax liability, with an offsetting credit to additional paid-in capital resulting from the excess tax benefits related to exercised stock options. No such amounts were recognized during the years ended December 31, 2018 and 2017, due to the implementation of ASU 2016-09.

Stock Option Valuation Information

The weighted-average assumptions used to estimate the fair value of employee stock options granted during the periods presented are as follows:

	2018	2017	2016
Expected volatility	56.7%	57.8%	63.3%
Risk-free interest rate	2.8%	2.2%	1.6%
Expected term (in years)	6.9	6.9	7.0
Expected dividend yield	0.0%	0.0%	0.0%

For the years ended December 31, 2018, 2017, and 2016, the weighted-average estimated fair value per option granted was $4.65, $6.32 and $9.20, respectively.

Restricted Stock Units

From time to time we grant restricted stock units to certain employees and directors. Restricted stock units are valued at the closing market price of our common stock on the day of grant and the total value of the units is recognized as expense ratably over the vesting period of the grants. The following table summarizes restricted stock unit activity during the year ended December 31, 2018:

	Number of Shares	Weighted Average Grant-Date Fair Value Per Unit
Outstanding as of December 31, 2016	—	$ —
Granted	481,250	$ 10.74
Cancelled	(85,350)	$ 12.54
Exercised	(14,000)	$ 12.65
Outstanding as of December 31, 2017	381,900	$ 10.27
Granted	381,820	$ 7.92
Cancelled	(121,690)	$ 8.54
Exercised	(106,202)	$ 10.17
Outstanding as of December 31, 2018	535,828	$ 9.01

As of December 31, 2018, we expect to recognize $2,955,000 of stock-based compensation for outstanding restricted stock units over a weighted-average period of 1.7 years.

10. Income Taxes

Income tax expense (benefit) consists of the following (in thousands):

	Years Ended December 31,		
	2018	2017 (As Revised)	2016
Current income taxes:			
Federal	$ (1,931)	$ (12,474)	$ 5,916
State and local	81	(188)	554
Total current income tax	(1,850)	(12,662)	6,470
Deferred income taxes:			
Federal	(45)	19,237	(7,762)
State and local	(5)	3,065	2,126
Total deferred income tax	(50)	22,302	(5,636)
Income tax expense (benefit)	$ (1,900)	$ 9,640	$ 834

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act. The 2017 Tax Act made broad and complex changes to the U.S. tax code, including, but not limited to: reduced the federal statutory income tax rate from 35% to 21% effective January 1, 2018, eliminated the ability to carryback NOLs arising after 2017 and instead would permit such NOLs to be carried forward indefinitely, repealed the domestic production deduction, further limited deductions for executive compensation and legal settlements, accelerated expensing for capital expenditures, and reduced the orphan drug credit to 25% from 50% of qualified clinical testing expenses. During the year ended December 31, 2017, we recognized, as a provisional estimate, a $7.5 million non-cash tax expense through income from continuing operations for the re-measurement of deferred tax assets and liabilities due to changes in tax laws included in the 2017 Tax Act. This re-measurement of deferred taxes had no impact on cash flows.

On December 22, 2017, the SEC issued *Staff Accounting Bulletin No. 118* ("SAB 118") which addressed income tax accounting implications of the 2017 Tax Act. The purpose of SAB 118 was to address any uncertainty or diversity of view in applying ASC Topic 740, "Income Taxes" in the reporting period in which the 2017 Tax Act was enacted. SAB 118 addressed situations where the accounting is incomplete for certain income tax effects of the 2017 Tax Act upon issuance of a company's financial statements for the reporting period which includes the enactment date. SAB 118 allowed for a provisional amount to be recorded if it is a reasonable estimate of the impact of the 2017 Tax Act. Additionally, SAB 118 allowed for a measurement period to finalize the impacts of the 2017 Tax Act, not to extend beyond one year from the date of enactment.

Due to the timing of the enactment and the complexity involved in applying the provisions of the 2017 Tax Act, we made reasonable estimates for certain effects of the 2017 Tax Act and recorded provisional amounts in our financial statements as of December 31, 2017. The Company completed its analysis of the 2017 Tax Act in conjunction with the completion of the Company's tax returns for 2017 and recorded a $1.0 million reduction of tax expense during the year ended December 31, 2018.

Estimates were used in determining the balance of deferred tax assets and liabilities subject to changes in tax laws included in the 2017 Tax Act. In addition, estimates were used in determining the timing of reversals of deferred tax assets and liabilities in assessing the ability to realize certain deferred tax assets, which impacted the valuation allowance adjustment we recorded as part of the effects of the 2017 Tax Act. In conjunction with the completion of the Company's tax returns for 2017, additional analysis was performed to accurately determine the deferred tax assets and liabilities affected by the 2017 Tax Act, as well as determine the reversal pattern of such deferred tax assets and liabilities in assessing the ability to realize deferred tax assets. This analysis resulted in a gross $7.3 million reduction of the Company's deferred tax assets and liabilities for the year ended December 31, 2018, the impact of which is offset by a full valuation allowance.

Deferred Income Taxes

The tax effects of temporary differences and carry forwards that give rise to the deferred tax assets and liabilities are comprised of the following as of December 31 (in thousands):

	2018	2017 (As Revised)
Deferred income tax assets:		
NOLs and credits	$ 63,770	$ 38,725
Start-up expenditures	1,342	1,480
Stock-based compensation	7,365	6,439
Allowances	341	931
Expenses currently not deductible for tax purposes	8,467	6,345
Deferred revenue	—	251
Intangibles	1,055	—
Other	1,376	1,167
Gross deferred tax assets	83,716	55,338
Deferred income tax asset valuation allowance	(78,313)	(49,713)
Deferred income tax assets	5,403	5,625
Deferred income tax liabilities:		
Federal impact of state taxes	—	(643)
Property and equipment	(4,316)	(4,058)
Prepaid expenses	(1,087)	(924)
Net deferred income tax assets	$ —	$ —

As of December 31, 2018, we had approximately $112.3 million of federal NOLs and $233.8 million of state NOLs. With the exception of the federal NOLs that were generated in 2018 and can be carried forward indefinitely, $1.1 million of the federal NOLs and $41.0 million of state NOLs will begin to expire in 2030 and 2019, respectively. As of December 31, 2018, we had approximately $13.5 million of federal tax credits and $6.8 million of state tax credits, of which $0.4 million and $0.1 million will begin to expire in 2034 and 2030, respectively.

We record valuation allowances to reduce the book value of our deferred tax assets to amounts that are estimated on a more likely than not basis to be realized. In assessing the realization of deferred tax assets, we evaluate both positive and negative evidence with greater weight given to information that is objectively verifiable. Based on this evidence, we consider whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. We also consider the scheduled reversal of deferred tax liabilities, projected future taxable income or losses, and tax planning strategies in making this assessment. As a result of this evaluation, we increased the valuation allowance for deferred taxes by $28.6 million for the year ended December 31, 2018. The increase of a valuation allowance does not impact cash, nor does it preclude us from using our tax credits, loss carryforwards and other deferred tax assets in the future.

Effective Tax Rate Reconciliation:

Our federal statutory tax rate is 21.0%, while our effective tax rate was 1.5% for the year ended December 31, 2018, as set forth below:

	2018	2017 (As Revised)	2016
U.S. statutory tax rate	21.0%	35.0%	35.0%
Increase (reduction) of income taxes resulting from:			
State income taxes, net of federal benefit	(0.4)%	0.7%	(0.1)%
Non-deductible litigation expense	—	—	3.4%
Non-deductible and includible items	(0.1)%	(0.9)%	7.5%
Non-deductible lobbying expense	—	—	8.3%
Research and other credits	2.4%	1.3%	(63.5)%
Uncertain tax positions	1.5%	—	4.2%
Domestic manufacturing deduction	—	—	(14.6)%
Stock based compensation	(0.2)%	(1.3)%	5.1%
Tax exempt interest income	—	—	(1.5)%
Non-deductible settlement expenses	—	(24.3)%	—
Adjustment of net deferred tax assets for U.S. tax reform	0.1%	(3.5)%	—
Other	(0.1)%	0.0%	0.6%
Change in valuation allowance	(22.7)%	(11.4)%	25.5%
Total provision for income taxes	1.5%	(4.4)%	9.9%

The following is a reconciliation of the beginning and ending amounts of unrecognized tax benefits (in thousands):

	Years Ended December 31,	
	2018	2017 (As Revised)
Beginning balance	$ 7,788	$ 9,800
Additions based on current year's tax positions	22	17
Deductions based on prior year's tax positions	(2,999)	(2,584)
Additions based on prior year's tax positions	249	555
Ending balance	$ 5,060	$ 7,788

We establish reserves when it is more likely than not that we will not realize the full tax benefit of a position. We had a reserve of $5.1 million as of December 31, 2018, mostly related to tax credits of $2.1 million, and state and local income tax filing positions of $2.9 million. If recognized, $5.1 million would affect our effective tax rate.

Although it is reasonably possible that certain unrecognized tax benefits may increase or decrease within the next 12 months due to tax examination changes, settlement activities, expirations of statutes of limitations, or the impact on recognition and measurement considerations related to the results of published tax cases or other similar activities, we do not anticipate any significant changes to unrecognized tax benefits over the next 12 months. Approximately $0.8 million of interest has been included in income taxes and accounted for on the balance sheet related to unrecognized tax positions as of December 31, 2018.

We recently completed an examination in the U.S. for tax years 2014 and 2015. As a result of this examination, we reduced our uncertain tax benefit reserve by approximately $3.0 million and recognized a deferred tax asset of $1.1 million, which was offset by a full valuation allowance during the year ended December 31, 2018. Because of NOLs and research credit carryovers, substantially all of our tax years remain open to examination.

11. Net Income (Loss) per Share

Basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of common shares outstanding during the period. The diluted income (loss) per share further includes any common shares available to be issued upon exercise of outstanding stock options if such inclusion would be dilutive.

The following table sets forth the computation of basic and diluted net income (loss) per common share (in thousands, except per share amounts):

	Years Ended December 31,		
	2018	2017 (As Revised)	2016 (As Revised)
Historical net income (loss) per share - Basic			
Numerator:			
Net income (loss)	$ (124,507)	$ (226,835)	$ 7,590
Denominator:			
Weighted average number of common shares outstanding	74,073,665	72,636,780	71,639,856
Basic net income (loss) per common share	$ (1.68)	$ (3.12)	$ 0.11
Historical net income (loss) per share - Diluted			
Numerator:			
Net income (loss)	$ (124,507)	$ (226,835)	$ 7,590
Denominator:			
Weighted average number of common shares outstanding	74,073,665	72,636,780	71,639,856
Effect of dilutive stock options	—	—	2,527,125
Weighted average number of common shares outstanding	74,073,665	72,636,780	74,166,981
Diluted net income (loss) per common share	$ (1.68)	$ (3.12)	$ 0.10

The calculation of diluted net income (loss) per common share excludes the effects of 6,663,030, 6,714,315 and 2,596,324 outstanding stock options and restricted stock awards for the years ended December 31, 2018, 2017, and 2016, respectively, as the impact of these options was anti-dilutive.

12. Product Lines, Concentration of Credit Risk and Significant Customers

We are engaged in the business of developing and selling pharmaceutical products. In 2018, we have two product lines, SUBSYS® and SYNDROS®. Our CODM evaluates revenues and gross profits based on product lines and routes to market.

The following tables summarize our net revenue by product line, as well as the percentages of revenue by route to market (in thousands):

	Net Revenue by Product Line Years Ended December 31,		
	2018	2017	2016
SUBSYS ®	$ 78,759	$ 139,250	$ 242,275
SYNDROS ®	3,321	1,443	—
Total net revenue	$ 82,080	$ 140,693	$ 242,275

	Percent of Revenue by Route to Market Years Ended December 31,		
	2018	2017	2016
Pharmaceutical wholesalers	61%	63%	67%
Specialty pharmaceutical retailers	39%	37%	33%
	100%	100%	100%

All our products are sold in the United States of America.

Product shipments to our three largest pharmaceutical wholesaler customers accounted for 33%, 15% and 10% of total shipments and product shipments to two specialty pharmaceutical retailers accounted for 21% and 18% of total shipments for the year ended December 31, 2018. Product shipments to our three largest pharmaceutical wholesaler customers accounted for 26%, 18% and 11% of total shipments and product shipments to two specialty pharmaceutical retailers accounted for 23% and 14% of total shipments for the year ended December 31, 2017. Product shipments to our four largest pharmaceutical wholesaler customers accounted for 17%, 16%, 15% and 14% of total shipments and product shipments to one specialty pharmaceutical retailer accounted for 32% of total shipments for the year ended December 31, 2016. One pharmaceutical wholesalers' accounts receivable balance accounted for 58% of accounts receivable as of December 31, 2018, and two specialty pharmaceutical retailers' accounts receivable balances accounted for 19% and 11% of accounts receivable as of December 31, 2018. Three pharmaceutical wholesalers' accounts receivable balances accounted for 44%, 18% and 10% of accounts receivable as of December 31, 2017, and two specialty pharmaceutical retailers' accounts receivable balances accounted for 13% and 12% of accounts receivable as of December 31, 2017.

Currently, for SUBSYS®, we use one vendor as our sole supplier of the active pharmaceutical ingredient in this product.

Financial instruments that potentially subject us to concentrations of credit risk consist principally of cash and trade accounts receivable. We place our cash with high credit quality financial institutions and generally limit the amount of credit exposure to the amount of FDIC coverage. However, periodically during the year, we maintain cash in financial institutions in excess of the current FDIC insurance coverage limit of $250,000. We are exposed to credit risk in the event of a default by the institutions holding our cash to the extent recorded on the Consolidated Balance Sheet. We perform ongoing credit evaluations of our customers' financial condition but do not typically require collateral to support customer receivables. We establish an allowance for doubtful accounts based upon factors surrounding the credit risk of specific customers, historical trends and other information.

13. Supplemental Financial Information

A summary of additions and deductions related to the allowances for accounts receivable for the years ended December 31, 2018, 2017 and 2016 are as follows (in thousands):

	Balance at Beginning of Year	Charged to Costs and Expenses	Utilization	Balance at End of Year
Allowance for doubtful accounts:				
Year ended December 31, 2018	$ —	$ —	$ —	$ —
Year ended December 31, 2017	$ 685	$ —	$ (685)	$ —
Year ended December 31, 2016	$ 811	$ (96)	$ (30)	$ 685
Allowance for wholesaler discounts, prompt pay discounts, stocking allowances, and chargebacks:				
Year ended December 31, 2018	$ 3,832	$ 9,292	$ (9,814)	$ 3,310
Year ended December 31, 2017	$ 5,459	$ 14,525	$ (16,152)	$ 3,832
Year ended December 31, 2016	$ 7,556	$ 27,968	$ (30,065)	$ 5,459

14. Quarterly Results of Operations (Unaudited)

The following table sets forth a summary of our unaudited quarterly operating results for each of the last eight quarters in the period ended December 31, 2018. We have derived this data from our Unaudited Condensed Consolidated Interim Financial Statements that, in our opinion, have been prepared on substantially the same basis as the audited Consolidated Financial Statements contained elsewhere in this report and include all normal recurring adjustments necessary for a fair presentation of the financial information for the periods presented. These unaudited quarterly results should be read in conjunction with our Consolidated Financial Statements and notes thereto included elsewhere in this report. The operating results in any quarter are not necessarily indicative of the results that may be expected for any future period (in thousands, except per share data).

	Quarter Ended			
	12/31/18	9/30/18	6/30/18	3/31/18
Net revenue	$ 16,357	$ 18,346	$ 23,466	$ 23,911
Gross profit	$ 13,733	$ 15,967	$ 19,870	$ 21,707
Net loss (1)(2)	$ (46,293)	$ (30,494)	$ (27,350)	$ (20,370)
Net loss per common share:				
Basic	$ (0.62)	$ (0.41)	$ (0.37)	$ (0.28)
Diluted	$ (0.62)	$ (0.41)	$ (0.37)	$ (0.28)

	Quarter Ended			
	12/31/17 (As Revised)	9/30/17 (As Revised)	6/30/17 (As Revised)	3/31/17 (As Revised)
Net revenue	$ 31,485	$ 30,670	$ 42,576	$ 35,962
Gross profit (3)	26,874	23,198	38,655	31,323
Net loss (4) (5)	(45,927)	(166,280)	(8,088)	(6,540)
Net loss per common share:				
Basic	$ (0.63)	$ (2.28)	$ (0.11)	$ (0.09)
Diluted	$ (0.63)	$ (2.28)	$ (0.11)	$ (0.09)

(1) The fourth quarter of 2018 includes an accrual of $14,000 related to potential settlement of insurance litigation.
(2) The third quarter of 2018 reflects an $1,123 of out-of-period income tax benefit related to 2017.
(3) The fourth quarter of 2017 includes an allowance of $2,100 for excess and obsolete inventory as the result of a change in estimate.

(4) The third quarter of 2017 includes an accrual of $150,000 related to the DOJ Investigation.
(5) The fourth quarter of 2017 includes a provisional tax expense of $7,500 related to the 2017 Tax Act, and an increase in tax expense associated with the accrual of $22,600 related to the valuation allowance against deferred tax assets.

15. Subsequent Events

On January 30, 2019, we received insurance proceeds of approximately $3.9 million for the reimbursement of costs and expenses associated with shareholder litigation.

As discussed in Note 7, in February 2019, we, through our manufacturing subsidiary, entered into a further amendment to our Renaissance manufacturing and supply agreement. This amendment effectively eliminates any prior and future minimum purchase (and batch) obligations that had been set forth in the amendment dated April 2018. In addition, we entered into an Asset Purchase Agreement in which we agreed to sell, and Renaissance agreed to purchase, certain of our manufacturing equipment. In accordance with ASC 855, Subsequent Events, this amendment is not reflected in these Consolidated Financial Statements. The amendment will result in a loss on disposal of property and equipment of approximately $0.9 million and will be reflected in our Interim Unaudited Condensed Financial Statements for the three months ended March 31, 2019.

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 President and Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that the Company's disclosure controls and procedures were effective as of December 31, 2018.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)). 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment, we used the criteria set forth in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control — Integrated Framework. Based on our assessment using those criteria, our management concluded that our internal control over financial reporting was effective as of December 31, 2018.

Our independent registered public accounting firm, BDO USA, LLP, has audited the effectiveness of our internal controls over financial reporting as of December 31, 2018, as stated in its audit report which is included herein.

Change in Internal Controls Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) that occurred during the quarter ended December 31, 2018, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within any company have been detected.

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Insys Therapeutics, Inc.
Chandler, Arizona

Opinion on Internal Control over Financial Reporting

We have audited Insys Therapeutics, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company and subsidiaries as of December 31, 2018 and 2017, and the related consolidated statements of comprehensive income (loss), stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated March 12, 2019, expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Item 9A, Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's 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. A company's 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 the transactions and dispositions of the assets of the company; (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 receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's 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.

/s/ BDO USA, LLP

Phoenix, Arizona
March 12, 2019

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be included in our Proxy Statement to be filed pursuant to Regulation 14A within 120 days after our year ended December 31, 2018 in connection with our 2019 Annual Meeting of Stockholders, or the 2019 Proxy Statement, and is incorporated herein by reference.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to employees, officers and directors, including our executive management team, such as our Chief Executive Officer and Chief Financial Officer. This Code of Business Conduct and Ethics is posted on our website at www.insysrx.com. We intend to satisfy the requirements under Item 5.05 of Form 8-K regarding disclosure of amendments to, or waivers from, provisions of the Code of Business Conduct and Ethics by posting such information on our website.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be included in the 2019 Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item will be included in the 2019 Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item will be included in the 2019 Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item will be included in the 2019 Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as part of this report.

(1) *Financial Statements*. The Consolidated Financial Statements listed on the index to Part II Item 8 of this Annual Report on Form 10-K are filed as a part of this Annual Report.

(2) *Financial Statement Schedules.* All financial statement schedules have been omitted since the information is either not applicable or required or is included in the Consolidated Financial Statements or notes thereof.

(3) *Exhibits.* Those exhibits marked with a (*) refer to exhibits filed or furnished herewith. The other exhibits are incorporated herein by reference, as indicated in the following list. Those exhibits marked with a (+) refer to management contracts or compensatory plans or arrangements. Portions of the exhibits marked with a (Ω) are the subject of a Confidential Treatment Request under 17 C.F.R. §§ 200.80(b)(4), 200.83 and 240.24b-2. Omitted material for which confidential treatment has been requested has been filed separately with the SEC.

Table of Contents

EXHIBIT INDEX

Exhibit Number	Description of Document
2.1	Agreement and Plan of Merger Among the Registrant, Insys Therapeutics, Inc. and ITNI Merger Sub Inc. dated October 29, 2010 (1)
3.1	Registrant's Amended and Restated Certificate of Incorporation (2)
3.2	Registrant's Amended and Restated Bylaws (3)
3.3	Certificate of Designation of Series A Junior Participating Preferred Stock (4)
4.1	Form of Common Stock Certificate of the Registrant (19)
4.2	Rights Agreement dated August 15, 2014 between the Insys Therapeutics, Inc. and Computershare Trust Company, N.A. (5)
10.1+	Form of Indemnity Agreement by and between the Registrant and its directors and officers (6)
10.2+	Insys Therapeutics, Inc. 2006 Equity Incentive Plan, as amended (7)
10.3+	Insys Pharma, Inc. Amended and Restated Equity Incentive Plan (8)
10.4+	2013 Equity Incentive Plan and Form of Stock Option Grant Notice and Form of Stock Option Agreement thereunder (9)
10.5+	2013 Employee Stock Purchase Plan (10)
10.6+	Amended and Restated Employment Agreement by and between the Registrant and Michael Babich dated April 18, 2013 (11)
10.7+	Employment Agreement by and between the Registrant and Darryl Baker dated April 18, 2013 (12)
10.8Ω	Manufacturing Agreement dated as of May 24, 2011 by and between the Registrant and DPT Lakewood, LLC, as amended on October 29, 2013 and April 30, 2015 (13)
10.9Ω	Letter Agreement dated April 23, 2012, amending the DPT Lakewood, LLC Manufacturing Agreement dated as of May 24, 2011 (14)
10.10	Amendment to Manufacturing and Supply Agreement, dated as of July 14, 2016 by and between the Registrant and DPT Lakewood, LLC (18)
10.11Ω	Amended and Restated Supply, Development & Exclusive Licensing Agreement dated as of October 30, 2015 by and between the Registrant and AptarGroup, Inc. (22)
10.12	Amendment to Restated Supply, Development & Exclusive Licensing Agreement dated as of April 6, 2017, by and between the Registrant and AptarGroup, Inc. (20)
10.13+	Non-Employee Director Compensation Policy (15)
10.14+	Employment Offer Statement effective January 31, 2014 by and between Registrant and Franc Del Fosse (16)
10.15+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Grant Agreement thereunder (19)

Exhibit Number	Description of Document
10.16+	Executive Employment Agreement, dated as of April 17, 2017, by and between the Registrant and Saeed Motahari (21)
10.17+	Executive Employment Agreement, dated as of August 7, 2017, by and between the Registrant and Andrew Long (23)
10.18+	Executive Employment Agreement, dated as of October 10, 2018, by and between the Registrant and Mark Nance (24)
10.19	Voting Trust Agreement by and among Insys Therapeutics, Inc., Dr. John N. Kapoor, Bessemer Trust Company of Delaware, N.A., as the initial trustee thereunder and certain other specified beneficiaries (25)
10.20	Registration Rights Agreement among Insys Therapeutics, Inc., Dr. John N. Kapoor and certain beneficiaries (26)
10.21	Amendment to Manufacturing and Supply Agreement, dated as of April 10, 2018 by and between the Registrant and Renaissance (27)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of BDO USA, LLP, Independent Registered Public Accounting Firm
24.1	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K)
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32*	Certification by Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (furnished herewith)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

(1) Previously filed as Exhibit 2.1 to the Company's Form S-1 Registration Statement (No. 333-173154) on March 30, 2011.
(2) Previously filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2014.
(3) Previously filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on May 9, 2016.
(4) Previously filed as 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on August 18, 2014.

(5) Previously filed as 4.1 to the Registrant's Current Report on Form 8-K filed with the SEC on August 18, 2014.
(6) Previously filed as Exhibit 10.1 to the Company's Form S-1 Registration Statement (No. 333-173154) on March 30, 2011.
(7) Previously filed as Exhibit 10.3 to the Company's Form S-1 Registration Statement (No. 333-173154) on March 30, 2011.
(8) Previously filed as Exhibit 10.4 to the Company's Form S-1 Registration Statement (No. 333-173154) on March 30, 2011.
(9) Previously filed as Exhibit 99.3 to the Company's Form S-8 Registration Statement (No. 333-188306) on May 2, 2013.
(10) Previously filed as Exhibit 99.4 to the Company's Form S-8 Registration Statement (No. 333-188306) on May 2, 2013.
(11) Previously filed as Exhibit 10.6 to the Company's Form S-1/A Registration Statement (No. 333-173154) on April 25, 2013.
(12) Previously filed as Exhibit 10.8 to the Company's Form S-1/A Registration Statement (No. 333-173154) on April 25, 2013.
(13) Previously filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2015.
(14) Previously filed as Exhibit 10.17 to the Company's Form S-1/A Registration Statement (No. 333-173154) on February 27, 2013.
(15) Previously filed as Exhibit 10.22 to the Company's Form S-1/A Registration Statement (No. 333-173154) on April 15, 2013.
(16) Previously filed as 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2014.
(17) Previously filed as Exhibit 4.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2014.
(18) Previously filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016.
(19) Previously filed as Exhibit 10.17 to the Company's Annual Report on Form 10-K for the year ended December 31, 2016.
(20) Previously filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017.
(21) Previously filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017.
(22) Previously filed as Exhibit 10.12 to the Company's Annual Report on Form 10-K for the year ended December 31, 2015.
(23) Previously filed as Exhibit 10.19 to the Company's Annual Report on Form 10-K for the year ended December 31, 2017.
(24) Previously filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the SEC on October 11, 2018.
(25) Previously filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the SEC on March 1, 2018.
(26) Previously filed as Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the SEC on March 1, 2018.
(27) Previously filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018.

ITEM 16. FORM 10-K SUMMARY

None.

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 on March 12, 2019.

Insys Therapeutics, Inc.

By /s/ Saeed Motahari
Saeed Motahari
President and Chief Executive Officer
(Principal Executive Officer)

By /s/ Andrew G. Long
Andrew G. Long
Chief Financial Officer
(Principal Financial Officer and
Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Andrew G. Long and Mark Nance, jointly and severally, his or her attorney-in-fact, with the power of substitution, for him or her 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 his or her 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 Annual Report on Form 10-K 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/ Saeed Motahari Saeed Motahari	President, Chief Executive Officer and Member of the Board of Directors *(Principal Executive Officer)*	March 12, 2019
/s/ Andrew G. Long Andrew G. Long	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 12, 2019
/s/ Steven Meyer Steven Meyer	Executive Chairman of the Board of Directors	March 12, 2019
/s/ Elizabeth Bolen Elizabeth Bolen	Member of the Board of Directors	March 12, 2019
/s/ Pierre Lapalme Pierre Lapalme	Member of the Board of Directors	March 12, 2019
/s/ Vaseem Mahboob Vaseem Mahboob	Member of the Board of Directors	March 12, 2019
/s/ Trudy Vanhove Trudy Vanhove	Member of the Board of Directors	March 12, 2019
/s/ Dr. Rohit Vishnoi Dr. Rohit Vishnoi	Member of the Board of Directors	March 12, 2019