# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 10-K

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

**For the fiscal year ended December 31, 2017**

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

**Commission File No. 001-36913**

# KemPharm, Inc.
**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **20-5894398** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(I.R.S. Employer Identification No.)** |
| **2500 Crosspark Road, Suite E126, Coralville, IA 52241** | **(319) 665-2575** |
| **(Address of Principal Executive Offices and Zip Code)** | **(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, $0.0001 par value** | **The NASDAQ Stock Market LLC (NASDAQ Global Market)** |

**Securities registered pursuant to Section 12(g) of the Act: None**

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

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

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. Yes ☒ No ☐

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $46,538,484, based upon the closing sales price for the registrant's common stock, as reported on the NASDAQ Global Market. The calculation of the aggregate market value of voting and non-voting common equity excludes 3,022,809 shares of common stock the registrant held by executive officers, directors and stockholders that the registrant concluded were affiliates of the registrant on that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of March 28, 2018, the registrant had 15,104,848 shares of common stock outstanding.

**Documents Incorporated by Reference**

Portions of the registrant's definitive proxy statement for its 2018 annual meeting of stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2017. Except with respect to information specifically incorporated by reference in this Annual Report on Form 10-K, the definitive proxy statement is not deemed to be filed as part of this Annual Report on Form 10-K.

**KEMPHARM, INC.**
**FORM 10-K**

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

*This Annual Report on Form 10-K, including the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations," contains forward-looking statements regarding future events and our future results that are subject to the safe harbors created under the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements relate to future events or our future financial performance. We generally identify forward-looking statements by terminology such as "may," "will," "would," "should," "expects," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "predicts," "assume," "intend," "potential," "continue" or other similar words or the negative of these terms. We have based these forward-looking statements largely on our current expectations about future events and financial trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described in "Risk Factors" and elsewhere in this report. Accordingly, you should not place undue reliance upon these forward-looking statements. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur, the timing of events and circumstances and actual results could differ materially from those anticipated in the forward-looking statements. Forward-looking statements contained in this report include, but are not limited to, statements about:*

- *the progress of, timing of and amount of expenses associated with our research, development and commercialization activities;*
- *the timing, conduct and success of our clinical studies for our product candidates;*
- *our ability to obtain U.S. and foreign regulatory approval for our product candidates and the ability of our product and product candidates to meet existing or future regulatory standards;*
- *our expectations regarding federal, state and foreign regulatory requirements;*
- *the therapeutic benefits and effectiveness of our product and product candidates;*
- *the size and characteristics of the markets that may be addressed by our product and product candidates;*
- *our ability to manufacture sufficient amounts of our product candidates for clinical studies and products for commercialization activities;*
- *our intention to seek to establish strategic collaborations or partnerships for the development or sale of our product and product candidates;*
- *our expectations as to future financial performance, expense levels and liquidity sources;*
- *the timing of commercializing our product and product candidates;*
- *our ability to compete with other companies that are or may be developing or selling products that are competitive with our product and product candidates;*
- *anticipated trends and challenges in our potential markets;*
- *our ability to attract and retain key personnel;*
- *our expectations as to future development, acquisition, procurement, maintenance, utilization or defense of any and all intellectual property; and*
- *other factors discussed elsewhere in this report.*

*The forward-looking statements made in this report relate only to events as of the date on which the statements are made. We have included important factors in the cautionary statements included in this report, particularly in the section entitled "Risk Factors" that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. Except as required by law, we do not assume any intent to update any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events or circumstances or otherwise.*

## NOTE REGARDING COMPANY REFERENCE

*Unless the context otherwise requires, we use the terms "KemPharm," "Company," "we," "us" and "our" in this Annual Report on Form 10-K to refer to KemPharm, Inc. We have proprietary rights to a number of trademarks used in this Annual Report on Form 10-K that are important to our business, including KemPharm, APADAZ, LAT and the KemPharm logo. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.*

## NOTE REGARDING MARKET AND INDUSTRY DATA

*This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties.*

*Any information in this Annual Report on Form 10-K provided by Symphony Health Solutions, or SHS, is an estimate derived from the use of information under license from the following SHS service: SHS Pharmaceutical Audit Suite (PHAST), in each case, for the period January 2012 to December 2017.*

## PART I

### ITEM 1. BUSINESS.

**Overview**

We are a specialty pharmaceutical company focused on the discovery and development of proprietary prodrugs to treat serious medical conditions through our Ligand Activated Therapy, or LAT™, platform technology. We utilize our proprietary LAT platform technology to generate improved versions of U.S. Food and Drug Administration, or FDA, approved drugs in the high need areas of attention deficit hyperactivity disorder, or ADHD, pain and other central nervous system, or CNS, disorders. Our co-lead clinical development candidates are KP415 and KP484, both based on a prodrug of methylphenidate, but with differing extended-release, or ER, effect profiles for the treatment of ADHD. In addition, we have received FDA approval for APADAZ™, an immediate-release, or IR, combination product of benzhydrocodone, our prodrug of hydrocodone, and acetaminophen, or APAP. We are also advancing KP201/IR, an APAP-free IR formulation of our benzhydrocodone prodrug. Both APADAZ and KP201/IR are intended for the treatment of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Key members of our senior management, while at New River Pharmaceuticals Inc., were instrumental in the development of VYVANSE, a prodrug of amphetamine indicated for ADHD, through FDA marketing approval. New River Pharmaceuticals, Inc. was acquired by Shire plc in 2007 and Vyvanse generated over $2.2 billion in sales in 2017.

We employ our LAT platform technology to discover and develop prodrugs that are new molecules that can improve one or more of the attributes of approved drugs, such as enhanced bioavailability, extended duration of action, increased safety and reduced susceptibility to abuse. A prodrug is a precursor chemical compound of a drug that is inactive or less than fully active, which is then converted in the body to its active form through a normal metabolic process. Where possible, we seek, in part, to develop prodrugs that will be eligible for approval under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FFDCA, otherwise known as a 505(b)(2) NDA, which allows us to rely on the FDA's previous findings of safety and effectiveness for one or more approved products, if we demonstrate such reliance is scientifically appropriate.

We intend to advance our pipeline of product candidates for the treatment of ADHD, pain and other CNS indications, and we anticipate reporting pivotal efficacy trial data for KP415 in 2018, pivotal efficacy trial data for KP484 in 2019 and human proof-of-concept, or POC, data for KP201/IR in 2019. Further, we anticipate reporting human POC data in 2019 for KP511/ER and KP511/IR, our ER and IR formulations of KP511, our prodrug of hydromorphone. In addition, we anticipate submitting a new drug application, or NDA, to the FDA for KP415 in the first quarter of 2019, potentially followed by an NDA for each of KP484, KP201/IR, KP511/ER and KP511/IR in 2019. We plan to employ our LAT platform technology and development expertise to develop additional product candidates that address unmet medical needs in large, established markets. We believe our product candidates may be eligible for composition-of-matter patent protection and we intend to use the 505(b)(2) NDA pathway when available, which we believe may reduce drug development time, risk and expense.

As of December 31, 2017, our patent portfolio consisted of 87 granted patents and 125 pending patent applications worldwide. Within that patent portfolio, we have received granted U.S. composition-of-matter patents covering KP201, KP201-related compositions-of-matter, and prodrugs underlying two of our other product candidates.

**Our Strategy**

Our goal is to be a leading specialty pharmaceutical company focused on the discovery and development of novel prodrugs. Key components of our strategy include, for example:

- ***Leverage our LAT platform technology to improve the attributes of widely-prescribed, approved drugs***. We plan to employ our LAT platform technology to discover and develop prodrugs that can improve one or more of the attributes of approved drugs that are widely-prescribed. We intend to discover and develop prodrugs of FDA-approved drugs in multiple therapeutic areas.

- ***Advance the development of our pipeline product candidates***. We plan to advance the development of our co-lead product candidates, KP415 and KP484, for the treatment of ADHD. We plan to report pivotal efficacy trial data for KP415 and KP484, in 2018 and 2019, respectively, and we plan to report POC data for KP201/IR, KP511/ER and KP511/IR in 2019. In addition, we are developing KP303, our prodrug of quetiapine, for the treatment of schizophrenia and other CNS disorders, KP606, our IR formulation of our prodrug of oxycodone, for the management of moderate to severe pain where the use of an opioid analgesic is appropriate, and KP746, our prodrug of oxymorphone, for the management of moderate to severe pain where the use of an opioid analgesic is appropriate.

- ***Continue to build a global intellectual property portfolio***. We intend to vigorously pursue composition-of-matter patent protection for our prodrugs in markets covering a majority of the global commercial opportunity.

- ***Commercialize APADAZ.*** We are evaluating potential U.S. commercialization options for APADAZ, including pursuing a commercial collaboration with pharmacy benefit managers who would agree to Tier 1 or equivalent reimbursement status, including the most favorable co-pay level in return for price parity with available generic products, or a partnership with a U.S.-based or global generic pharmaceutical manufacturer and distributor, or pursuing a strategic transaction. We may also license the international commercial rights to APADAZ to one or more collaborators.

**Our LAT Prodrug Platform Technology**

We employ our LAT platform technology to create prodrugs that are new molecules by chemically attaching one or more molecules, referred to as ligands, to an FDA-approved parent drug. We typically use ligands that have been demonstrated to be safe in toxicological studies or have been granted Generally Recognized as Safe, or GRAS, status by the FDA. When the prodrug is administered, human metabolic processes, such as those in the gastrointestinal, or GI, tract, separate the ligand from the prodrug and release the parent drug, which can then exert its therapeutic effect. We select ligands that, when combined with the parent drug, create prodrugs believed to have improved drug attributes while maintaining efficacy potentially equivalent to the parent drug.

We believe that our LAT platform technology offers the following potential benefits:

- ***Improved drug properties***. We seek to discover and develop prodrugs that are new molecules with potentially improved attributes over FDA-approved drugs, such as enhanced bioavailability, extended duration of action, increased safety and reduced susceptibility to abuse.

- ***Composition-of-matter patent protection***. Our prodrugs are new molecules and thus may be eligible for patent protection as novel compositions of matter, provided that all other applicable requirements are met. We seek patent protection not only for our prodrug product candidates, but also for related compounds with the intention of creating potential heightened barriers to market entry.

- ***Eligibility for 505(b)(2) NDA pathway***. Our LAT platform technology allows us to discover and develop prodrugs that may be eligible to use the 505(b)(2) NDA pathway. Under that regulatory pathway, if we are able to provide an adequate bridge between our product candidates and appropriate approved drugs, we will then be able to reference the FDA's previous findings of safety and effectiveness of the approved drugs in our 505(b)(2) NDA submissions. This may allow us to avoid the significant time and expense of conducting large clinical trials and eliminate the need for some preclinical activities.

**The Unmet Need for Addressing Early Morning Behavioral Deficits and Maintaining Consistent, Sustained Efficacy in Daily ADHD Treatment**

The ADHD market is relatively well served by a number of methylphenidate and amphetamine stimulant products. However, we believe there is a significant need for longer duration products. While many of the currently marketed methylphenidate products provide good symptom control for up to 12 hours post-dose, there is increasing attention to addressing late afternoon/early evening behavioral deficits, while maintaining early symptom control.

A study published in a peer-reviewed journal characterized the frequency and severity of ADHD symptoms throughout the day in children and adolescents treated with stable doses of stimulant medications. Results of that particular study indicated that the time from awakening to arriving at school can comprise up to 20% of waking hours per day (2-3 hours), and therefore such symptoms can cause significant distress for both children and caregivers. As a result, we believe there is a need to develop a methylphenidate product that provides early-morning control of symptoms.

In addition to early onset, patients require sustained, consistent efficacy throughout the day and into the early evening hours. While currently marketed methylphenidate products offer efficacy for up to 12 hours, this duration may not be sufficient for all patients. Particularly adolescents and adults may often require longer effects as they have longer waking hours compared to younger patients. It has been reported in a peer-reviewed journal that these patients are typically using dose-augmentation strategies by taking additional doses of stimulant later in the day. We believe a single dose therapy that provides effective symptom control without requiring additional doses may have several benefits including, potentially, improved dosage compliance by regularly and consistently taking medication as indicated, reduced social embarrassment by avoiding the need to take medication during working hours, and overall improvement in quality of life through more consistent therapy. Based on this evidence, we believe there is a need to develop a methylphenidate product that can deliver long duration of efficacy. There may also be a need to develop a long-duration stimulant with and without very early onset depending on individual patient preference and requirements.

**The Epidemic of Prescription Drug Abuse in the United States**

The United States is facing an epidemic of prescription drug abuse. According to the U.S. Department of Health and Human Services, or HHS, prescription drug overdose death rates in the United States have increased five-fold since 1980, and by 2009, drug overdose deaths outnumbered deaths due to motor vehicle crashes. HHS also estimates that opioid analgesics were involved in approximately 60% of U.S. drug overdose deaths where a drug was specified in 2010. The economic costs of this public health problem are significant. A study published in 2011 in a peer-reviewed medical journal estimated that the costs of the non-medical use of prescription opioids in the United States are over $50 billion annually, including medical and substance abuse treatment costs, lost work productivity and criminal justice costs.

The increasing negative social consequences and costs of prescription drug abuse have led to a number of regulatory and legislative actions and proposals, including:

- ***FDA Guidance***. In January 2013, the FDA published draft guidance with regard to the evaluation and labeling of abuse-deterrent opioids. The guidance was published in final form in April 2015. The FDA guidance provides direction as to the studies and data required for obtaining abuse-deterrent claims in a product label. The draft guidance describes four categories of label claims for abuse-deterrent products. Depending on product and study data, a combination of categories can be included in the label claims. The FDA guidance lists the following theoretical examples:

- Category 1–in vitro data demonstrate the product has physical and chemical properties that are expected to deter intravenous abuse. However, abuse is still possible by the oral and nasal routes.

- Category 1 and 2–in vitro data demonstrate that the product has physical and chemical properties that are expected to deter oral, nasal and intravenous abuse. However, abuse of intact product is still possible by the oral route.

- Category 2 and 3–pharmacokinetic and clinical abuse potential studies indicate that the product has properties that are expected to deter abuse via the oral, intranasal and intravenous routes. However, abuse of product by these routes is still possible.

- Category 4–data demonstrated a reduction in the abuse of the product in the community setting compared to the levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available. This reduction in abuse appears to be attributable to the product's formulation, which deters abuse by injection or snorting of the manipulated product. However, such abuse of this product is still possible, and the product's abuse deterrence properties do not deter abuse associated with swallowing the intact formulation.

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

- ***FDA Authority***. In an April 2013 letter to the U.S. House of Representatives' Committee on Energy and Commerce, the FDA outlined its authority to address the issue of prescription opioid abuse in the United States. The FDA asserted that, if it determines that a formulation of an extended-release opioid drug product has abuse-deterrent properties, it has the authority to refrain from approving non-abuse-deterrent formulations of the drug and to initiate procedures to withdraw the non-abuse-deterrent formulations already on the market.

- ***FDA Action***. The FDA has approved the inclusion of language regarding the ability to deter abuse in the product labels for ten abuse-deterrent opioids, OxyContin, Targiniq ER, Embeda, Hysingla, MorphaBond, Xtampza, Troxyca, Arymo, Vantrela and RoxyBond. These actions reinforce the FDA's public statement that the development of abuse-deterrent opioid analgesics is a public health priority.

- ***FDA Public Meetings***. In October 2014, the FDA hosted a public meeting to discuss the development, assessment and regulation of abuse-deterrent formulations of opioid medications. In the announcement for the public meeting, the FDA anticipated that, after abuse-deterrent formulations become available for a number of different opioid medications and after it gains more experience with formulations with meaningful abuse-deterrent properties, the FDA may determine that the risks outweigh the benefits for all or most opioid products without abuse-deterrent properties. On October 31 and November 1, 2016, the FDA convened a public meeting for Abuse-Deterrent Generic Products and Standardization of *In Vitro* Testing. The public meeting was held to review and evaluate FDA draft guidance to establish a pathway for generic abuse-deterrent formulation approvals and to standardize testing requirements for *In Vitro* testing regimes. The FDA has not indicated a timeline for finalizing this draft guidance.

**Our Prodrug Product and Product Candidates**

We have employed our LAT platform technology to create a portfolio of product candidates that we believe will offer significant improvements over FDA-approved and widely-prescribed drugs. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Our product and pipeline of product candidates is summarized in the table below:

**Selected KemPharm Prodrug Product and Product Candidates**

| Indication / Parent Drug | Product Candidate | Development Status | Key Milestone |
|---|---|---|---|
| **ADHD** | | | |
| Methylphenidate (ER) | KP415 | Clinical | NDA Submission - 2019<br>Pivotal Efficacy Trial Data - 2018 |
| Methylphenidate (ER) | KP484 | Clinical | NDA Submission - 2019<br>Pivotal Efficacy Trial Data - 2019 |
| **PAIN** | | | |
| Hydrocodone/APAP | APADAZ | Approved | Potential Commercial Partnerships |
| Hydrocodone | KP201/IR | Clinical | NDA Submission with Expected Priority Review - 2019<br>Human POC Data - 2019 |
| Hydromorphone | KP511/ER | Clinical | NDA Submission with Expected Priority Review - 2019<br>Human POC Data - 2019 |
| Hydromorphone | KP511/IR | Clinical | NDA Submission with Expected Priority Review - 2019<br>Human POC Data - 2019 |
| Oxycodone | KP606 | Preclinical | |
| Oxymorphone | KP746 | Preclinical | |
| **MULTIPLE CNS DISORDERS** | | | |
| Quetiapine | KP303 | Preclinical | |

***KP415 and KP484***

***Overview***

The prodrug in KP415 and KP484 is our prodrug of methylphenidate, which we are developing for the treatment of ADHD. The ADHD market is largely served by the stimulant products methylphenidate and amphetamine. KP415 and KP484 are designed to be controlled release, or CR, methylphenidate products.

We intend to seek approval of KP415 and KP484 under the 505(b)(2) NDA pathway, which will allow us to rely on the FDA's previous findings of safety and effectiveness for one or more approved products. We anticipate reporting additional pharmacokinetic, or PK, and pivotal efficacy trial data for KP415 in 2018 and KP484 in 2019 and submitting a 505(b)(2) NDA for both KP415 and KP484 in 2019.

Under our asset purchase agreement with Shire Pharmaceuticals, LLC, or Shire, we granted Shire a right of first refusal to acquire, license or commercialize KP415 and KP484. The right of first refusal may be exercised by Shire for a period of 30 business days following Shire's receipt of written notice from us of the existence of a bona fide offer from a third party to acquire, license or commercialize KP415 and KP484.

We are also party to an agreement with MonoSol Rx, LLC, or MonoSol, pursuant to which MonoSol has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415 and KP484, and any product candidates arising therefrom, including royalty payments on any license of KP415 or KP484, the sale of KP415 or KP484 to a third party or the commercialization of KP415 or KP484.

***Market Opportunity***

We believe the ADHD market would be receptive to new branded drugs that have improved properties when compared to current treatments. We believe a new product in the form of a prodrug that has differentiated features and potentially a more consistent controlled release drug delivery mechanism may provide a new treatment option in this large market segment. While methylphenidate is available as a generic product, the branded formulations, FOCALIN XR, CONCERTA, QUILLIVANT XR and DAYTRANA, accounted for sales of $1.0 billion in 2017.

***Key Features of KP415***

Based on our preclinical and clinical data, we believe KP415, if approved by the FDA, may have valuable product features and may provide significant benefits to patients, physicians, and society when compared to other FDA-approved and widely-prescribed methylphenidate products:

- ***Faster early-morning symptom control and sustained effectiveness***. In December 2016, we announced the results of our Phase 1 POC clinical trial of KP415. This trial was designed to assess the relative PK of 32 mg of KP415 compared with 36 mg of Concerta after oral administration under fasted conditions. Following an analysis of the data, dexmethylphenidate was added to the formulation to provide a PK profile that may provide quicker onset of action than existing alternatives, thereby providing faster control of symptoms following administration early in the morning, as well as sustained, consistent effectiveness through the day and into the early evening hours.

- ***Reduced abuse potential***. In order to evaluate the potential for reduced abuse of our prodrug of methylphenidate in the formulation of KP415, we conducted preclinical studies in rats to compare the exposure to methylphenidate following intranasal and intravenous, or IV, administration of the prodrug as compared to intranasal and IV administration of methylphenidate hydrochloride. We observed significantly lower concentrations of methylphenidate following intranasal and IV administration of the prodrug compared to intranasal and IV administered methylphenidate hydrochloride. Our prodrug of methylphenidate incorporates our LAT platform technology and, based on our preclinical and clinical studies, we believe it may have lower abuse potential compared to methylphenidate.

- ***Once-daily dosing***. PK data from our preclinical studies suggest that the time to maximum plasma concentration of methylphenidate after oral administration of KP415 is approximately three times longer than that after oral administration of currently marketed IR methylphenidate. We believe this continual release, or CR, attribute of KP415 may allow for convenient, once-daily dosing.

- ***Amenable to patient-friendly formulations***. We believe our prodrug in KP415 may possess a lower abuse potential, our preclinical and clinical data shows that KP415 could ultimately be used in a variety of patient-friendly dosage forms such as oral thin film, orally dissolving tablets, chewable tablets and liquids as a means of increasing patient convenience and dosage compliance by regularly and consistently taking the medication as indicated.

- ***Composition-of-matter patent protection***. We have a U.S. composition-of-matter patent that will expire, after utilizing all appropriate patent term adjustments but excluding possible term extensions, in 2032 that generally covers at least one component of KP415. Our patent strategy is focused primarily on key geographic markets, and, as of December 31, 2017, we have composition-of-matter patents in over 30 countries in Europe, Malaysia, Mexico, Indonesia, Israel, China, Japan, Philippines, South Korea, Russia, Singapore, New Zealand, Vietnam and South Africa, and additional patent filings were pending in the United States and an additional 15 foreign jurisdictions. In addition, subject to further discussions with the FDA, we believe additional patent protection may be eligible for new chemical entity, or NCE, exclusivity status, which could allow for five years of U.S. market exclusivity following the FDA's approval of an NDA for KP415.

- ***No generic equivalent product***. KP415 contains a prodrug that we believe will be given a new chemical name by the U.S. Adopted Names Council, or USAN, which could mean that there would be no generic equivalent product for KP415 in most states, making drug-equivalent substitution potentially difficult at the pharmacy.

***Key Features of KP484***

Based on our preclinical and clinical data, we believe KP484, if approved by the FDA, may have valuable product features and may provide significant benefits to patients, physicians, and society when compared to other FDA-approved and widely-prescribed methylphenidate products:

- ***Super-extended release***. We believe that this KP484 may provide sustained, consistent effectiveness through the day and into the evening hours.

- ***Reduced abuse potential***. The preclinical studies of the prodrug of methylphenidate discussed above in the KP415 “Reduced Abuse Potential” subsection are used for the abuse potential evaluation of the KP484 product candidate. As such, we believe our prodrug of methylphenidate may have abuse-deterrent characteristics as observed in the preclinical studies in rats exposed to methylphenidate following intranasal and intravenous, or IV, administration of the prodrug as compared to intranasal and IV administration of methylphenidate hydrochloride

- ***Once-daily dosing***. PK data from our clinical studies suggest that under fasted conditions, the time to maximum plasma concentration of methylphenidate after oral administration of KP484 is potentially five to seven times longer compared to oral administration of currently marketed IR methylphenidate. We believe this CR attribute of KP484 may allow for convenient, once-daily dosing.

- ***Amenable to patient-friendly formulations***. Our preclinical and clinical data shows that KP484 could ultimately be used in a variety of patient-friendly dosage forms such as oral thin film, orally dissolving tablets, chewable tablets and liquids as a means of increasing patient convenience and dosage compliance by regularly and consistently taking the medications as indicated.

- ***Composition-of-matter patent protection***. KP484 is generally protected by a U.S. composition-of-matter patent that will expire, after utilizing all appropriate patent term adjustments but excluding possible term extensions, in 2032. Our patent strategy is focused primarily on key geographic markets, and, as of December 31, 2017, we have composition-of-matter patents on KP484 in New Zealand and South Africa, and additional KP484 patent filings were pending in the United States and an additional 23 foreign jurisdictions. In addition, subject to further discussions with the FDA, we believe KP484 may be eligible for new chemical entity, or NCE, exclusivity status, which could allow for five years of U.S. market exclusivity following the FDA's approval of an NDA for KP484.

- ***No generic equivalent product***. KP484 contains a prodrug that we believe will be given a new chemical name by the USAN which could mean that there would be no generic equivalent product for KP484 in most states, making drug-equivalent substitution potentially difficult at the pharmacy.

***APADAZ***

***Overview***

On February 23, 2018, we announced that the FDA approved our NDA for APADAZ for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. APADAZ is an IR combination of our prodrug, benzhydrocodone, and APAP. Benzhydrocodone was developed with our proprietary LAT platform technology. We are evaluating potential U.S. commercialization options for APADAZ, including pursuing a commercial collaboration with pharmacy benefit managers who would agree to Tier 1 or equivalent reimbursement status, including the most favorable co-pay level in return for price parity with available generic products, or as parnership with a U.S.-based or global generic pharmaceutical manufacturer and distributor, or pursuing a strategic transaction. We may also license the international commercial rights to APADAZ to one or more collaborators.

***Market Opportunity***

IMS Health estimates that in 2017, IR hydrocodone/APAP combination products represented the most frequently prescribed opioid products in the United States, accounting for 73 million U.S. prescriptions, representing 4.8 billion tablets. Typically, patients are instructed to take four pills per day and prescriptions provide approximately 14 days of therapy. Hydrocodone is associated with more drug abuse and diversion than any other opioid and IR hydrocodone abuse results in more emergency department visits than any other prescription opioid. Currently, there are no IR hydrocodone/APAP combination products approved in the United States with an abuse-deterrent label.

***Key Product Features of APADAZ***

We believe APADAZ has many valuable product features and may p rovide significant benefits to patients, physicians and society when compared to other FDA-approved and widely-prescribed IR hydrocodone/APAP combination products:

- ***Composition-of-matter patent protection***. APADAZ is protected by a U.S. composition-of-matter patent on KP201, the prodrug of hydrocodone contained in APADAZ, that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2031. Our patent strategy is focused primarily on key geographic markets, and, as of December 31, 2017, KP201 had received granted, issued or allowed patent status in 20 foreign jurisdictions and patent applications covering KP201 were pending in an additional 11 foreign jurisdictions.

- ***No generic equivalent product***. KP201, the APADAZ active pharmaceutical ingredient, or API, is a prodrug with a new chemical name given by the USAN, benzhydrocodone. APADAZ has a lower prescribed milligram strength of KP201 than the therapeutic equivalent amount of hydrocodone bitartrate used in existing IR hydrocodone/APAP combination products. The difference in chemical structure and prescription strength means that there is no generic equivalent product for APADAZ in most states, making substitution difficult at the pharmacy.

- ***Convenient dosing***. Based on data from our food-effect clinical trial, APADAZ can be administered under both fed and fasting conditions and, accordingly, APADAZ will be as convenient as existing IR hydrocodone/APAP combination products.

***KP201/IR***

***Overview***

KP201/IR, is an IR formulation of APADAZ without any APAP. We are developing KP201/IR for the short-term management of acute pain. KP201/IR is designed to be a differentiated opioid product that offers comparable efficacy to the existing standard-of-care, IR hydrocodone/APAP combination products, such as Vicodin, Norco and Lortab, but with the potential safety advantage of having no added APAP.

We anticipate conducting human clinical trials in 2019, including an intranasal human abuse liability study. Based on our current development timelines, we anticipate submitting an NDA utilizing the 505(b)(2) pathway for KP201/IR in 2019. We believe that KP201/IR, will receive priority review. KP201/IR has received "Fast Track" designation by the FDA.

***Market Opportunity***

Currently, there are no IR hydrocodone products approved in the United States that are formulated APAP-free, with or without an abuse-deterrent label. We believe KP201/IR, if approved, would provide physicians an APAP-free hydrocodone product not currently available, thereby offering an alternative treatment option to patients with acute pain. We believe such an alternative would be particularly valuable to patients who already take other APAP-containing products concomitantly or have liver disease.

***Key Features of KP201/IR***

We believe KP201/IR, if approved by the FDA, may have many valuable product features and may provide significant benefits to patients, physicians and society:

- ***Abuse-deterrent technology***. KP201/IR uses our KP201 prodrug, which incorporates our LAT platform technology, as well as additional formulation barriers which we believe may potentially provide a higher level of abuse deterrence than many existing abuse-deterrent formulation products.

- ***No added APAP***. KP201/IR contains no acetaminophen. According to the FDA, overdoses of APAP are the most common cause of drug-related liver injury. In 2011, the FDA limited the amount of APAP in prescription combination products and required warnings be added to all APAP prescription products.

- ***Composition-of-matter patent protection***. KP201/IR is protected by a U.S. composition-of-matter patent on KP201 that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, no earlier than 2030.

- ***No generic equivalent product***. We believe the difference in chemical name, prescription strength and lack of APAP in the formulation may potentially mean that there will be no generic equivalent product for KP201/IR in most states, making drug equivalent substitution potentially difficult at the pharmacy.

- ***Convenient dosing***. We believe that KP201/IR will be as convenient as existing IR hydrocodone/APAP combination products.

***KP511***

***Overview***

KP511 is our prodrug of hydromorphone, which we are developing for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. KP511 combines hydromorphone with one or more ligands. We believe KP511 does not release its hydromorphone component until it is metabolized in the GI tract following oral administration. We believe KP511 is highly tamper-resistant and is stable under most tampering conditions that can potentially defeat many formulation-based abuse-deterrent technologies. We are currently working on an ER and IR formulation of KP511. KP511 will be formulated as an abuse-deterrent opioid product that offers equivalent efficacy to approved hydromorphone products.

We plan to seek approval of KP511/ER and KP511/IR under the 505(b)(2) NDA pathway. Based on our preclinical data, we believe that KP511 may release hydromorphone after oral administration in humans in a manner that is comparable to the appropriate approved hydromorphone drug. We anticipate reporting additional human data for KP511/ER and KP511/IR in 2019 and submitting a 505(b)(2) NDA for KP511/ER and KP511/IR in 2019.

In June 2016, we announced results from a Phase 1 POC trial of KP511. In the trial, we observed comparable hydromorphone exposure between 4 mg Dilaudid Oral Liquid and an equimolar 8 mg dose of KP511. Additionally, in January 2017, we announced the results of our exploratory Phase 1, double-blind, single-dose, 2-treatment, 2-period, randomized, crossover study, intended to assess the PK, safety and intranasal abuse potential of KP511, compared to equivalent doses of hydromorphone hydrochloride, or HM. In this trial, KP511 produced statistically significant reduction in peak and overall hydromorphone exposure with KP511 versus HM. The improved PK of KP511 resulted in meaningful, statistically lower scores in the exploratory pharmacodynamic measures of "Drug Liking," "Feeling High," "Overall Drug Liking" and "Take Drug Again" when compared to HM.

***Market Opportunity***

ER oral hydromorphone products are typically used for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in opioid tolerant patients and for which alternative treatment options are inadequate. SHS estimates that in 2017 there were nearly 2.6 million dispensed prescriptions of hydromorphone in the United States. Currently, there are no hydromorphone products approved in the United States with an abuse-deterrent label.

***Key Features of KP511***

Based on our clinical and preclinical data, we believe KP511/ER and KP511/IR, if approved by the FDA, may have valuable product features and provide significant benefits to patients, physicians and society when compared to FDA-approved hydromorphone products:

- ***Abuse-deterrent technology***. In order to evaluate the abuse-deterrent qualities of KP511, we conducted clinical and preclinical studies of KP511. As described above, our Phase 1 POC trial of KP511 produced meaningful, statistically lower scores in the exploratory pharmacodynamic measures of "Drug Liking," "Feeling High," "Overall Drug Liking" and "Take Drug Again" when compared to HM. We also conducted preclinical studies in rats to compare the exposure to hydromorphone following intranasal and IV administration of KP511 as compared to intranasal and IV administration of hydromorphone hydrochloride. We observed significantly lower concentrations of hydromorphone following IV administration of KP511 compared to intranasal and IV administered hydromorphone hydrochloride. KP511 incorporates our LAT platform technology to create its abuse-deterrent properties and, based on our preclinical and clinical studies, we believe it may have abuse-deterrent characteristics.

- ***Oral overdose protection***. In our preclinical studies, we observed that hydromorphone blood levels in rats increased more slowly and to a lesser extent after oral administration of increasing excessively large doses of KP511, as compared to increasing equimolar oral doses of hydromorphone hydrochloride. Thus, as to KP511, we believe it is possible that the metabolic processes of releasing hydromorphone from the prodrug become saturated at excessively large oral doses. If confirmed by further studies, this could potentially mean that KP511 may reduce the risk of oral overdosing.

- ***Composition-of-matter patent protection***. KP511/ER and KP511/IR are generally protected by a U.S. composition-of-matter patent on KP511 that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2032. Our patent strategy is focused primarily on key geographic markets, and, as of December 31, 2017, we have composition-of-matter patents on KP511 in Australia, Canada, China, Kazakhstan, Japan, Philippines, New Zealand, South Africa, South Korea, Ukraine and Singapore, and applications covering KP511 were pending in the United States and an additional 20 foreign jurisdictions.

- ***No generic equivalent product***. KP511 is a prodrug that was given a new chemical name by the USAN, asalhydromorphone, which means that there may be no generic equivalent product for KP511/ER or KP511/IR in most states, making drug equivalent substitution difficult at the pharmacy.

***Other Product Candidates***

We are using our LAT platform technology to develop other product candidates in pain. One example is KP606, an IR formulation of KP606, our prodrug of oxycodone, which we are developing for the management of moderate to severe pain where the use of an opioid analgesic is appropriate. KP606 is designed to be an IR abuse-deterrent opioid product that may potentially offer equivalent efficacy to OXYCONTIN. KP606 combines oxycodone with one or more ligands. Another example is KP746, our prodrug of oxymorphone, which is currently in preclinical development. We are developing KP746 for the management of moderate to severe pain where the use of an opioid analgesic is appropriate.

In addition to our product candidates in pain, we are using our LAT platform technology to develop product candidates for the treatment of CNS disorders. KP303, a prodrug of an antipsychotic, is our product candidate for the treatment of CNS disorders including, for example, schizophrenia and bipolar disorder. Existing therapies for these disorders may result in side effects that can include weight gain, fatigue, high cholesterol and triglycerides, diabetes and low blood pressure/dizziness when standing up. Compliance and side effects, which may be triggered by undesirable metabolites, are some challenges associated with current therapies. Early research suggests that KP303 may allow for more compliant dosage forms and/or demonstrate changes in the metabolism that could improve the adverse events of existing treatments.

**Our Intellectual Property**

Our intellectual property strategy includes seeking composition-of-matter patents, among other patents, for our prodrugs and product candidates and conjugates of our prodrugs while also protecting, where appropriate as trade secrets, our LAT platform technology, the process by which we identify, screen, evaluate and select ligands to be conjugated with parent drugs to create our prodrugs. Our current prodrugs all consist of an approved parent drug and one or more ligands that we have selected using our LAT platform technology. The parent drug and ligand or ligands together may potentially constitute a new molecule and thus may be eligible for composition-of-matter patent protection, among other patent protections, in the United States and abroad.

As of December 31, 2017, we have been granted 23 issued patents within the United States, and an additional 64 foreign patents covering our prodrugs or product candidates. The terms of the 23 issued U.S. patents extend to various dates ranging, for example, between 2030 and 2032. The term of our overall domestic and foreign patent portfolio related to our prodrugs and product candidates, including patent term adjustments but excluding possible patent term extensions, extend to various dates ranging, for example, between 2030 and 2032, if pending patent applications in each of our patent families issue as patents. As of December 31, 2017, we had filed 14 pending patent applications under active prosecution in the United States, and an additional 101 pending foreign patent applications potentially covering our prodrugs and product candidates. Our issued and granted patents provide protection in jurisdictions that include the United States, Australia, Canada, China, Colombia, Cuba, Europe, Israel, Japan, Kazakhstan, Malaysia, Mexico, New Zealand, Philippines, Russia, Ukraine, Vietnam, Singapore, Indonesia, South Africa and South Korea.

In 2013, the United States Patent and Trademark Office, or the USPTO, issued a composition-of-matter patent covering KP201, which will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, no earlier than 2030. Further, there are granted or recently allowed compositions-of-matter patents covering KP201 in Australia, Belarus, Canada, Chile, China, Colombia, Cuba, Israel, Japan, Kazakhstan, Malaysia, Mexico, New Zealand, Russia, Ukraine, Indonesia, Philippines, Singapore, South Africa and South Korea. In addition, five U.S. patent applications covering KP201-related compositions-of-matter were pending as of December 31, 2017, and patent applications covering KP201 were pending as of December 31, 2017, in the United Arab Emirates, Brazil, Costa Rica, Egypt, Europe, Hong Kong, India, Oman, Thailand and Vietnam.

In August 2014, the USPTO issued a composition-of-matter patent covering KP511, which will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2032. We have received composition-of-matter patents and also additionally filed composition-of-matter patent applications related to the KP415, KP484 and KP511 families in the United States and in Argentina, Australia, Brazil, Canada, Chile, China, Egypt, Hong Kong, Europe, India, Israel, Indonesia, Japan, South Korea, Kazakhstan, Mexico, Malaysia, New Zealand, Philippines, Russia, Singapore, Thailand, Ukraine, Vietnam and South Africa. We anticipate filing additional patent applications for our prodrug product candidates.

We also depend upon the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our LAT platform technology, as well as any proprietary know-how and show-how beyond that which is patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we generally require our employees, consultants and advisors to enter into confidentiality agreements prohibiting the disclosure of confidential information and, in some cases, requiring disclosure and assignment to us of the ideas, developments, discoveries, inventions and improvements important to our business.

**Commercialization**

On February 23, 2018, we announced that the FDA approved our NDA for APADAZ for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. We are evaluating potential U.S. commercialization options for APADAZ, including pursuing a commercial collaboration with pharmacy benefit managers who would agree to Tier 1 or equivalent reimbursement status, including the most favorable co-pay level in return for price parity with available generic products, or a partnership with a U.S.-based or global generic pharmaceutical manufacturer and distributor, or pursuing a strategic transaction. We may also license the international commercial rights to APADAZ to one or more collaborators.

With the exception of APADAZ, we have not yet begun commercialization activities for our product candidates in active development. Because many of our product candidates may have large potential market opportunities, and may require significant marketing resources, we may conclude that the most appropriate approach to their commercialization, if they receive regulatory approval, will involve forming a commercial collaboration or strategic relationship, or consummating some type of strategic transaction, with a larger pharmaceutical or other marketing organization. Alternatively, we may conclude that building our own focused sales and marketing organization will be most appropriate, perhaps as part of a co-promotional arrangement, or some other form of collaboration. As we get closer to potential approval of our product candidates, we will work to identify and implement the commercialization strategies that we conclude are the most desirable with regard to the specific product candidates.

**Research and Development**

Historically, we have devoted a significant amount of resources to develop our product and product candidates. For the years ended December 31, 2017, 2016 and 2015, we recorded $20.6 million, $20.5 million and $13.9 million, respectively, in research and development expenses. We plan to increase our research and development expense for the foreseeable future as we continue our efforts to further advance the development of our product candidates and commercialize APADAZ and our product candidates, if approved, subject to the availability of additional funding.

**Competition**

Our industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We will face competition and potential competition from a number of sources, including pharmaceutical and biotechnology companies, specialty pharmaceutical companies, generic drug companies, drug delivery companies and academic and research institutions. We believe the key competitive factors that will affect the development and commercial success of our products and product candidates include their potential degree of abuse deterrence, onset of action, bioavailability, therapeutic efficacy, convenience of dosing, safety, tolerability and cost. Many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as more experience in the development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Consequently, our competitors may develop differentiated products for the treatment of ADHD, the short-term management of acute pain, or for other indications we are pursuing or may pursue in the future, and such competitors' products may be more effective, better tolerated and less costly than our products or product candidates. Our competitors may also be more successful in manufacturing and marketing their products than we are. We will also face competition in recruiting and retaining qualified personnel and establishing clinical trial sites and patient enrollment in clinical trials.

If approved, KP415 and KP484 will compete against currently marketed, branded and generic methylphenidate products for the treatment of ADHD. Some of these currently marketed products include Johnson & Johnson's Concerta, Novartis AG's RITALIN, Pfizer's Quillivant, FOCALIN and Focalin XR, UCB S.A.'s METADATE CD, and Noven Pharmaceuticals' Daytrana, in addition to multiple other branded and generic methylphenidate products marketed by companies including Allergan plc and Mallinckrodt plc. In addition, if approved, KP415 and KP484 will face potential competition from any other methylphenidate products for the treatment of ADHD that are currently in or which may enter into clinical development.

APADAZ and, if approved, KP201/IR, will compete against currently marketed, branded and generic IR hydrocodone/APAP combination products indicated for the short-term management of acute pain. Some of these currently marketed products include AbbVie's VICODIN, Allergan's NORCO, Shionogi's XODOL and UCB Pharma's LORTAB, in addition to multiple other branded and generic hydrocodone/APAP combination products marketed by companies including Allergan plc, Endo International plc and Mallinckrodt plc. In addition, APADAZ and, if approved, KP201/IR, will face potential competition from any IR or hydrocodone/APAP combination or other APAP-free products for the short-term management of acute pain that are currently in or may enter into clinical development.

If approved, KP511/ER and KP511/IR will compete against currently marketed, branded and generic, ER and IR hydromorphone products. KP511/ER would compete against products approved for use in opioid-tolerant patients for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. KP511/IR would compete against products approved for use in patients for the management of pain severe enough to require opioid analgesic and for which alternative treatments are inadequate. Some of these currently marketed products include Purdue Pharma L.P.'s DILAUDID and Mallinckrodt plc's EXALGO, in addition to multiple other branded and generic IR and ER hydromorphone products marketed by companies including Allergan plc, Mallinckrodt plc, Rhodes Pharmaceuticals L.P. and Roxanne Laboratories, Inc. In addition, if approved, KP511/ER and KP511/IR will face potential competition from any abuse-deterrent or other IR and ER hydromorphone products for the treatment of pain that are currently in or which may enter into clinical development.

If approved, our other opioid product candidates will face competition from commercially available branded and generic opioid drugs, including hydrocodone, hydromorphone, oxycodone, fentanyl, morphine, oxymorphone and methadone, as well as other marketed non-opioid products for the treatment of pain, and potential competition from opioid and non-opioid products for the treatment of pain that are currently in clinical development. In addition, our product candidates will face competition from approved and abuse-deterrent labeled opioid drugs and potential competition from abuse-deterrent opioid drugs that are currently in clinical development. We may compete with multiple companies that have developed and are developing abuse-deterrent technologies that may be applied to a variety of drugs, including those being developed for the short-term management of acute pain as well as for other indications that we are pursuing or may pursue in the future. If approved, our other opioid product candidates may face competition from opioid products or abuse-deterrent technologies from companies including Allergan plc, Acura Pharmaceuticals, Inc., Cara Therapeutics, Inc., Collegium Pharmaceutical, Inc., Depomed, Inc., DURECT Corporation, Egalet Corporation, Elite Pharmaceuticals, Inc., Endo International plc, Grünenthal Group, Inspirion Delivery Technologies, LLC, IntelliPharmaceutics International Inc., Mallinckrodt plc, Mylan Inc., Nektar Therapeutics, Pain Therapeutics, Inc., Pfizer Inc., Purdue Pharma L.P., Signature Pharmaceuticals, Teva Pharmaceutical Industries Ltd., Trevena Inc. and UCB S.A.

If approved, KP303 will compete against currently marketed, branded and generic, quetiapine and olanzine products approved for use in the treatment of multiple CNS disorders. Some of these currently marketed products include AstraZeneca's SEROQUEL and SEROQUEL XR and Eli Lilly's ZYPREXA and ZYPREXA ZYDIS, in addition to multiple other branded and generic quetiapine and olanzine products marketed by companies Teva Pharmaceutical Industries Ltd. and Dr. Reddy's Laboratories Ltd. In addition, if approved, KP303 will face potential competition from any abuse-deterrent or other quetiapine or olanzine products for the treatment of multiple CNS disorders which are currently in or which may enter into clinical development.

**Manufacturing**

Our manufacturing strategy is to rely on contract manufacturers to produce our prodrug product candidates for clinical trials and, if approved, drug product for commercial sale. We currently have no manufacturing facilities and limited personnel with manufacturing experience. We rely on Johnson Matthey Inc., or JMI, a third-party manufacturer, to produce the bulk quantities of KP201 required to manufacture APADAZ and KP201/IR used in our clinical trials and pre-commercial activity under a supply agreement. JMI is also currently contracted to manufacture KP511 to be used in our non-clinical, clinical and formulation development programs needed to support an NDA filing. We have contracted with another third-party manufacturer to supply KP415 and KP484 to be used in our non-clinical, clinical and formulation development programs necessary to support an NDA filing. We plan to continue to rely on these manufacturers to manufacture commercial quantities of KP201, KP511, KP415 and KP484, respectively, for sale in the United States, if and when we receive approval by the FDA. We expect to contract with third-party manufacturers for the manufacture of all API supply needs outside the United States if and when we receive approval by regulatory authorities outside the United States.

Our current and any future third-party manufacturers, their facilities and all lots of drug substance and drug products used in our clinical trials are required to be in compliance with current good manufacturing practices, or cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements and FDA satisfaction before any product is approved and we can manufacture commercial products. Our current and any future third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreements to resolve allegations of non-compliance with these laws, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and individual imprisonments.

**Supply Agreement with Johnson Matthey**

Under our supply agreement with JMI, or the Supply Agreement, JMI has agreed to supply us with all of the KP201 necessary for clinical trials and commercial sale for a price equal to JMI's manufacturing cost and to provide process development services for KP201. In exchange, we issued shares of our common stock to JMI, provided that the commercial supply arrangement for KP201 would be exclusive to them in the United States. In addition, for further process optimization and manufacture of NDA registration batches, we agreed to pay a minimum royalty on the net sales on the commercial sale of any products which utilize KP201 as the API, if approved by the FDA. The percentage royalty rate ranges from the high teens at low volumes to the mid-single digits at higher volumes. Under the agreement, JMI has completed manufacture of our registration batches of any products which utilize KP201 as the API, and stability testing for those batches is in process.

Under the Supply Agreement, we retain sole ownership of KP201 and are required to use commercially reasonable efforts to develop and to pursue FDA marketing approval of any products which utilize KP201 as the API. We are responsible for product development, including formulation, preclinical studies and clinical trials, and for regulatory approval, quality assurance and commercialization. If any products which utilize KP201 as the API are subject to a U.S. Drug Enforcement Agency, or DEA, scheduling quota, then each quarter, both we and JMI are responsible for using commercially reasonable efforts to obtain a quota from the DEA for the production of KP201 for use with any products that utilize KP201 as an API.

JMI is responsible for all costs of any KP201 manufactured during a specified validation process for any products which utilize KP201 as an API. After completion of the validation process, but prior to the commercial launch of any products that utilize KP201 as the API, JMI will manufacture batches of KP201 at a negotiated price. Upon commercial launch, JMI will manufacture and supply KP201 at a price equal to JMI's fully allocated manufacturing cost after commercial launch of APADAZ, as well as for KP201/IR or any other product that may utilize KP201 as an API, should we obtain approval for marketing from the FDA.

We must purchase all of our U.S. KP201 needs from JMI and JMI cannot supply KP201 to other companies. After the commercial launch of any product that utilizes KP201 as the API, JMI is required to identify a secondary manufacturing site and qualify and validate that site for the production of KP201.

The term of the Supply Agreement extends as long as we hold a valid and enforceable patent for KP201 or until the tenth anniversary of the commercial launch of any product that utilizes KP201 as the API, whichever date is later. Upon the expiration of such term, the agreement will automatically renew for a period of two years unless either party provides 12 months' prior notice of its intent not to renew.

**Asset Purchase Agreement with Shire**

In March 2012, as a result of a litigation settlement, we and our chief executive officer, Travis C. Mickle, Ph. D., entered into an asset purchase agreement with Shire pursuant to which we sold assets and intellectual property to Shire for proceeds of $5.1 million. Pursuant to this agreement, we also granted Shire a right of first refusal to acquire, license or commercialize KP415 and KP484.

**Third-Party Reimbursement**

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third-party payors, such as state and federal governmental authorities, including those that administer the Medicare and Medicaid programs, and private managed care organizations and health insurers. Decisions regarding the extent of coverage and amount of reimbursement to be provided for each of our product and product candidates will be made on a plan-by-plan basis. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Each third-party payor determines whether or not it will provide coverage for a drug, what amount it will pay providers for the drug, and on what tier of its formulary the drug will be placed. These decisions are influenced by the existence of multiple drug products within a therapeutic class and the net cost to the plan, including the amount of the prescription price, if any, rebated by the drug's manufacturer. Typically, generic versions of drugs are placed in a preferred tier. The position of a drug on the formulary generally determines the co-payment that a patient will need to make to obtain the drug and can strongly influence the adoption of a drug by patients and physicians. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. 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. Additionally, a third-party payor's decision to provide coverage for a drug does not imply that an adequate reimbursement rate will be approved. Also, third-party payors are developing increasingly sophisticated methods of controlling healthcare costs. As a result, coverage, reimbursement and placement determinations are complex and are often the subject of extensive negotiations between the payor and the owner of the drug.

Unless we enter into a strategic collaboration under which our collaborator assumes responsibility for seeking coverage and reimbursement for a given product, we will be responsible for negotiating coverage, reimbursement and placement decisions for our product candidates. Coverage, reimbursements and placement decisions for a new product are based on many factors including the coverage, reimbursement and placement of already marketed branded drugs for the same or similar indications, the safety and efficacy of the new product, availability of generics for similar indications, the clinical need for the new product and the cost-effectiveness of the product. Increasingly, both purchasers and payors are also conducting comparative clinical and cost effectiveness analyses involving application of metrics, including data on patient outcomes, provided by manufacturers.

Within the Medicare program, as self-administered drugs, our product and product candidates would be reimbursed under the expanded prescription drug benefit known as Medicare Part D. This program is a voluntary Medicare benefit administered by private plans that operate under contracts with the federal government. These plans develop formularies that determine which products are covered and what co-pay will apply to covered drugs. The plans have considerable discretion in establishing formularies and tiered co-pay structures, negotiating rebates with manufacturers and placing prior authorization and other restrictions on the utilization of specific products, subject to review by the Centers for Medicare and Medicaid Services, or CMS, for discriminatory practices. These Part D plans negotiate discounts with drug manufacturers, which are passed on, in whole or in part, to each of the plan's enrollees through reduced premiums. Historically, Part D beneficiaries have been exposed to significant out-of-pocket costs after they surpass an annual coverage limit and until they reach a catastrophic coverage threshold. However, changes made by the Patient Protection and Affordable Care Act as amended by the Health Care Education and Reconciliation Act, or the ACA, will reduce this patient coverage gap, known as the "donut hole", by transitioning patient responsibility in that coverage range from 100% in 2010 to only 25% in 2019. To help achieve this reduction, pharmaceutical manufacturers are required to provide quarterly discounts of 50%, and 70% commencing January 1, 2019, off the negotiated price of branded drugs dispensed to Medicare Part D patients in the donut hole.

If a drug product is available for reimbursement by Medicare or Medicaid, its manufacturer must comply with various health regulatory requirements and price reporting metrics, which may include, as applicable, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, or the OBRA, and the Veterans Health Care Act of 1992, or the VHCA, each as amended. Among other things, the OBRA requires drug manufacturers with certain drugs covered by Medicaid to pay rebates on prescription drugs to state Medicaid programs. States may also negotiate "supplemental" Medicaid rebates on drug products dispensed under Medicaid. Manufacturers participating in Medicaid are also generally required to participate in the Public Health Service 340B Drug Discount Program, which imposes a mandatory discount on purchases by certain customers. Manufacturers of innovator drugs, including 505(b)(2) drugs, that participate in the Medicaid program are also required to offer the drugs on the Federal Supply Schedule purchasing program of the General Services Administration for purchase by the Department of Veterans Affairs, the Department of Defense and other authorized users at a mandatory discount. Additional laws and requirements apply to these contracts. Participation in such federal programs may result in prices for our future products that will likely be lower than the prices we might otherwise obtain.

Third-party payors, including the U.S. government, continue to apply downward pressure on the reimbursement of pharmaceutical products. Also, the trend towards managed health care in the United States and the concurrent growth of organizations such as health maintenance organizations may result in lower reimbursement for pharmaceutical products. We expect that these trends will continue as these payors implement various proposals or regulatory policies, including various provisions of the recent health reform legislation that affect reimbursement of these products. There are currently, and we expect that there will continue to be, a number of federal and state proposals to implement controls on reimbursement and pricing, directly and indirectly.

**Government Regulation**

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, packaging, recordkeeping, tracking, approval, import, export, distribution, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- non-clinical laboratory and animal tests that must be conducted in accordance with good laboratory practices, or GLPs;
- submission of an investigational new drug application, or IND, which must be received by the FDA and become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, for each clinical site or centrally before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed product candidate for its intended use, performed in accordance with good clinical practices, or GCPs;
- submission of a NDA to the FDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with cGMP and GCPs; and
- FDA approval of an NDA to permit commercial marketing for particular indications for use.

Prior to the commencement of marketing of controlled substances, the DEA must also determine the controlled substance schedule, taking into account the recommendation of the FDA.

The testing and approval process requires substantial time, effort and financial resources. Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity and drug product formulation, as well as animal studies to assess potential safety and efficacy. Prior to commencing the first human clinical trial with a product candidate, we must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Additional non-clinical studies may be required even after the IND is submitted. The IND becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the conduct of the clinical trial by imposing a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each study site proposing to conduct the clinical trial must review and approve the plan for any clinical trial, its informed consent form and other communications to study subjects before the clinical trial commences at that site. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans. Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, if the drug has been associated with unexpected serious harm to subjects, or based on evolving business objectives or competitive climate. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise us to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

In general, for purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- *Phase 1*—Studies are initially conducted to test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 trials may also be used to gain an initial indication of product effectiveness.

- *Phase 2*—Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- *Phase 3*—These clinical trials are undertaken in larger subject populations to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded subject population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. These trials may be done globally to support global registrations so long as the global sites are also representative of the U.S. population and the conduct of the study at global sites comports with FDA regulations and guidance, such as compliance with GCPs.

In the case of a 505(b)(2) NDA, which is a marketing application in which sponsors may rely on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted, some of the above-described studies and preclinical studies may not be required or may be abbreviated. Bridging studies may be needed, however, to demonstrate the relevance of the studies that were previously conducted by other sponsors to the drug that is the subject of the NDA.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4, or post-market, studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information.

Clinical trials must be conducted under the supervision of qualified investigators in accordance with GCP requirements, which includes the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, and the review and approval of the study by an IRB. Investigators must also provide information to the clinical trial sponsors to allow the sponsors to make specified financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FFDCA. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events occur.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

***505(b)(2) Approval Process***

Section 505(b)(2) of the FFDCA, or 505(b)(2), provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, 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 or use from the person by or for whom the investigations were conducted. The applicant may rely upon the FDA's prior findings of safety and effectiveness for an approved product that acts as the reference listed drug for purposes of a 505(b)(2) NDA. The FDA may also require 505(b)(2) applicants to perform additional studies or measurements to support any changes from the reference listed drug. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Our current and anticipated product candidates are or will be based on already approved APIs in combination with a ligand. Accordingly, we have and expect to be able to continue to rely on information from studies previously conducted by the companies that obtained approval for drugs containing such APIs.

***Orange Book Listing***

Section 505 of the FFDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. ANDAs are termed "abbreviated" because they are generally not required to include preclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the Orange Book. These products may be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

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

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the holder of the NDA for the reference listed drug and the patent owner once the application has been accepted for filing by the FDA. The NDA holder or patent owner 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 application until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the applicant or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a Paragraph IV certification, the NDA holder or patent owner regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. The applicant may also elect to submit a statement certifying that its proposed label does not contain, or carves out, any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.

***Exclusivity***

The FDA provides periods of regulatory exclusivity, which provides the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA's approval of the NDA. Five years of exclusivity are available to NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent derivatives, such as a complex, chelate, or clathrate, of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. Applicants may also seek to carve out certain drug labeling that is protected by exclusivity.

If a product is not eligible for the NCE exclusivity, it may be eligible for three years of exclusivity. Three-year exclusivity is available to the holder of an NDA, including a 505(b)(2) NDA, for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical trials, other than bioavailability or bioequivalence trials, was essential to the approval of the application and was conducted or sponsored by the applicant. This three-year exclusivity period protects against FDA approval of ANDAs and 505(b)(2) NDAs for the condition of the new drug's approval. As a general matter, three-year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

***NDA Submission and Review by the FDA***

Assuming successful completion of the required clinical and preclinical testing, among other items, the results of product development, including chemistry, manufacture and controls, non-clinical studies and clinical trials are submitted to the FDA, along with proposed labeling, as part of an NDA. The submission of an NDA requires payment of a substantial application user fee to the FDA. These user fees must be filed at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in some circumstances. One basis for a waiver of the application user fee is if the applicant employs fewer than 500 employees, including employees of affiliates, the applicant does not have an approved marketing application for a product that has been introduced or delivered for introduction into interstate commerce, and the applicant, including its affiliates, is submitting its first marketing application.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA must refer applications for drugs that contain active ingredients, including any ester or salt of the active ingredients, that have not previously been approved by the FDA to an advisory committee or provide in an action letter a summary of the reasons for not referring it to an advisory committee. The FDA may also refer drugs which present difficult questions of safety, purity or potency to an advisory committee. An advisory committee is a panel that typically includes clinicians and other experts who review, evaluate and make a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontracts, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

Once the FDA receives an application, it has 60 days to review the NDA to determine if it is substantially complete to permit a substantive review, before it accepts the application for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The timeline for the FDA to complete its review of a NDA may differ based on whether the application is a standard review or priority review application. The FDA may give a priority review designation to drugs that are intended to treat serious conditions and provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has set the review goal of ten months from the 60-day filing date to complete its initial review of a standard NDA for a new molecular entity, or NME, and make a decision on the application. For non-NME standard applications, the FDA has set the review goal of ten months from the submission date to complete its initial review and to make a decision on the application. For priority review applications, the FDA has set the review goal of reviewing NME NDAs within six months of the 60-day filing date and non-NME applications within six months of the submission date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal and the FDA does not always meet its PDUFA dates. The review process and the PDUFA date may also be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding the submission.

Once the FDA's review of the application is complete, the FDA will issue either a Complete Response Letter, or CRL, or approval letter. A CRL indicates that the review cycle of the application is complete, and the application is not ready for approval. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing, or other information or analyses in order for the FDA to reconsider the application. The FDA has the goal of reviewing 90% of application resubmissions in either two or six months of the resubmission date, depending on the kind of resubmission (Class 1 or Class 2). Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product, or impose other conditions, including distribution restrictions or other risk management mechanisms. For example, the FDA may require a risk evaluation and mitigation strategy, or REMS, as a condition of approval or following approval to mitigate any identified or suspected serious risks and ensure safe use of the drug. The FDA may prevent or limit further marketing of a product, or impose additional post-marketing requirements, based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements, FDA notification and FDA review and approval. Further, should new safety information arise, additional testing, product labeling or FDA notification may be required.

FDA approval of any NDA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings or precautions in the product labeling, including a black box warning. If the FDA requires a boxed warning, we would also be subject to specified promotional restrictions, such as the prohibition of reminder advertisements. The FDA also may not approve the inclusion of labeling claims necessary for successful marketing. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

***Post-approval Requirements***

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including manufacturing, periodic reporting, product sampling and distribution, advertising, promotion, drug shortage reporting, compliance with any post-approval requirements imposed as a conditional of approval such as Phase 4 clinical trials, REMS and surveillance, recordkeeping and reporting requirements, including adverse experiences. For example, we are required to conduct pediatric studies related to Apadaz, which was approved by the FDA in February 2018, to determine the safety and effectiveness of Apadaz for the claimed indication in pediatric patients.

After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any approved products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and to list their drug products, and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP regulations and other FDA regulatory requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented, or FDA notification. FDA regulations also require investigation and correction of any deviations from cGMPs and specifications and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in withdrawal of marketing approval, mandatory revisions to the approved labeling to add new safety information or other limitations, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program, among other consequences.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA. Physicians, in their independent professional medical judgment, may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. We, however, are prohibited from marketing or promoting drugs for uses outside of the approved labeling.

In addition, the distribution of prescription pharmaceutical products, including samples, is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration 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. The Drug Supply Chain Security Act also imposes obligations on manufacturers of pharmaceutical products related to product tracking and tracing.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and individual imprisonment. Any of these sanctions could result in adverse publicity, among other adverse consequences.

***Risk Evaluation and Mitigation Strategy***

The FDA has the authority to require a REMS to ensure the safe use of the drug. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecule. If the FDA determines a REMS is necessary, the drug sponsor must develop the REMS program, which the FDA reviews and approves. A REMS may be required for a single drug or an entire class of drugs.

A REMS may be required to include various elements, including, but not limited to, a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, elements to assure safe use, or ETASU, an implementation system, or other measures that the FDA deems necessary to assure the safe use of the drug. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under specified circumstances, special monitoring, and the use of patient registries. In addition, the REMS must include a timetable to periodically assess the strategy. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks. The requirement for a REMS can materially affect the potential market and profitability of a drug.

Based upon currently approved product REMS programs and class-wide REMS programs, including the class-wide REMS programs for extended-release and long-acting opioid analgesics, we believe that most of our products and product candidates, if approved, may be subject to a REMS. Accordingly, we expect to have to take prescribed measures to ensure the safe use of our products, once they are approved. For example, we are required to prepare a REMS program for Apadaz, the plan for which was approved by the FDA, along with the NDA for Apadaz, in February 2018.

***Prescription Drug Program Fees***

In general, each applicant named in a human drug application is required to pay an annual prescription drug program fee for each prescription drug product that is identified in such a human drug application approved as of October 1 of such fiscal year. Applicants may not be assessed more than five prescription drug program fees for a fiscal year for prescription drug products identified in a single approved application.

A prescription drug product is not assessed a prescription drug program fee if the product is on the list compiled under section 505(j)(7) with a potency described in terms of per 100 milliliters (large volume parenteral), the product is the same as another product approved under an application filed under sections 505(b) or 505(j) of the Federal Food, Drug and Cosmetic Act and that other product is not in the list of discontinued products compiled under 505(j)(7) of the Federal Food, Drug and Cosmetic Act or an abbreviated application filed under section 507 of the Federal Food, Drug and Cosmetic Act, or an ANDA prior the implementation of the Drug Price Competition and Patent Term Restoration Act of 1984.

Like application user fees, fee waivers or reductions are available for prescription drug program fees in some circumstances.

***DEA Regulation***

Most of our products and product candidates, if approved, will be regulated as "controlled substances" as defined in the Controlled Substances Act of 1970, or CSA, and the DEA's implementing regulations, which establish registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA. These requirements are directly applicable to us and also applicable to our contract manufacturers and to distributors, prescribers and dispensers of our product candidates. The DEA regulates the handling of controlled substances through a closed chain of distribution. This control extends to the equipment and raw materials used in their manufacture and packaging 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 no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Schedule II drugs are those that meet the following criteria:

- the drug has a high potential for abuse;
- the drug has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions; and
- abuse of the drug may lead to severe psychological or physical dependence.

The DEA has determined that APADAZ will be listed as a Schedule II controlled substance under the CSA, and we expect that most of our other products and product candidates may be listed in the same manner, if approved. In 2014, the DEA rescheduled hydrocodone combination products into Schedule II from Schedule III. If our product candidates are ultimately listed as Schedule II controlled substances, then the importation of APIs for our product candidates, as well as the manufacture, shipping, storage, sales and use of the products, will be subject to a high degree of regulation. In addition to maintaining an importer and/or exporter registration, importers and exporters of controlled substances must obtain a permit for every import of a Schedule I or II substance and a narcotic substance in Schedule III, IV and V, as well as every export of a Schedule I or II substance and a narcotic substance in Schedule III and IV. For all other drugs in Schedule III, IV and V, importers and exporters must submit an import or export declaration. Schedule II drugs are subject to the strictest requirements for registration, security, recordkeeping and reporting. Also, distribution and dispensing of these drugs are highly regulated. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Electronic prescriptions may also be permissible depending on the state, so long as the prescription complies with the DEA's requirements for electronic prescriptions.

Controlled substances classified in Schedule III, IV, and V are also subject to registration, recordkeeping, reporting, and security requirements. For example, Schedule III drug prescriptions must be authorized by a physician and may not be refilled more than six months after the date of the original prescription or more than five times. A prescription for controlled substances classified in Schedules III, IV, and V issued by a physician, may be communicated either orally, in writing or by facsimile to the pharmacies. Controlled substances that are also classified as narcotics, such as hydrocodone, oxycodone and hydromorphone, are also subject to additional DEA requirements, such as manufacturer reporting of the import of narcotic raw material.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized. Similarly, separate registrations are also required for separate facilities. Acquisition and distribution transactions must also be reported for Schedule I and II controlled substances, as well as Schedule III narcotic substances.

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

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance or Schedule III narcotic must also be accompanied by special order forms, with copies provided to the DEA. Because most of our current product candidates may be regulated as Schedule II controlled substances, they may be subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for how much of a controlled substance may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. The limited aggregate amount of opioids and stimulants that the DEA allows to be produced in the United States each year is allocated among individual companies, which must submit applications annually to the DEA for individual production and procurement quotas. We and our contract manufacturers must receive an annual quota from the DEA in order to produce or procure any Schedule I or Schedule II for use in manufacturing of our product candidates. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Our, or our contract manufacturers', quota of an active ingredient may not be sufficient to meet commercial demand or complete clinical trials. Any delay, limitation 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. To enforce these requirements, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in administrative, civil or criminal enforcement action that could have a material adverse effect on our business, results of operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate administrative proceedings to revoke those registrations. In some circumstances, violations could result in criminal proceedings.

Individual states also independently regulate controlled substances. We and our contract manufacturers will be subject to state regulation on distribution of these products, including, for example, state requirements for licensures or registration.

***Other Healthcare Regulations***

Our business activities, including but not limited to, research, sales, promotion, distribution, medical education and other activities are subject to regulation by numerous regulatory and law enforcement authorities in the United States in addition to the FDA, including potentially the Department of Justice, the U.S. Department of Health and Human Services and its various divisions, including the CMS and the Health Resources and Services Administration, the Department of Veterans Affairs, the Department of Defense and state and local governments. Our business activities must comply with numerous healthcare laws, including those described below.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for, or purchasing, leasing, ordering, or arranging for the purchase, lease or order of, any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the ACA amended the intent requirement of the federal Anti-Kickback Statute, and some other healthcare criminal fraud statutes, so that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute, or the specific intent to violate it, to have violated those statutes. The ACA also provided that a violation of the federal Anti-Kickback Statute is grounds for the government or a whistleblower to assert that a claim for payment of items or services resulting from such violation constitutes a false or fraudulent claim for purposes of the False Claims Act.

The federal civil and criminal false claims laws, including the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or *qui tam* actions, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government, including the Medicare and Medicaid programs, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government.

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Additionally, the ACA amended the intent requirement of some of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

Additionally, the federal Open Payments program, created under Section 6002 of the ACA and its implementing regulations, require some manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with specified exceptions) to report annually information related to specified payments or other transfers of value provided to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually specified ownership and investment interests held by physicians and their immediate family members.

Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in significant civil monetary penalties.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes requirements covered entities, including certain healthcare providers, health plans and healthcare clearinghouses, and their respective business associates, independent contractors or agents of covered entities that receive or obtain individually identifiable health information in connection with providing a service on behalf of a covered entity, relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Many states have also adopted laws similar to each of the above federal laws, which may be broader in scope and apply to items or services reimbursed by any third-party payor, including commercial insurers. Several states and local jurisdictions have also enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, or register their sales representatives, as well as prohibiting pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and prohibiting certain other sales and marketing practices.

Depending on the circumstances, failure to comply with these laws can result in penalties, including criminal, civil and/or administrative penalties, damages, fines, disgorgement, debarment from government contracts, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion from government programs, refusal to allow us to enter into supply contracts, including government contracts, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our business.

***Healthcare Reform Measures***

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals designed to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States 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 United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, in March 2010, the ACA was passed. The ACA has substantially changed health care financing by both governmental and private insurers, and significantly affected the U.S. pharmaceutical industry. The ACA, among other things, subjected manufacturers to new annual fees and taxes for specified branded prescription drugs, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, expanded health care fraud and abuse laws, revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated, imposed an inflation penalty on new formulations of drugs, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, expanded the 340B program which caps the price at which manufacturers can sell covered outpatient pharmaceuticals to specified hospitals, clinics and community health centers, and provided incentives to programs that increase the federal government's comparative effectiveness research. There have been judicial and congressional challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by ACA. Concurrently, Congress has considered legislation to repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". We continue to evaluate the effect that the ACA has on our business. Final regulations, guidance, amendments and judicial orders are anticipated in the future and we will continue to assess the ACA's impact on us as final regulations, guidance, amendments and judicial orders are issued.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 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 of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In addition, in January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

***The Foreign Corrupt Practices Act***

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the companies to maintain books and records that accurately and fairly reflect all transactions of the companies, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

***Foreign Regulation***

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any products outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

**Employees**

As of December 31, 2017, we employed 32 full-time employees. We have never had a work stoppage, and none of our employees are represented by a labor organization or under any collective bargaining arrangements. We consider our employee relations to be good.

**Segments and Geographic Information**

We view our operations and manage our business as one operating segment. See our financial statements for a discussion of revenues, operating loss, net loss and total assets. All of our assets were held in the United States for the years ended December 31, 2017, 2016 and 2015.

**Corporate Information**

We were incorporated under the laws of the State of Iowa in October 2006 and were reincorporated under the laws of the State of Delaware in May 2014. Our principal executive offices are located at 2500 Crosspark Road, Suite E126, Coralville, IA 52241 and our telephone number is (319) 665-2575.

Our website address is www.kempharm.com. The information contained on our website is not incorporated by reference into this Annual Report on Form 10-K.

**ITEM 1A. RISK FACTORS.**

You should carefully consider all the risk factors and uncertainties described below, in addition to other information contained in this Annual Report on Form 10-K, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes, before investing in our common stock. If any of the following risks materialize, our business, financial condition and results of operations could be seriously harmed. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements because of factors that are described below and elsewhere in this Annual Report on Form 10-K.

**Risks Related to Our Financial Position and Capital Needs**

***We have incurred significant operating losses since our inception. We expect to incur operating losses over the next several years and may never achieve or maintain profitability.***

We have incurred operating losses since our inception and, as of December 31, 2017, had an accumulated deficit of $164.7 million. Our loss from operations for the years ended December 31, 2017, 2016 and 2015, were $33.4 million, $37.5 million and $22.8 million, respectively. We have financed our operations to date with $25.3 million raised in private placements of redeemable convertible preferred stock, $115.9 million in convertible promissory notes and term debt and $59.9 million in aggregate net proceeds from our initial public offering. In addition, as of March 28, 2018, we have raised $2.9 million in gross proceeds from the sales of 446,111 shares of our common stock under our Common Stock Sales Agreement, or ATM Agreement, with Cowen and Company, LLC, or Cowen.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We are still in the early stages of development of many of our product candidates, and we have only completed development of, and received regulatory approval for, one of our product candidates, APADAZ. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our ongoing preclinical studies, clinical trials and our product development activities for our pipeline of product candidates;
- seek regulatory approvals for product candidates that successfully complete clinical trials;
- continue research and preclinical development and initiate clinical trials of our product candidates;
- seek to discover and develop additional product candidates either internally or in partnership with other pharmaceutical companies;
- potentially establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize APADAZ and any of our product candidates for which we may obtain regulatory approval;
- increase chemistry, manufacturing and controls, or CMC, activities related to the potential commercialization of APADAZ and any of our product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- incur additional legal, accounting and other expenses in operating as a public company; and
- add operational systems and personnel, including systems and personnel, if needed, to support any future commercialization efforts.

To become and remain profitable, we must succeed in developing and eventually commercializing prodrugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials and obtaining regulatory approval of our product candidates, and manufacturing, marketing and selling APADAZ and any of our product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. For instance, we have not yet determined our strategy for commercializing APADAZ, and we cannot guarantee that any strategy we adopt will be successful. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with prodrug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, obtain product approvals, diversify our product offerings or continue our operations. A decline in our value could also cause you to lose all or part of your investment.

***The auditor's opinion on our audited financial statements for the fiscal year ended December 31, 2017, 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, 2017 includes an explanatory paragraph stating that our recurring losses from operations, stockholders' deficit and negative operating cash flows raise substantial doubt about our ability to continue as a going concern. While we believe that we will be able to raise the capital we need to continue our operations, 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, 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.

***We will need substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to delay, reduce or altogether cease our prodrug development programs or commercialization efforts.***

Based on our current operating plan, existing resources are not expected to be sufficient to fund operating expense and capital investment requirements through the first quarter of 2019. Because of this, the auditor's opinion on our audited financial statements for the year ended December 31, 2017, includes an explanatory paragraph stating that our recurring losses from operations and negative cash flows raise substantial doubt about our ability to continue as a going concern. We will need to obtain substantial additional funding in connection with our continuing operations from one or more equity offerings, including pursuant to our ATM Agreement, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements, and we cannot guarantee that we will be able to generate sufficient proceeds from sales under our ATM Agreement or otherwise, or be successful in completing other transactions, that will fund our operating expenses. Our future capital requirements will depend on many factors, including:

- the progress and results of our preclinical studies, clinical trials, CMC and other product development and commercialization activities;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the ability to obtain differentiating claims in the labels for our product candidates;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the efforts necessary to institute post-approval regulatory compliance requirements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for APADAZ and any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of APADAZ or our product candidates for which we receive marketing approval , which may be affected by market conditions, including obtaining coverage and adequate reimbursement of APADAZ or our product candidates from third-party payors, including government programs and managed care organizations, and competition within the therapeutic class to which APADAZ or our product candidates are assigned;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may not generate the necessary data or results required to obtain regulatory approval for our product candidates or claims necessary to make such candidates profitable and achieve product sales. In addition, APADAZ or our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of prodrug products and we do not currently know when, APADAZ or any of our product candidates will be commercially available. We have not yet determined our strategy for commercializing APADAZ, and we cannot guarantee that any strategy we adopt will be successful. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or debt securities, the terms of these securities or this debt may restrict our ability to operate. On June 2, 2014 ,we entered into a $60 million facility agreement, or the Deerfield Facility Agreement, with Deerfield Private Design Fund III, LP, or Deerfield. The Deerfield Facility Agreement includes, and any future debt financing and equity financing, if available, may involve agreements that include, covenants limiting and restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, entering into profit-sharing or other arrangements or declaring dividends. Additionally, in February 2016, we issued 5.50% senior convertible notes due 2021, or the 2021 Notes. We are required to make periodic interest payments to the holders of the 2021 Notes and to make payments of principal upon maturity. In this regard, if holders of the 2021 Notes do not convert their 2021 Notes prior to the maturity date, we will be required to repay the principal amount of all then outstanding 2021 Notes plus any accrued and unpaid interest. We may also be required to repurchase the 2021 Notes for cash upon the occurrence of a change of control or certain other fundamental changes involving us. If our capital resources are insufficient to satisfy our debt service obligations, we will be required to seek to sell additional equity or debt or to obtain debt financing. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

***Our operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.***

We commenced active operations in 2006, and our operations to date have been largely focused on raising capital, identifying potential product candidates, broadening our expertise in the development of our prodrugs, undertaking preclinical studies and conducting clinical trials. To date, we have only had one of our product candidates approved by the FDA. For instance, on February 23, 2018, we announced that the FDA approved our NDA for APADAZ for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. We have not yet demonstrated an ability to manufacture a prodrug on a commercial scale, or arrange for a third party to do so, or conduct sales and marketing activities necessary for successful commercialization or enter into a collaboration for that purpose. We have not yet determined our strategy for commercializing APADAZ, and we cannot guarantee that any strategy we adopt will be successful. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

**Risks Related to the Development of Our Product Candidates**

***Our research and development activities are focused on discovering and developing proprietary prodrugs, and we are taking an innovative approach to discovering and developing prodrugs, which may never lead to marketable prodrug products.***

A key element of our strategy is to use our LAT platform technology to build a pipeline of prodrugs and progress product candidates based on these prodrugs through clinical development for the treatment of a variety of diseases and conditions. The scientific discoveries that form the basis for our efforts to discover and develop prodrugs are relatively new. As our scientific efforts are primarily focused on discovering novel prodrugs with new molecular structures, the evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Although our research and development efforts to date have resulted in a pipeline of prodrug product candidates, we may not be able to develop prodrugs that are bioequivalent, safe and effective and that have commercially significant improvements over already approved drugs. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, for reasons including being shown to have harmful side effects, a lack of efficacy, or other characteristics that indicate that they are unlikely to be prodrugs that will receive marketing approval and achieve market acceptance. For instance, in June 2016, we received a CRL from the FDA for our APADAZ NDA. In November 2016, we elected to continue the regulatory review process for APADAZ with the submission of a FDRR to the FDA. In September 2017, we announced completion of the FDRR process with the FDA for APADAZ. Following detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended NDA for APADAZ. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ. If we do not successfully commercialize APADAZ and develop and commercialize our product candidates based upon our LAT platform technology, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

***If we are not able to obtain required regulatory approvals for our product candidates, we will not be able to commercialize them and our ability to generate revenue or profits or to raise future capital could be limited.***

The research, testing, manufacturing, labeling, packaging, storage, approval, sale, marketing, advertising and promotion, pricing, export, import and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country and change over time. We are not permitted to market any of our product candidates in the United States until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite approvals in such countries. In the United States, the FDA generally requires the completion of non-clinical testing and clinical trials of each drug to establish its safety and efficacy and extensive pharmaceutical development to ensure its quality and other factors before an NDA is approved. Regulatory authorities in other jurisdictions impose similar requirements. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

Even if regulatory approval is obtained, subsequent safety, efficacy, quality or other issues can result in a product approval being suspended or withdrawn. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ. Even with the regulatory approval of APADAZ by the FDA, we cannot guarantee that the FDA will approve any of our other product candidates for commercial sale. If our development efforts for our product candidates, including regulatory approval, are not successful for their planned indications or are delayed, or if adequate demand for our product candidates that are approved for marketing, if any, is not generated, our business will be harmed.

The success of our product candidates will depend on the receipt and maintenance of regulatory approval and the issuance and maintenance of such approval is uncertain and subject to a number of risks, including the following:

- the FDA or comparable foreign regulatory authorities, institutional review boards, or IRBs, or ethics committees may disagree with the design or conduct of our clinical trials;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or other regulatory agencies for marketing approval or for us to receive approval for claims that are necessary for commercialization;
- the dosing in a particular clinical trial may not be at an optimal level;
- patients in our clinical trials may suffer adverse effects for reasons that may or may not be related to our product candidates;
- the data collected from clinical trials may not be sufficient to support submissions to regulatory authorities or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies or may later suspend or withdraw such approval;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; and
- even if we obtain marketing approval in one or more countries, future safety or other issues could result in the suspension or withdrawal of regulatory approval in such countries.

We have only limited experience in filing the applications necessary to gain regulatory approvals and have relied, and expect to continue to rely, on consultants and third-party contract research organizations, or CROs, with expertise in this area to assist us in this process. Securing FDA approval requires the submission of extensive non-clinical and clinical data, information about product manufacturing processes and inspection of facilities and supporting information to the FDA for each therapeutic indication to establish a product candidate's safety and efficacy for each indication and manufacturing quality. Additionally, we cannot guarantee that regulators will agree with our assessment of the results of the clinical trials we have conducted or that any future trials will be successful. For example, in May 2016, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA voted 16 to four for the approval of APADAZ, but voted 18 to two against inclusion of abuse-deterrent labeling for APADAZ. Additionally, in June 2016, we received a CRL from the FDA for our APADAZ NDA. In November 2016, we elected to continue the regulatory review process for APADAZ with the submission of a FDRR to the FDA. In September 2017, we announced completion of the FDRR process with the FDA for APADAZ. Following detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended NDA for APADAZ. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ.

Any product candidates we develop may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use with respect to one or all intended indications.

The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon, among other things, the type, complexity and novelty of the product candidates involved, the jurisdiction in which regulatory approval is sought and the substantial discretion of the regulatory authorities. Changes in the regulatory approval policy during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for a submitted product application may cause delays in the approval or rejection of an application or may result in future withdrawal of approval. Regulatory approval obtained in one jurisdiction does not necessarily mean that a product candidate will receive regulatory approval in all jurisdictions in which we may seek approval, but the failure to obtain approval in one jurisdiction may negatively impact our ability to seek approval in a different jurisdiction. Failure to obtain regulatory marketing approval of our product candidates in any indication will prevent us from commercializing those product candidates for that indication, and our ability to generate revenue will be impaired.

***We are early in our development efforts and have only one product which has completed development and obtained regulatory approval by the FDA, APADAZ. All our other active product candidates are in clinical or preclinical development. If we are unable to commercialize APADAZ or our product candidates, or experience significant delays in doing so, our business will be harmed.***

We are early in our development efforts and have only one product that has completed development and been approved by the FDA, APADAZ. All of our other active product candidates are in clinical or preclinical development. We currently generate no revenue from the sale of any prodrugs and we may never be able to commercialize a prodrug product. For instance, we have not yet determined our strategy for commercializing APADAZ, and we cannot guarantee that any strategy we adopt will be successful. We have invested substantially all our efforts and financial resources in the development of our LAT platform technology, the identification of potential product candidates and the development of our product candidates. Our ability to generate revenue from APADAZ and our product candidates will depend heavily on their successful development and eventual commercialization. The success of APADAZ and our product candidates will depend on several factors, including:

- successful completion of preclinical studies and requisite clinical trials;
- successful completion and achievement of endpoints in our clinical trials;
- demonstration that the risks involved with APADAZ and our product candidates are outweighed by the benefits;
- successful development of our manufacturing processes for APADAZ and our product candidates, including entering into and maintaining arrangements with third-party manufacturers;
- successful completion of an FDA preapproval inspection of the facilities used to manufacture APADAZ and our product candidates, as well as select clinical trial sites;
- receipt of timely marketing approvals from applicable regulatory authorities, including, if applicable, the determination by the U.S. Drug Enforcement Administration, or DEA, of the controlled substance schedule for APADAZ and a product candidate, taking into account the recommendation of the FDA;
- obtaining differentiating claims in the labels for our product candidates;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for APADAZ and our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs;
- launching commercial sales of APADAZ and our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of APADAZ and our prodrug product candidates, if approved, by patients, the medical community and third-party payors;
- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement; and
- maintaining a continued acceptable safety and efficacy profile of the prodrug products following approval.

Whether regulatory approval will be granted is unpredictable and depends upon numerous factors, including the substantial discretion of the regulatory authorities. If, following submission, our NDA for a product candidate is not accepted for substantive review or approval, the FDA or other comparable foreign regulatory authorities may require that we conduct additional studies or clinical trials, provide additional data, take additional manufacturing steps or require other conditions before they will reconsider our application. If the FDA or other comparable foreign regulatory authorities require additional studies, clinical trials or data, we would incur increased costs and delays in the marketing approval process, which may require us to expend more resources than we have available. In addition, the FDA or other comparable foreign regulatory authorities may not consider sufficient any additional required studies, clinical trials, data or information that we perform and complete or generate, or we may decide to abandon the program.

Although APADAZ obtained regulatory approval on February 23, 2018, it is possible that none of our other existing product candidates or any of our future product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize APADAZ or our product candidates, which would harm our business.

***Our ability to market and promote our products in the United States by describing their abuse-deterrent features will be determined by the FDA-approved labeling for them.***

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

FDA approval is required to make claims that a product has an abuse-deterrent effect. In January 2013, the FDA published draft guidance with regard to the evaluation and labeling of abuse-deterrent opioids. This guidance was published in final form in April 2015. The FDA guidance provides direction as to the studies and data required for obtaining abuse-deterrent claims in a product label. The guidance describes four categories of label claims for abuse-deterrent products. Depending on product and study data, a combination of categories can be included in the label claims. The FDA guidance lists the following theoretical examples:

- Category 1–in vitro data demonstrate the product has physical and chemical properties that are expected to deter intravenous abuse. However, abuse is still possible by the oral and nasal routes.

- Category 1 and 2–in vitro data demonstrate that the product has physical and chemical properties that are expected to deter oral, nasal and intravenous abuse. However, abuse of intact product is still possible by the oral route.

- Category 2 and 3–pharmacokinetic and clinical abuse potential studies indicate that the product has properties that are expected to deter abuse via the oral, intranasal and intravenous routes. However, abuse of product by these routes is still possible.

- Category 4–data demonstrated a reduction in the abuse of the product in the community setting compared to the levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available. This reduction in abuse appears to be attributable to the product's formulation, which deters abuse by injection or snorting of the manipulated product. However, such abuse of this product is still possible, and the product's abuse-deterrent properties do not deter abuse associated with swallowing the intact formulation.

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

There can be no assurance that any of our product candidates will receive FDA-approved labeling that describes the abuse-deterrent features of such products. The FDA may find that our trials do not support abuse-deterrent labeling or that our product candidates do not provide substantial abuse deterrence because, for example, their deterrence mechanisms do not address the way they are most likely to be abused. For instance, in May 2016, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA voted 18 to two against inclusion of abuse-deterrent labeling for APADAZ. Subsequently, in June 2016, the FDA issued a CRL for our APADAZ NDA indicating that the FDA considered the review cycle for the APADAZ NDA complete and that the application was not ready for approval in its present form. In its CRL, the FDA advised us that it did not believe our proposed labeling included in the application accurately conveyed the outcome of our abuse-deterrent studies of APADAZ. In November 2016, we elected to continue the regulatory review process for APADAZ with the submission of a FDRR to the FDA. In September 2017, we announced completion of the FDRR process with the FDA for APADAZ. Following detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended NDA for APADAZ. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ. The final label approved by the FDA for APADAZ determined it was not expected to deter abuse.

As with all claims, we will be required to provide adequate substantiation. For example, we will need to demonstrate that our product candidates have abuse-deterrent properties sufficient to achieve abuse-deterrent labeling.

Further, the FDA is not required to follow its guidance and could change this guidance, which could require us to conduct additional trials. If the FDA does not approve abuse-deterrent labeling, we will not be able to promote such products based on their abuse-deterrent features and may not be able to differentiate such products from other comparable products.

Even if we do receive FDA approval for abuse-deterrent claims, the claims may not be broad enough to demonstrate a substantial benefit to health care providers and patients. For instance, the claims may not encompass the more common forms of abuse for products like our product candidates. Moreover, continued investigation in Phase 4 studies following product approval may not support the continued use of abuse-deterrent claims.

***If we attempt to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act and the FDA does not conclude that our product candidates are sufficiently bioequivalent, or have comparable bioavailability, to approved drugs, or if the FDA does not allow us to pursue the 505(b)(2) NDA pathway as anticipated, the approval pathway for our product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and the FDA may not ultimately approve our product candidates.***

A key element of our strategy is to seek FDA approval for most of our product candidates under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, otherwise known as the 505(b)(2) NDA pathway with any NDA submitted thereunder a 505(b)(2) NDA, where possible. The 505(b)(2) NDA pathway 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. Such reliance is typically predicated on a showing of bioequivalence or comparable bioavailability to an approved drug.

If the FDA does not allow us to pursue the 505(b)(2) NDA pathway as anticipated, or if we cannot demonstrate bioequivalence or comparable bioavailability of our product candidates to approved products, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. Moreover, even if the FDA does allow us to pursue the 505(b)(2) NDA pathway, depending on the product candidate, we may still need to conduct additional clinical trials, including clinical trials to assess product safety or efficacy. For instance, we currently plan on relying on the 505(b)(2) pathway for any NDA we submit for KP415 or KP484 and KP201/IR. However, we do not anticipate that the 505(b)(2) pathway will be available for every product candidate. For instance, it is possible we will only be permitted to utilize the 505(b)(2) NDA pathway for either KP415 or KP484, but not both. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates, and complications and risks associated with our product candidates, would likely substantially increase.

To rely on the FDA's previous findings of safety and effectiveness for an approved product in a 505(b)(2) NDA, the approved product must be an NDA product. For our amended APADAZ NDA, because there are no approved NDAs for hydrocodone/APAP combination products, we were required to rely on two NDAs (one containing hydrocodone and another containing APAP) to bridge previous findings of safety and efficacy from those NDAs to APADAZ. We also referenced published medical and scientific literature for hydrocodone and APAP in our amended APADAZ NDA to support the safety and effectiveness of APADAZ and we were required to demonstrate bioequivalence to NORCO to establish that APADAZ is not a new drug combination. If this is deemed insufficient, we may need to conduct additional clinical trials and provide additional data and information regarding the safety and effectiveness of APADAZ.

Moreover, our inability to pursue the 505(b)(2) NDA pathway could result in new competitive products reaching the market more quickly than our product candidates, which could hurt our competitive position and our business prospects. Even if we are allowed to pursue the 505(b)(2) NDA pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization on a timely basis, if at all. Other companies may achieve product approval of similar products before we do, which would delay our ability to obtain product approval, expose us to greater competition, and would require that we seek approval via alternative pathways, such as an abbreviated new drug application, or ANDA, which is used for the development of generic drug products.

In addition, notwithstanding the approval of several products by the FDA under 505(b)(2) over the last few years, pharmaceutical companies and others have objected to the FDA's interpretation of 505(b)(2). If the FDA's interpretation of 505(b)(2) is successfully challenged, the FDA may change its policies and practices with respect to 505(b)(2) regulatory approvals, which could delay or even prevent the FDA from approving any NDA that we submit under 505(b)(2).

Even if our product candidates are approved under 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed, including more limited subject populations than we request, may require that contraindications, warnings or precautions be included in the product labeling, including a black box warning, may be subject to other conditions of approval, or may contain requirements for costly post-marketing clinical trials, testing and surveillance to monitor the safety or efficacy of the products, or other post-market requirements, such as a Risk Evaluation and Mitigation Strategy, or REMS. The FDA also may not approve a product candidate with a label that includes the labeling claims necessary or desirable for the successful commercialization of that product candidate. Based upon currently approved products, we anticipate that we will be required to conduct Phase 4 studies and to implement a REMS and will have a black box warning for at least some of our product candidates.

***The FDA may determine that any NDA we may submit under the 505(b)(2) regulatory pathway for any of our product candidates in the future is not sufficiently complete to permit a substantive review.***

If we were to submit an NDA under the 505(b)(2) regulatory for any of our product candidates, within 60 days of the agency's receipt of our NDA, the FDA will make a threshold determination of whether the NDA is sufficiently complete to permit a substantive review. This 60-day review period is referred to as the filing review. If the NDA is sufficiently complete, the FDA will file the NDA. If the agency refuses to file the NDA, it will notify us and state the reason(s) for the refusal. The FDA may refuse to file our NDA for various reasons, including but not limited to, if:

- the NDA is incomplete because it does not on its face contain the information required under the Federal Food, Drug and Cosmetic Act or the FDA's regulations;
- the NDA does not contain a statement that each non-clinical laboratory study was conducted in compliance with good laboratory practices requirements, or for each study not so conducted, a brief statement of the reason for the noncompliance;
- the NDA does not contain a statement that each clinical trial was conducted in compliance with the IRB regulations or was not subject to those regulations, and the agency's informed consent regulations or a brief statement of the reason for noncompliance; or
- the drug is a duplicate of a listed drug approved before receipt of the NDA and is eligible for approval under an ANDA for generic drugs.

In its procedures, the FDA has stated that it could find an NDA submitted under the Section 505(b)(2) regulatory pathway incomplete and refuse to file it if the NDA, among other reasons:

- fails to include appropriate literature or a listed drug citation to support the safety or efficacy of the drug product;
- fails to include data necessary to support any aspects of the proposed drug that represent modifications to the listed drug(s) relied upon;
- fails to provide a bridge, for example by providing comparative bioavailability data, between the proposed drug product and the listed drug product to demonstrate that such reliance is scientifically justified;
- uses an unapproved drug as a reference product for the bioequivalence study; or
- fails to provide a patent certification or statement as required by the FDA's regulations where the 505(b)(2) NDA relies on one or more listed drugs.

Additionally, the FDA will refuse to file an NDA if an approved drug with the same active moiety is entitled to five years of exclusivity, unless the exclusivity period has elapsed, or unless four years of the five-year period have elapsed and the NDA contains a certification of patent invalidity or non-infringement. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bond) or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the therapeutic activity of the drug substance.

If the FDA refuses to file an NDA submitted by us, we may amend the NDA and resubmit it. In such a case, the FDA will again review the NDA and determine whether it may be filed. There can be no assurance that the FDA will file any NDA submitted by us in the future. If the agency refuses to file an NDA, we will need to address the deficiencies cited by the FDA, which could substantially delay the review process.

***Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

The risk of failure for our product candidates is high. It is impossible to predict when or if any of our current product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Interpretation of results from early, usually smaller, studies that suggest positive trends in some subjects, requires caution. Results from later stages of clinical trials enrolling more subjects may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidates. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints, or lack of trial endpoints in exploratory studies, subject population, number of subjects, subject selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. For instance, in June 2016, the FDA issued a CRL for our APADAZ NDA. In its CRL, the FDA advised us that it did not believe our proposed labeling included in the application accurately conveyed the outcome of our abuse-deterrent studies of APADAZ. In November 2016, we elected to continue the regulatory review process for APADAZ with the submission of a FDRR to the FDA. In September 2017, we announced completion of the FDRR process with the FDA for APADAZ. Following detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended NDA for APADAZ. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or IRBs may not authorize us or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site or amend clinical trial protocols as needed;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites and CROs;
- clinical trials of our product candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance in cases where that is required, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon prodrug development programs;
- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or trial protocols, or meet their contractual obligations to us in a timely manner, or at all;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate, including if we are not able to pursue the 505(b)(2) NDA pathway for approval of our product candidates;
- we will need to pay substantial application user fees, which we may not be able to afford;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- we may abandon our development program or programs based on the changing regulatory or commercial environment;
- regulatory authorities may not agree with our trial design or implementation; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval but without the claims necessary for us to successfully commercialize our product candidates;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing, surveillance, or other requirements, such as REMS; or
- have the product removed from the market after obtaining marketing approval.

Our prodrug development costs may also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

***Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.***

As product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, various aspects of the development program, such as manufacturing methods and formulation, may be altered along the way in an effort to optimize processes and results. Such changes may not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence product sales and generate revenue.

***Our decision to seek approval of our product candidates under the 505(b)(2) NDA pathway, if available, may increase the risk that patent infringement suits are filed against us, which would delay the FDA's approval of such product candidates.***

Regarding any NDA that we may submit under the 505(b)(2) NDA pathway, if there are patents that claim the approved drug contained in our product candidates and referenced in our 505(b)(2) NDA, we must certify to the FDA and notify the patent holder that any patents listed for the approved drug in the FDA's Orange Book publication are invalid, unenforceable or will not be infringed by the manufacture, use or sale of our prodrug. If a patent infringement lawsuit is filed against us within 45 days of its receipt of notice of our certification, the FDA is automatically prevented from approving our 505(b)(2) NDA until the earliest of 30 months, expiration of the patent, settlement of the lawsuit or a court decision in the infringement case that is favorable to us, or such shorter or longer period as may be ordered by a court. Such actions are routinely filed by patent owners. Accordingly, we may invest considerable time and expense in the development of our product candidates only to be subject to significant delay and patent litigation before our product candidates may be commercialized. We may not be successful in defending any patent infringement claim. Even if we are found not to infringe, or a plaintiff's patent claims are found invalid or unenforceable, defending any such infringement claim would be expensive and time-consuming, and would delay launch of our product candidates and distract management from their normal responsibilities.

***We may not be successful in our efforts to develop a prodrug-based product that might allow us to seek a rare pediatric disease priority review voucher.***

The FDA has awarded rare pediatric disease priority review vouchers to sponsors of drug candidates to treat rare pediatric disease, if the treatment sponsors apply for this designation and meet certain criteria. Under this program, upon the approval of a qualifying NDA, for the treatment of a rare pediatric disease, the sponsor of such an application would be eligible for a rare pediatric disease priority review voucher that can be used to obtain priority review for a subsequent NDA. The priority review voucher may be sold or transferred an unlimited number of times.

We recently announced a technology licensing agreement with Genco Sciences, LLC to develop prodrug-based therapy for potential rare pediatric indications of Tourette's Syndrome with ADHD. We cannot guarantee that we will be successful in this effort to develop such a prodrug-based therapy. Additionally, we cannot guarantee that the FDA would grant us a rare pediatric disease designation for such a prodrug-based product candidate. Even if the FDA grants us a rare pediatric disease designation for one of our prodrug-based product candidates, designation of a drug as a drug for a rare pediatric disease does not guarantee that an NDA for such drug will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved.

***APADAZ is, and we anticipate most of our current product candidates, if approved by the FDA, will be, subject to mandatory REMS programs, which could increase the cost, burden and liability associated with the commercialization of APADAZ and certain product candidates.***

The FDA has indicated that some opioid drugs formulated with the active ingredients hydrocodone, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxymorphone and others will be required to have a REMS to ensure that the benefits of the drugs continue to outweigh the risks. The FDA has already approved a REMS for ER and long-acting opioids as part of a federal initiative to address inappropriate prescribing and prescription drug abuse and misuse, which the FDA continually updates. The Commissioner of the FDA recently announced his intention to expand the REMS program to include IR opioids in the near future. The REMS plan introduces new safety measures designed to reduce risks and improve the safe use of ER and long-acting opioids, while ensuring access to needed medications for patients in pain. The ER and long-acting opioid REMS affects more than 25 companies that manufacture these opioid analgesics. Under the new REMS, companies are required to make education programs available to prescribers. It is expected that companies will meet this obligation by taking specific steps to ensure that health care providers are aware of the availability of the training and by providing educational grants to continuing education providers, who will develop and deliver the training. The REMS also requires companies to make available FDA-approved patient education materials on the safe use of these drugs. The companies must perform periodic assessments of the implementation of the REMS and the success of the program in meeting its goals. The FDA will review these assessments and may require additional elements to achieve the goals of the program. Independent audits must also be conducted of the educational efforts.

APADAZ is subject to REMS, and we anticipate that most of our product candidates, if approved by the FDA, are likely to also be subject to a REMS requirement. As part of the FDA's approval of the NDA for APADAZ in February 2018, they also approved our plan for the APADAZ REMS program. There may be increased cost, administrative burden and potential liability associated with the marketing and sale of these types of product candidates subject to a REMS requirement, which could increase the costs to us and reduce the commercial benefits to us from the sale of these product candidates.

***APADAZ and our product candidates contain controlled substances, the manufacture, use, sale, importation, exportation, prescribing and distribution of which are subject to regulation by the DEA.***

Before we can commercialize any of our product candidates, if approved, the DEA will need to determine the controlled substance schedule, taking into account the recommendation of the FDA. This may be a lengthy process that could delay our marketing of a product candidate and could potentially diminish any regulatory exclusivity periods for which we may be eligible. For APADAZ, the DEA has completed its process for determining the controlled substance schedule and determined that it will be a Schedule II drug. We expect that most of our products and our product candidates, KP415, KP484, KP201/IR, KP511/ER, KP511/IR, KP606 and KP746, if approved, will be regulated as "controlled substances" as defined in the Controlled Substances Act, or the CSA, and the implementing regulations of the DEA, which establish registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA. These requirements are applicable to us, to our contract manufacturers and to distributors, prescribers and dispensers of our product candidates. The DEA regulates the handling of controlled substances through a closed chain of distribution. This control extends to the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce. A number of states and foreign countries also independently regulate these drugs as controlled substances.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Schedule II drugs are those that meet the following characteristics:

- the drug has a high potential for abuse;
- the drug has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions; and
- abuse of the drug may lead to severe psychological or physical dependence.

We expect that most of our current product candidates may be listed by the DEA as Schedule II controlled substances under the CSA. If our product candidates are listed as Schedule II controlled substances, then the importation of the APIs for our product candidates, as well as the manufacture, shipping, storage, sales and use of the products, will be subject to a high degree of regulation. In addition to maintaining an importer and/or exporter registration, importers and exporters of controlled substances must obtain a permit for every import of a Schedule I or II substance and a narcotic substance in Schedule III, IV and V, as well as every export of a Schedule I or II substance and a narcotic substance in Schedule III and IV. For all other drugs in Schedule III, IV and V, importers and exporters must submit an import or export declaration. Schedule II drugs are subject to the strictest requirements for registration, security, recordkeeping and reporting. Also, distribution and dispensing of these drugs are highly regulated. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Electronic prescriptions may also be permissible depending on the state, so long as the prescription complies with the DEA's requirements for electronic prescriptions.

Controlled substances classified in Schedule III, IV, and V are also subject to registration, recordkeeping, reporting and security requirements. For example, Schedule III drug prescriptions must be authorized by a physician and may not be refilled more than six months after the date of the original prescription or more than five times. A prescription for controlled substances classified in Schedules III, IV and V issued by a physician, may be communicated either orally, in writing or by facsimile to the pharmacies. Controlled substances that are also classified as narcotics, such as hydrocodone, oxycodone and hydromorphone, are also subject to additional DEA requirements, such as manufacturer reporting of the import of narcotic raw material.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized. Similarly, separate registrations are also required for separate facilities. Acquisition and distribution transactions must also be reported for Schedule I and II controlled substances, as well as Schedule III narcotic substances.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Because most of our product candidates may be regulated as Schedule II controlled substances, they may be subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for how much of a controlled substance may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. Manufacturers of Schedule I and II controlled substances are required to apply for quotas on an annual basis. If we or our contract manufacturers or suppliers do not obtain a sufficient quota from the DEA, we may not be able to obtain sufficient quantities of these controlled substances in order to complete our clinical trials or meet commercial demand, if our product candidates are approved for marketing.

Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates containing controlled substances. States may also have their own controlled substance laws that may further restrict and regulate controlled substances. Failure to comply with these laws and regulations could also result in withdrawal of our DEA registrations, disruption in manufacturing and distribution activities, consent decrees, criminal and civil penalties and state actions, among other consequences.

***If we experience delays or difficulties in the enrollment of subjects in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.***

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible subjects to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. We cannot predict how successful we will be at enrolling subjects in future clinical trials. If we are not successful at enrolling subjects in one clinical trial, it may affect when we are able to initiate our next clinical trial, which could result in significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and subjects who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. Subject enrollment is affected by other factors including:

- the size and nature of the subject population specified in the trial protocol;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the fact that the product candidate is a controlled substance;
- severe or unexpected drug-related adverse events experienced by subjects in a clinical trial;
- the availability of drugs approved to treat the diseases or conditions under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the severity of the disease or condition under investigation;
- the ability to obtain and maintain subject informed consent;
- the ability to retain subjects in the clinical trial and their return for follow-up;
- the clinical trial design, including required tests, procedures and follow-up;
- the ability to monitor subjects adequately during and after treatment;
- delays in adding new investigators and clinical sites;
- withdrawal of clinical trial sites from clinical trials; and
- the proximity and availability of clinical trial sites for prospective subjects.

Our inability to enroll a sufficient number of subjects for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which could cause our value to decline and limit our ability to obtain additional financing.

***Our clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent or delay regulatory approval and commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.***

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication.

If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The FDA or an IRB may also require that we suspend, discontinue, or limit our clinical trials based on safety information. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the product candidate.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and management resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***Social issues around the abuse of opioids and stimulants, including law enforcement concerns over diversion and regulatory efforts to combat abuse, could decrease the potential market for APADAZ or our product candidates.***

Media stories regarding prescription drug abuse and the diversion of opioids, stimulants and other controlled substances are commonplace. Law enforcement and regulatory agencies may apply policies that seek to limit the availability of opioids and stimulants. Such efforts may inhibit our ability to commercialize APADAZ or our product candidates. Aggressive enforcement and unfavorable publicity regarding, for example, the use or misuse of hydrocodone or other opioid drugs, the limitations of abuse-deterrent formulations, public inquiries and investigations into prescription drug abuse, litigation or regulatory activity, sales, marketing, distribution or storage of our products could harm our reputation. Such negative publicity could reduce the potential size of the market for APADAZ or our product candidates and decrease the revenue we are able to generate from their sale, if approved. Similarly, to the extent prescription drug abuse becomes a less prevalent or less urgent public health issue, regulators and third-party payors may not be willing to pay a premium for formulations with improved attributes of opioids or stimulants.

Additionally, efforts by the FDA and other regulatory bodies to combat abuse of opioids and stimulants may negatively impact the market for APADAZ and our product candidates. For example, in April 2014, the FDA approved class-wide labeling changes to the indications for use of all approved ER and long-acting opioids so that ER and long-acting opioids will be indicated only for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. It is possible that such changes could reduce the number of prescriptions for opioids written by physicians and negatively impact the potential market for APADAZ or our product candidates. The FDA also held a public meeting in October 2014, on the development and regulation of abuse-deterrent formulations of opioid medications. Further, the Centers for Disease Control and Prevention recently issued draft guidelines for the prescribing of opioids for chronic pain, providing recommendations for primary care providers prescribing opioids for chronic pain on when to initiate or continue opioids, opioid selection and discontinuation, and the assessment of the risk and addressing harms of opioid use, among other areas. It is possible that FDA, or other regulatory bodies, will announce new regulatory initiatives at any time that may increase the regulatory burden or decrease the commercial opportunity for APADAZ or our product candidates.

**Risks Related to Our Dependence on Third Parties**

***We rely on and expect to continue to rely on third parties to conduct our clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.***

We have engaged and expect to continue to engage CROs for our planned clinical trials of our product candidates. We rely on and expect to continue to rely on CROs, as well as other third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Agreements with such third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our drug development activities would be delayed.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, investigators and trial sites. We also are required to register specified ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. In addition, we must conduct our clinical trials with product produced under cGMP requirements. Failure to comply with these regulations may require us to repeat preclinical studies and clinical trials, which would delay the regulatory approval process. Failure to comply with the applicable requirements related to clinical investigations by us, our CROs or clinical trial sites can also result in clinical holds and termination of clinical trials, debarment, FDA refusal to approve applications based on the clinical data, warning letters, withdrawal of marketing approval if the product has already been approved, fines and other monetary penalties, delays, adverse publicity and civil and criminal sanctions, among other consequences.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may 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, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA we submit by the FDA. Any such delay or rejection could prevent us from commercializing our product candidates. Further, our arrangements with investigators are also subject to scrutiny under other health care regulatory laws, such as the federal Anti-Kickback Statute.

We also rely on and expect to continue to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

If the third parties with whom we contract do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, we may need to conduct additional trials, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be adversely affected.

***We contract with third parties for the manufacture of our product and product candidates that utilize KP415, KP484, KP201 and KP511 as the API used in our clinical trials and with a sole source supplier for the manufacture of bulk quantities of KP415, KP484, KP201 and KP511 used in products and product candidates that utilize these moieties as the API and we expect to continue to do so. This reliance on third-party manufacturers increases the risk that we will not have sufficient quantities of KP415, KP484, KP201 or KP511, or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not have any manufacturing facilities. We procure the bulk drug substances for KP415, KP484, KP201 and KP511 from sole-source, third-party manufacturers and the products and product candidates that utilize these moieties as the API used in our clinical trials from other third parties. We anticipate we will continue to do so for the foreseeable future. We also expect to continue to rely on third parties as we proceed with preclinical and clinical testing of our product candidates, as well as for commercial manufacture or APADAZ or our product candidates should they receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of KP415, KP484, KP201, KP511, other bulk drug substances or our products or product candidates, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts.

We may be unable to establish any future agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to maintain our existing third-party relationships or establish any such agreements with other third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for FDA and DEA regulatory compliance and quality assurance;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- disruption and costs associated with changing suppliers, including additional regulatory filings;
- the possible breach, termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms; and
- carrier disruptions or increased costs that are beyond our control.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

***The facilities used by our contract manufacturers to manufacture APADAZ and our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing application to the FDA, and these facilities could fail to obtain FDA approval.***

While we are ultimately responsible for the manufacturing of APADAZ and our product candidates, we do not, other than through our contractual arrangements, control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, we will not be able to secure and maintain regulatory approval for their manufacturing facilities. In addition, other than through our contractual agreements, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacturing of APADAZ or our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market APADAZ or our product candidates, if approved.

Further, for APADAZ and our product candidates, if approved, our suppliers will be subject to regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to APADAZ or our product candidates, if approved, and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements, as well as market disruption related to any necessary recalls or other corrective actions.

Third-party manufacturers may not be able to comply with current cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including warning letters, clinical holds or termination of clinical trials, fines, injunctions, restitution, disgorgement, civil penalties, delays, suspension or withdrawal of approvals or other permits, FDA refusal to approve pending applications, product detentions, FDA or DEA consent decrees placing significant restrictions on or suspending manufacturing and distribution operations, debarment, refusal to allow import or export, product detentions, adverse publicity, dear-health-care-provider letters or other warnings, license revocation, seizures or recalls of product candidates, operating restrictions, refusal of government contracts or future orders under existing contracts and civil and criminal liability, including False Claims Act liability, exclusion from participation in federal health care programs, and corporate integrity agreements among other consequences, any of which could significantly and adversely affect supplies of our prodrugs.

***APADAZ, our product candidates and any prodrugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities, and we may be unable to obtain access to these facilities on favorable terms.***

There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for KP415, KP484, KP201 or KP511 bulk drug substance. If our current contract manufacturer for KP415, KP484, KP201 or KP511 bulk drug substance cannot perform as agreed, we may be required to replace such manufacturer and we may incur added costs and delays in identifying and qualifying any such replacement.

***We may seek collaborations with third parties for the development or commercialization of APADAZ or our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of APADAZ or these product candidates.***

We have not yet determined our strategy for commercializing APADAZ, but we may see k third-party collaborators for the commercialization of APADAZ or the development or commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators include large and mid-size pharmaceutical companies, regional, national and international pharmaceutical companies and biotechnology companies. In addition, we may seek alternative collaborative strategies with pharmacy benefit managers or generic pharmaceutical manufacturers to develop and implement non-traditional commercialization options of APADAZ. If we do enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of APADAZ or our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving APADAZ or our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of APADAZ or any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with APADAZ or our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of APADAZ or our product candidates;
- a collaborator with marketing and distribution rights to APADAZ or one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of APADAZ or our product candidates, might lead to additional responsibilities for us with respect to APADAZ or our product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of APADAZ or the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of APADAZ or our product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

***If we are not able to establish collaborations, we may have to alter our development and commercialization plans.***

Our prodrug development programs and the potential commercialization of APADAZ or our product candidates will require substantial additional capital. For some of our product candidates, we may need, and for APADAZ, we anticipate we will need, to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of APADAZ or those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for APADAZ or the subject product candidate, the costs and complexities of manufacturing and delivering APADAZ or such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for APADAZ or our product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of product candidates, reduce or delay one or more of our development programs, delay potential commercialization of APADAZ or our product candidates or reduce the scope of any sales or marketing activities of APADAZ or our product candidates, or increase our expenditures and undertake development or commercialization activities at our own expense of APADAZ or our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring APADAZ or our product candidates to market and generate product revenue.

***Provisions in our agreements with Shire and MonoSol may inhibit our ability to enter into future collaborations with third parties.***

Under our asset purchase agreement with Shire, we granted Shire a right of first refusal to acquire, license or commercialize KP415 and KP484. The right of first refusal may be exercised by Shire for a period of 30 business days following Shire's receipt of written notice from us of the existence of a bona fide offer from a third party to acquire, license or commercialize KP415 and KP484.

We are also party to a termination agreement with MonoSol that may limit the value of any sale, license or commercialization of KP415 or KP484. Under this termination agreement, MonoSol has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415 or KP484, and any product candidates arising therefrom, including royalty payments on any license of KP415 or KP484, the sale of KP415 or KP484 to a third party or the commercialization of KP415 or KP484.

***Provisions in our facility agreement with Deerfield may inhibit our ability to enter into specified transactions, including any joint venture, partnership or any other profit sharing arrangement.***

Pursuant to the Deerfield facility, we may not enter into specified transactions, including any joint venture, partnership or any other profit sharing arrangement, without the prior approval of Deerfield. Deerfield's interests may not always coincide with our corporate interests or the interests of our other stockholders, and Deerfield may act in a manner with which you may not agree or that may not be in the best interests of our other stockholders. If Deerfield does not approve our entry into specified transactions, it could significantly delay or inhibit the commercialization APADAZ or our product candidates.

**Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain trade secret protection or patent protection for our technology, APADAZ and our product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology, APADAZ and our product candidates may be impaired.***

Our success depends in large part on our ability to obtain and maintain trade secret protection of our LAT platform technology as well as patent protection in the United States and other countries with respect to APADAZ and our product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product technology and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents, licensed to third parties by us.

Further, we may also not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents, licensed from third parties to us. Therefore, any such patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors or licensees fail to maintain such patents, or lose rights to those patents, the rights we have in- or out-licensed may be reduced or eliminated.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States or visa-versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and utility, or equivalent, patent applications in the United States and other jurisdictions are typically not published until 18 months after the filing date of such patent applications, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Our patent position is subject to numerous additional risks, including the following:

- we may fail to seek patent protection for inventions that are important to our success;
- our pending patent applications may not result in issued patents;
- we cannot be certain that we are the first to invent the inventions covered by pending patent applications or that we are the first to file such applications and, if we are not, we may be subject to priority disputes or lose rights;
- we may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications;
- we may file patent applications but have claims restricted or we may not be able to supply sufficient data to support our claims and, as a result, may not obtain the original claims desired or we may receive restricted claims; alternatively, it is possible that we may not receive any patent protection from an application;
- even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, and may not be of sufficient scope or strength to provide us with any commercial advantage;
- our competitors may be able to design around our owned or licensed patents by developing similar or alternative technologies or drugs without infringing on our intellectual property rights;
- we could inadvertently abandon a patent or patent application, resulting in the loss of protection of intellectual property rights in a particular country, and we, our collaborators or our patent counsel may take action resulting in a patent or patent application becoming abandoned which may not be able to be reinstated or if reinstated, may suffer patent term adjustments;
- the claims of our issued patents or patent applications when issued may not cover our product candidates;
- no assurance can be given that our patents would be declared by a court to be valid or enforceable or that a competitor's technology or product would be found by a court to infringe our patents and our patents or patent applications may be challenged by third parties in patent litigation or in proceedings before the United States Patent and Trademark Office, or the USPTO, or its foreign counterparts, and may ultimately be declared invalid or unenforceable or narrowed in scope;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim and there may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim;
- third parties may develop products that have the same or similar effect as our products without infringing our patents;
- third parties may intentionally circumvent our patents by means of alternate designs or processes or file applications or be granted patents that would block or hurt our efforts;
- there may be dominating patents relevant to our product candidates of which we are not aware;
- obtaining regulatory approval for pharmaceutical products is a lengthy and complex process, and as a result, any patents covering our product candidates may expire before or shortly after such product candidates are approved and commercialized;
- the patent and patent enforcement laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions; and
- we may not develop additional proprietary technologies that are patentable.

Any of these factors could hurt our ability to gain full patent protection for our products. Registered trademarks and trademark applications in the United States and other countries are subject to similar risks as described above for patents and patent applications, in addition to the risks described below.

Further, a third party may misappropriate or reverse engineer our LAT platform technology, which could limit our ability to stop others from using or commercializing similar or identical technology and resultant product candidates, product technology or prodrugs, or limit the duration of the trade secret protection of our LAT platform technology.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, nullity, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to seek patent protection or to license, develop or commercialize current or future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts, patent offices and tribunals in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our product technology, product candidates and prodrugs.

***Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.***

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted in the United States, redefine prior art and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013.

Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For instance, the Leahy-Smith Act established the inter partes review and post grant review procedures that has lowered the burden of proof for invalidity challenges to issued patents and limited the ability to amend patent claims in response to such challenges. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our owned and licensed patents and/or patent applications.

***We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.***

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke those parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology or its prior use by a third party. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which would undermine our competitive position.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could significantly harm business.***

Our commercial success depends upon our ability, and the ability of any collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. In particular, we are focused on developing product candidates based on widely used therapeutic agents or drugs, many of which may be protected by proprietary rights of third parties.

Although we seek to develop proprietary prodrug formulations that do not infringe the intellectual property rights of others, we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our prodrugs or other aspects of our technology, including, for example, interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our technology and drugs. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some or all of our business operations.

Competing products may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patent, we could be prevented from marketing our products in one or more foreign countries. As a result, our ability to grow our business and compete in the market may be harmed.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could hurt the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

***We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.***

A third party may hold intellectual property rights, including patent rights, which are important or necessary to the development of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

***If we or our third-party licensors fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.***

We are currently party to license agreements for technologies that we anticipate using in our product development activities. In the future, we may become party to licenses that are important for product development and commercialization. If we or our third-party licensors fail to comply with the obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, we may be forced to terminate these agreement or we may no longer effectively rely on any licenses to us under these agreements, in which event we might not be able to develop, manufacture or market any product or utilize any technology that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially and adversely affect the value of a product candidate being developed under any such agreement or could restrict our drug discovery activities. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

***We may be required to reduce the scope of our intellectual property due to third-party intellectual property claims.***

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications, 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 ours that claims priority to an application filed prior to March 16, 2013, we may have to participate in an interference proceeding 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 such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. In addition, changes enacted on March 16, 2013, to the U.S. patent laws under the Leahy-Smith Act resulted in the United States changing from a "first to invent" country to a "first to file" country. As a result, we may lose the ability to obtain a patent if a third-party files with the USPTO first and could become involved in proceedings before the USPTO to resolve disputes related to inventorship. We may also become involved in similar proceedings in other jurisdictions.

Furthermore, recent changes in U.S. patent law under the Leahy-Smith Act allows for post-issuance challenges to U.S. patents, including ex parte re-examinations, inter partes reviews and post-grant reviews. There is significant uncertainty as to how the new laws will be applied. If our U.S. patents are challenged using such procedures, we may not prevail, possibly resulting in altered or diminished claim scope or loss of patent rights altogether. Similarly, some countries, notably Europe, also have post-grant opposition proceedings that can result in changes in scope or cancellation of patent claims.

***We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.***

Many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees do not use the proprietary information, show-how or know-how of others in their work for us, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. For example, in March 2012, we settled litigation regarding similar matters with Shire. We may also in the future be subject to claims that we have caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these potential claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A court could prohibit us from using technologies or features that are essential to our products, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and could be a distraction to management. In addition, any litigation or threat thereof may adversely affect our ability to hire employees or contract with independent service providers. Moreover, a loss of key personnel or their work product could hamper or prevent our ability to commercialize our products.

***Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.***

We expect to rely on trademarks as one means to distinguish APADAZ and any of our product candidates that are approved for marketing from the products of our competitors. We have solicited and applied for trademarks for APADAZ and LAT. For our other product candidates, we have not yet solicited trademarks and have not yet begun the process of applying to register trademarks. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. If our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to seeking patent and trademark protection for our APADAZ and our product candidates, we also rely on trade secrets, including unpatented show-how, know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets.

Monitoring unauthorized uses and disclosures of our intellectual property, including our trade secrets, is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop or reverse engineer knowledge, methods, show-how and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

***Outside of the U.S. we cannot be certain that any country's patent or trademark office will not implement new rules that could seriously affect how we draft, file, prosecute and maintain patents, trademarks and patent and trademark applications.***

We cannot be certain that the patent or trademark offices of countries outside the United States will not implement new rules that increase costs for drafting, filing, prosecuting and maintaining patents, trademarks and patent and trademark applications or that any such new rules will not restrict our ability to file for patent protection. For example, we may elect not to seek patent protection in some jurisdictions or for some inventions to save costs. We may be forced to abandon or return the rights to specific patents due to a lack of financial resources.

**Risks Related to the Commercialization of Our Product and Product Candidates**

***If we are unable to establish sales, marketing and distribution capabilities for APADAZ or any other product candidates, if approved, we may not be successful in commercializing APADAZ or any approved product candidate in the United States.***

We have only a limited sales and marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for APADAZ, or any product candidate for whi ch we may obtain marketing approval in the United States, we will need to enter into collaborations with one or more parties or establish our own sales and marketing organization. We have not yet determined our commercialization strategy for APADAZ or any of our product candidates. Should we decide to establish our own sales, marketing and distribution capabilities, we would encounter a number of risks. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of APADAZ, or a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize APADAZ, or our product candidates, on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our inability to access government and commercial health plan formularies or secure preferred coverage and adequate reimbursement levels;
- the inability of sales personnel to obtain access to physicians or achieve adequate numbers of physicians to prescribe any future prodrug products;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- liability for personnel, including sales personnel, failing to comply with applicable legal requirements; and
- costs associated with maintaining compliance with the FDA's marketing and promotional requirements, including ongoing training and monitoring, as well as unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we decide not to or are unable to establish our own sales, marketing and distribution capabilities and, instead, enter into arrangements with third parties to perform these services, our product revenue and our profitability, if any, are likely to be lower than if we were to sell, market and distribute APADAZ, or any product candidates that we develop, ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute APADAZ, or our product candidates, or may be unable to do so on terms that are favorable to us, including as a result of restrictions in the Deerfield facility. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market APADAZ, or our product candidates, effectively. Further, we may be liable for conduct of third parties acting on our behalf, including failure to comply with legal requirements applicable to sales and marketing of our products. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing APADAZ, or our product candidates.

***APADAZ, or any of our product candidates that may receive marketing approval, may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.***

APADAZ, or any of our product candidates that may receive marketing approval, may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If APADAZ, or our product candidates, do not achieve an adequate level of market acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of APADAZ, or our product candidates if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments, including less expensive generic treatments;
- the ability to obtain differentiating claims in the labels for most of our product candidates;
- our ability to offer our prodrug products for sale at competitive prices;
- the clinical indications for which our product candidates are approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the cost of treatment in relation to alternative treatments;
- the steps that prescribers and dispensers must take, since APADAZ and most of our product candidates are controlled substances, as well as the perceived risks based upon their controlled substance status;
- the ability to manufacture our product in sufficient quantities and yields;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement or willingness of patients to pay out of pocket in the absence of third-party coverage;
- the prevalence and severity of any side effects;
- any potential unfavorable publicity;
- any restrictions on the use, sale or distribution of APADAZ or our product candidates, including through REMS; and
- any restrictions on the use of our prodrug products together with other medications.

***We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.***

Our industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We will face competition and potential competition from a number of sources, including pharmaceutical and biotechnology companies, specialty pharmaceutical companies, generic drug companies, drug delivery companies and academic and research institutions. Our competitors may develop or market drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products. See *"Item 1 - Business - Competition"* of this Annual Report on Form 10-K for more information about our potential competitors.

Many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as more experience in the development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Consequently, our competitors may develop products for indications we are pursuing or may pursue in the future, and such competitors' products may be more effective, better tolerated and less costly than our product candidates. Our competitors may also be more successful in manufacturing and marketing their products than we are. We will also face competition in recruiting and retaining qualified personnel and establishing clinical trial sites and patient enrollment in clinical trials.

Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. If the competitor's product were similar to our product candidates, we may be required to seek approval via alternative pathways, such as the ANDA, which is used for the development of generic drug products. We may also be blocked from product marketing by periods of patent protection or regulatory exclusivity.

In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs or giving drugs with improved attributes sufficient weight in a comparative clinical cost effectiveness analysis. For some of the indications that we are pursuing, drugs used off-label serve as cheaper alternatives to our product candidates. Their lower prices could result in significant pricing pressure, even if our product candidates are otherwise viewed as a preferable therapy. Additional drugs may become available on a generic basis over the coming years.

Many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as more experience in the development of product candidates, obtaining FDA and other regulatory approvals of products, and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Consequently, our competitors may develop products for the treatment of ADHD, pain or for other indications we may pursue in the future, and such competitors' products may be more effective, better tolerated and less costly than our product candidates. Our competitors may also be more successful in manufacturing and marketing their products than we are. We will also face competition in recruiting and retaining qualified personnel and establishing clinical trial sites and subject enrollment in clinical trials.

***We may not be able to obtain either five-year FDA regulatory exclusivity as a new chemical entity or three-year FDA regulatory exclusivity.***

The FDA provides periods of regulatory exclusivity following their approval of an NDA, which provide the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug. Five-year exclusivity precludes approval of 505(b)(2) applications or ANDAs by delaying the submission or approval of the application, while three-year exclusivity precludes the approval of the application. We intend to seek new chemical entity, or NCE, status for any of our prodrug product candidates as appropriate. Five years of exclusivity are available to NCEs following the approval of an NDA by the FDA. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. If a product is not eligible for the NCE exclusivity, it may be eligible for three years of exclusivity. Three-year exclusivity is available to the holder of an NDA, including a 505(b)(2) NDA, for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical trials, other than bioavailability or bioequivalence trials, were essential to the approval of the application and were conducted or sponsored by the applicant.

There is a risk that the FDA may disagree with any claim that we may make that any of our prodrug product candidates are NCEs and therefore entitled to five-year exclusivity. The FDA may also take the view that the studies that we are conducting are not clinical trials, other than bioavailability and bioequivalence studies, that are essential to approval and therefore do not support three-year exclusivity. Further, to the extent that the basis for exclusivity is not clear, the FDA may determine to defer a decision until it receives an application which necessitates a decision.

If we do obtain either five or three years of exclusivity, such exclusivity will not block all potential competitors from the market. Competitors may be able to obtain approval for similar products with different forms of competitive differentiating mechanisms or may be able to obtain approval for similar products without a competitive differentiating mechanism.

***Even if we are able to commercialize APADAZ, or any of our product candidates, they may be subject to unfavorable pricing regulations, third-party coverage and reimbursement policies.***

Our ability to commercialize APADAZ, or any of our product candidates succ essfully will depend, in part, on the extent to which coverage and adequate reimbursement for APADAZ, or our product candidates, will be available from government payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and managed care plans and other third-party payors. Government authorities and other third-party payors decide which medical products they will pay for and establish reimbursement levels, including co-payments. A trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Inadequate reimbursement levels may adversely affect the demand for, or the price of, APADAZ, or any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our prodrug products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. Moreover, the trend has been for government and commercial health plans and their pharmacy benefit managers to commoditize drug products through therapeutic equivalence determinations, making formulary decisions based on cost. If coverage and adequate reimbursement are not available or reimbursement is available only at limited levels, we may not be able to successfully commercialize APADAZ, or any product candidates for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved prodrug products, and coverage may be more limited than the indications for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new prodrug products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for prodrug products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Private third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Except for certain government health care programs, such as the Department of Defense's TRICARE Uniform Formulary, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Even state Medicaid programs have their own preferred drug lists that may disadvantage non-preferred brand drugs. Therefore, coverage and reimbursement can differ significantly from payor to payor. 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 payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained at all. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved prodrug products that we develop could significantly harm our operating results, our ability to raise capital needed to commercialize prodrugs and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue able to be generated from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

There can be no assurance that APADAZ, or our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available, or that third-party payors' reimbursement policies will not adversely affect our ability to sell APADAZ, or our product candidates profitably if they are approved for sale.

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

The FDA closely regulates promotional materials and other promotional activities. Even if the FDA initially approves product labeling that includes a description of our improved attribute claims, the FDA may object to our marketing claims and product advertising campaigns. Failure to comply with the FDA's promotional, marketing and advertising laws and regulations could lead to the issuance of warning letters, cyber letters, or untitled letters, adverse publicity, the requirement for dear-health-care-provider letters or other corrective information, fines and other monetary penalties, civil or criminal prosecution, including False Claims Act liability, restrictions on our operations and other operating requirements through consent decrees or corporate integrity agreements, debarment, exclusion from participation in federal health care programs and refusal of government contracts or future orders under existing contracts, among other consequences. Any of these consequences would harm the commercial success of our products.

Further, our promotional materials, statements and training methods must comply with the FDA's prohibition of the promotion of unapproved, or off-label, use. Physicians may use our products off-label, as the FDA does not restrict or regulate a physician's independent choice of treatment within the practice of medicine. However, if the FDA determines that our promotional materials, statements or training constitutes promotion of an off-label use, it could request that we modify our promotional materials, statements or training methods or subject us to regulatory or enforcement actions, such as the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine, disgorgement of money, operating restrictions or criminal penalties. We may also be subject to actions by other governmental entities or private parties, such as the False Claims Act, civil whistleblower or "qui tam" actions. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our promotional or training materials to constitute promotion of an off-label use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. In that event, our reputation could be damaged and adoption of the products could be impaired. In addition, the off-label use of our products may increase the risk of product liability claims. Product liability claims are expensive to defend and could divert our management's attention, result in substantial damage awards against us and harm our reputation.

***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of APADAZ or any products that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk as we commercialize APADAZ, and any prodrug products that may be approved in the future. This includes the risk that our products may be misused. For example, APADAZ does, and we anticipate that our other product candidates if approved may, carry a boxed warning regarding lethality if our oral tablets are prepared for injection and hepatotoxicity, as is commonly done by abusers of opioids. If we cannot successfully defend ourselves against claims that APADAZ, and our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for APADAZ and any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- termination of clinical trial sites or entire trial programs;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- significant costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards paid to trial participants or patients;
- product recalls, withdrawals or labeling revisions and marketing or promotional restrictions;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize APADAZ or any prodrug products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or when we commence commercialization of APADAZ, or any other product approved in the future. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

***A variety of risks associated with international operations could materially adversely affect our business.***

We expect to engage in significant cross-border activities, and we will be subject to risks related to international operations, including:

- different regulatory requirements for maintaining approval of drugs in foreign countries;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- reduced protection for contractual and intellectual property rights in some countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in North America;
- tighter restrictions on privacy and the collection and use of patient data; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

**Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters**

***Failure to obtain marketing approval in international jurisdictions would prevent APADAZ and our product candidates from being marketed abroad.***

In order to market and sell our products in the European Union and any other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, failure to obtain approval in one jurisdiction may impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

***A variety of risks associated with marketing APADAZ and our product candidates internationally could affect our business.***

We may seek regulatory approval for APADAZ and our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market with low or lower prices rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may compromise our ability to achieve or maintain profitability.

***APADAZ is, and any product candidate for which we obtain marketing approval could be, subject to post-marketing restrictions or recall or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with APADAZ, or our product candidates when and if any of them are approved.***

APADAZ is, and any product candidate for which we obtain marketing approval could be, subject to a comprehensive regulatory scheme, which includes the regulation of manufacturing processes, post-approval clinical data, labeling, advertising, marketing, distribution and promotional activities for such product, by the FDA and other regulatory authorities. For example, we are required to conduct pediatric studies related to Apadaz to determine the safety and effectiveness of Apadaz for the claimed indication in pediatric patients. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, payment of substantial annual product and establishment fees, labeling requirements, promotional, marketing and advertising requirements, requirements related to further development, packaging, storage and distribution requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. If there are any modifications to the drug, including changes in indications, labeling, manufacturing processes or facilities, or new safety issues arise, a new or supplemental NDA, a post-implementation notification or other reporting may be required or requested depending on the change, which may require additional data or additional preclinical studies and clinical trials.

APADAZ is, and if marketing approval of a product candidate is granted may be, subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries. Our plan for the APADAZ REMS program was approved by the FDA as part of the NDA approval for APADAZ received in February 2018.

APADAZ does, and if any of our product candidates receive marketing approval it may, have a label that limits its approved uses, including more limited subject populations, than we request, and regulatory authorities may require that contraindications, warnings or precautions be included in the product labeling, including a black box warning, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, which could limit sales of the product. For instance, we expect that at least some of our product candidates would likely be required to carry black box warnings, including warnings regarding tampering, lethality if our oral tablets are prepared for injection and hepatotoxicity.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. APADAZ is subject to a post-marketing requirement for four deferred pediatric assessments that must be completed pursuant to the FDA's February 2018 approval letter. The FDA closely regulates the post-approval marketing and promotion of p roducts to ensure products are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our prodrug products, if any, for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act relating to the promotion of prescription drugs may lead to a number of actions and penalties, including warning letters, cyber letters, or untitled letters, adverse publicity, the requirement for dear-health-care-provider letters or other corrective information, fines and other monetary penalties, civil or criminal prosecution, including False Claims Act liability, restrictions on our operations and other operating requirements through consent decrees or corporate integrity agreements, debarment, exclusion from participation in federal health care programs and refusal of government contracts or future orders under existing contracts, among other consequences.

In addition, later discovery of previously unknown adverse events or other problems with our prodrug products, including those related to manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have negative consequences, including:

- adverse inspectional findings;
- restrictions on such prodrug products, distribution, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- additional warnings or otherwise restrict the product's indicated use, label, or marketing;
- issuance of safety alerts, dear-healthcare-provider letters, press releases or other communications containing warnings regarding the product;
- requirement to establish or modify a REMS;
- requirement to conduct post-marketing studies or surveillance;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- recall or withdrawal of the prodrug products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit and other delays;
- clinical holds, or the suspension or termination of ongoing clinical trials;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals or other permits or voluntary suspension of marketing;
- refusal to permit the import or export of our prodrug products;
- reputational harm;
- refusal of government contracts or future orders under existing contracts, exclusion from participation in federal health care programs, and corporate integrity agreements;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties, including False Claims Act liability.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of drugs for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

***Our employees, independent contractors, principal investigators, CROs, consultants, commercial collaborators, contract manufacturers, service providers and other vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.***

We are exposed to the risk of misconduct by employees and independent contractors, such as principal investigators, CROs, consultants, commercial collaborators, contract manufacturers, service providers and other vendors. Such misconduct could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards that we have established or that are established by regulation, to comply with federal and state contracting and healthcare fraud and abuse laws, to report drug pricing, financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing, advertising and promotion, sales commissions, customer incentive programs and other business arrangements. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct and self-disclose credible evidence of False Claims Act violations. It is not always possible to identify and deter employee and independent contractor misconduct, and any precautions we take to detect and prevent improper activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of warning letters, untitled letters, cyber letters, seizure or recall of products, injunctions, withdrawal of product approval or other permits, clinical holds and termination of clinical trials, FDA refusal to approve pending applications, product detentions, FDA or DEA consent decrees, restriction or suspension of manufacturing and distribution, debarment, refusal to allow product import or export, adverse publicity, refusal of government contracts or future orders under existing contracts, dear-health-care-provider letters or other warnings or corrective information, recalls, delays, civil, criminal and administrative penalties including False Claims Act liability, damages, monetary fines, disgorgement, restitution, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, corporate integrity agreements, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, among other consequences, any of which could adversely affect our ability to operate.

***Our current and future relationships with healthcare professionals, principal investigators, consultants, customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to penalties.***

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the False Claims Act, that may constrain the business or financial arrangements and relationships through which we sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or arranging for the purchase, lease or order of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid;

- federal civil and criminal false claims laws, including the False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making or using a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, including erroneous pricing information on which mandatory rebates, discounts and reimbursement amounts are based, or in the case of the False Claims Act, for violations of the federal Anti-Kickback Statute in connection with a claim for payment or for conduct constituting reckless disregard for the truth;

- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;

- HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by HITECH and their respective implementing regulations, which impose obligations on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Open Payments program, created under Section 6002 of the ACA, and its implementing regulations, which imposes new annual reporting requirements for manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with certain exceptions, to annually report certain payments and transfers of value provided to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals, and to report annually certain ownership and investment interests held by physicians and their immediate family members; and

- comparable state and foreign laws, which may be broader in scope than the analogous federal laws and may differ from each other in significant ways.

These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws, or that our compliance systems are inadequate to detect and report such conduct or to report accurate pricing information to the government. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, corporate integrity agreements or similar agreements to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, which could significantly harm our business. If any of the physicians or other healthcare providers or entities with whom we currently, or expect to, do business, including future collaborators, is found not to be in compliance with applicable laws, they and we may be subject to penalties and potential exclusion from participation in healthcare programs as a result of their non-compliance.

***Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of our product candidates and to commercialize APADAZ and any of our product candidates that may be approved in the future and affect the prices we may obtain.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell APADAZ and any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States 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 United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, President Obama signed into law the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded drugs and generic drugs, respectively;

- expansion of healthcare fraud and abuse laws, including the False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;

- establishment of a new and distinct methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices (generally as negotiated between the Medicare Part D plan and the pharmacy) of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations and extension of the inflation percentage applicable to existing branded drugs to new formulations for purposes of computing the inflation penalty component of Medicaid rebates;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- the new requirements under the federal Open Payments program and its implementing regulations;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial and congressional challenges to numerous provisions of the ACA, and we expect there will be additional challenges and amendments in the future. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provision of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress will likely consider additional legislation to repeal or repeal and replace other elements of the ACA. We continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In Aug ust 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, which went into effect in April 2013, and, due to subsequent legislative amendments, including the BBA, will stay in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. These new laws may result in additional reductions in Medicare and other healthcare funding, which could negatively impact customers for our product candidates, if approved, and, accordingly, our financial operations.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may, among other things, result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our prodrug product candidates.

Legislative and regulatory proposals and enacted statutes have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. For instance, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new legislation, manufacturers are required to provide specified information regarding the drug products they produce to individuals and entities to which product ownership is transferred, label drug products with a product identifier and keep specified records regarding the drug products. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers are also required to verify that purchasers of products are appropriately licensed. Further, under this legislation, manufacturers have drug product investigation, quarantine, disposition and FDA and trading-partner notification responsibilities related to counterfeit, diverted, stolen and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

***Governments outside the United States tend to impose strict price controls, which may affect our revenue, if any.***

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our prodrug products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from malicious human acts, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Moreover, despite network security and back-up measures, some of our and our vendors' servers are potentially vulnerable to physical or electronic break-ins, including cyber-attacks, computer viruses and similar disruptive problems. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business and could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was 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 development of our product candidates could be delayed.

**Risks Related to Employee Matters and Managing Our Growth**

***Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.***

We are highly dependent on the management, research and development, clinical, financial and business development expertise of Travis C. Mickle, Ph.D., our president and chief executive officer, Gordon K. Johnson, our chief business officer, R. LaDuane Clifton, CPA, our chief financial officer, Sven Guenther, Ph.D., our executive vice president research and development, and Daniel L. Cohen, our executive vice president government and public relations, as well as the other members of our scientific and clinical teams. Although we have employment agreements with each of our executive officers, these agreements do not obligate them to continue working for our company and they may terminate their employment with us at any time.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our prodrug product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

***We expect to potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

Following the approval of APADAZ, we may experience growth in the number of our employees and the scope of our operations, particularly in the areas including sales, marketing and/or distribution. To manage potential future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel, depending on the commercialization strategy ultimately adopted.

Due to our limited financial resources and the limited experience of our management team in managing a company with such potential growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The potential expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

**Risks Related to Ownership of Our Common Stock and Our Status as a Public Company**

***An active trading market for our common stock may not be sustained and you may not be able to resell your shares of our common stock for a profit, if at all.***

Prior to our initial public offering, or IPO, there had been no public market for our common stock. An active trading market for our shares may not be sustained. If an active market for our common stock is not sustained, it may be difficult for you to sell our shares at an attractive price or at all.

***The trading price of the shares of our common stock is likely to be volatile, and purchasers of our common stock could incur substantial losses.***

Our stock price has been, and is likely to continue to be, volatile. Since shares of our common stock were sold in our IPO in April 2015 at a price of $11.00 per share, our stock price has ranged from $2.45 to $26.15 through March 28, 2018. In addition, the stock market in general and the market for pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- actual or anticipated variations in our operating results;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the pharmaceutical industry;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- adverse regulatory announcements or determinations regarding our product candidates;
- capital commitments;
- investors' general perception of us and our business;
- recruitment or departure of key personnel; and
- sales of our common stock, including sales by our directors and officers or specific stockholders.

Many of the factors described above are not within our control. For instance, in May 2016, we announced that the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA voted 16 to four for the approval of APADAZ but voted 18 to two against inclusion of abuse-deterrent labeling for APADAZ. The announcement was followed by a substantial decrease in the trading price of our common stock on The NASDAQ Global Market. Additionally, when we announced in June 2016 that the FDA had issued a CRL for our APADAZ NDA, the trading price of our common stock on The NASDAQ Global Market was subject to another substantial decrease. We cannot guarantee that future announcements will not have similar effects on the trading price of our common stock.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. For instance, in December 2016, we received notice of a class action suit filed against us in the Iowa District Court in Johnson County by a stockholder alleging that we, certain of our senior executives and directors who signed the registration statement in connection with our IPO, and each of the investment banks that acted as underwriters for the offering negligently issued untrue statements of material facts and omitted to state material facts required to be stated in the registration statement and incorporated offering materials that we filed with the SEC in support of the offering. The plaintiff does not quantify any alleged damages in his complaint but, in addition to attorneys' fees and costs, the plaintiff seeks to recover damages and obtain other relief on behalf of himself and all other persons who purchased our common stock pursuant or traceable to the offering and the registration statement and who were allegedly damaged thereby. In January 2017, the suit was removed to the U.S. District Court for the Southern District of Iowa. The plaintiff subsequently filed a motion to remand the case to the Iowa District Court, and that motion was granted. In January 2018, the Iowa District Court issued an order postponing all deadlines and the setting of any schedule in the case pending a decision by the United States Supreme Court in *Cyan, Inc. v. Beaver County Employees Retirement Fund*. On March 20, 2018, the Supreme Court issued its decision in *Cyan* and held that state courts have subject matter jurisdiction over putative class actions like the one filed against us, which assert claims arising under the Securities Act. Accordingly, the case will proceed in Iowa District Court. The suit against us is still in a preliminary stage and has not yet been set for trial. As such, we are unable to predict the timing or outcome of this litigation as of the date of this report. Such litigation could cause us to incur substantial costs and divert management's attention and resources from our business. Further, companies listed on The NASDAQ Global Market, and biotechnology and pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

***If we fail to maintain compliance with the listing requirements of The NASDAQ Global Market, we may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.***

Our common stock is currently listed on The NASDAQ Global Market. To maintain the listing of our common stock on The NASDAQ Global Market, we are required to meet certain listing requirements, including, among others, either: (i) a minimum closing bid price of $1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least $5 million and stockholders' equity of at least $10 million; or (ii) a minimum closing bid price of $1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors, affiliates and 10% or more stockholders) of at least $15 million and a total market value of listed securities of at least $50.0 million. On September 18, 2017, we received a notice from The NASDAQ Stock Market indicating we were not in compliance with NASDAQ Listing Rule 5450(b)(2)(a) for continued listing on the NASDAQ Global Market, as the market value of our listed securities was less than $50.0 million for the previous 30 consecutive business days, and , if we were unable to demonstrate compliance with this requirement during the applicable grace periods, our common stock would be delisted after that time. We were notified that we had regained compliance with NASDAQ Listing Rule 5450(b)(2)(a) on September 29, 2017, because the market value of our listed securities was at least $50.0 million for the previous 10 consecutive business days.

Notwithstanding our ability to regain compliance with NASDAQ Listing Rule 5450(b)(2)(a) within the applicable grace period, we may fail to satisfy one or more NASDAQ Global Market requirements for continued listing of our common stock in the future. There can be no assurance that we will be successful in maintaining the listing of our common stock on the NASDAQ Global Market, or, if transferred, on the NASDAQ Capital Market. This could impair the liquidity and market price of its common stock. In addition, the delisting of our common stock from a national exchange could have a material adverse effect on our access to capital markets, and any limitation on market liquidity or reduction in the price of our common stock as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all.

***If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.***

The trading market for our common stock is influenced by the research and reports that securities or industry analysts publish about us or our business, our market and our competitors. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our shares or change their opinion of our shares, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

***We may incur substantial costs as a result of ongoing litigation.***

In December 2016, we received notice of a class action suit filed against us in the Iowa District Court in Johnson County by a stockholder alleging that we, certain of our senior executives and directors who signed the registration statement in connection with our initial public offering, and each of the investment banks that acted as underwriters for the offering negligently issued untrue statements of material facts and omitted to state material facts required to be stated in the registration statement and incorporated offering materials that we filed with the SEC in support of the offering. The plaintiff does not quantify any alleged damages in his complaint but, in addition to attorneys' fees and costs, the plaintiff seeks to recover damages and obtain other relief on behalf of himself and all other persons who purchased our common stock pursuant or traceable to the offering and the registration statement and who were allegedly damaged thereby. In January 2017, the suit was removed to the U.S. District Court for the Southern District of Iowa. The plaintiff subsequently filed a motion to remand the case to the Iowa District Court, and that motion was granted. In January 2018, the Iowa District Court issued an order postponing all deadlines and the setting of any schedule in the case pending a decision by the United States Supreme Court in *Cyan, Inc. v. Beaver County Employees Retirement Fund.* On March 20, 2018, the Supreme Court issued its decision in *Cyan* and held that state courts have subject matter jurisdiction over putative class actions like the one filed against us, which assert claims arising under the Securities Act. Accordingly, the case will proceed in Iowa District Court. The suit against us is still in a preliminary stage and has not yet been set for trial. We cannot predict the timing or outcome of this litigation and irrespective of its outcome, this litigation may cause us to incur substantial costs in related legal fees and divert management's attention and resources from our business.

***A significant portion of our outstanding warrants and convertible securities are entitled to certain anti-dilution protections which, if triggered, may cause substantial dilution to your investment.***

In June 2014, we issued to Deerfield (i) a warrant to purchase 14,423,076 shares of Series D redeemable convertible preferred stock at an exercise price of $0.78 per share, which is exercisable until June 2, 2024, or the Deerfield Warrant, and (ii) a convertible note under the Deerfield Facility Agreement, in the principal amount of $10.0 million, which bears interest at 9.75% per annum, or the Deerfield Note. Upon completion of our IPO, the Deerfield Warrant automatically converted into a warrant to purchase 1,923,077 shares of our common stock at an exercise price of $5.85 per share and the outstanding principal and accrued interest under the Deerfield Note became convertible into shares of our common stock at a conversion price of $5.85 per share. The Deerfield Warrant and Deerfield Note each include an exercise or conversion, as applicable, price protection provision, pursuant to which the exercise or conversion, as applicable, price of the warrant or note will be adjusted downward on a broad-based weighted-average basis if we issue or sell any shares of common stock, convertible securities, warrants or options at a sale or exercise price per share less than the greater of the Deerfield Warrant's exercise price or the Deerfield Note's conversion price, as applicable, or the closing sale price of our common stock as reported on The NASDAQ Global Market on the last trading date immediately prior to such issuance or, in the case of a firm commitment underwritten offering, on the date of execution of the underwriting agreement between us and the underwriters for such offering. Additionally, pursuant to the terms of our fourth amendment to the Deerfield Warrant and Deerfield Note, if we effect an "at the market offering" as defined in Rule 415 of the Securities Act, of our common stock, the exercise price of the Deerfield Warrant and conversion price of the Deerfield Note will be adjusted downward pursuant to this anti-dilution adjustment only if such sales are made at a price less than $5.85 per share.

***Future sales and issuances of equity and debt could result in additional dilution to our stockholders.***

We expect that we will need significant additional capital in the future to fund our planned operations, including to complete potential clinical trials for our product candidates. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time.

Additionally, we previously issued to Deerfield the Deerfield Note in the principal amount of $10.0 million. The Deerfield Note bears interest at 9.75% per annum. Deerfield may convert all or any portion of the outstanding principal and any accrued but unpaid interest on the Deerfield Note into shares of our common stock at a conversion price of $5.85 per share.

According to the terms of the Deerfield Note, in no event may Deerfield convert the Deerfield Note to the extent such conversion would result in Deerfield beneficially owning more than 9.985% of the then issued and outstanding shares of our common stock. This conversion limitation may not be waived and any purported conversion that is inconsistent with this conversion limitation will be null and void. This conversion limitation will not apply to any conversion made immediately prior to a change of control transaction. If Deerfield is only able to convert the Deerfield Note into a limited number of shares due to this conversion limitation, the Deerfield Note could subsequently become convertible into the remainder of the shares as a result of a variety of events. This could occur, for example, if we issue more shares or Deerfield sells some of its existing shares. Without regard to this conversion limitation, the Deerfield Note is convertible into 1,751,410 shares of our common stock, assuming a conversion date of December 31, 2017. The conversion price of the Deerfield Note will be adjusted downward if we issue or sell any shares of common stock, convertible securities, warrants or options at a sale or exercise price per share less than the greater of the Deerfield Note's conversion price or the closing sale price of our common stock as reported on The NASDAQ Global Market on the last trading date immediately prior to such issuance, or, in the case of a firm commitment underwritten offering, on the date of execution of the underwriting agreement between us and the underwriters for such offering. Although, if we effect an "at the market offering" as defined in Rule 415 of the Securities Act, of our common stock, the exercise price of the Deerfield Warrant and conversion price of the Deerfield Note will be adjusted downward pursuant to this anti-dilution adjustment only if such sales are made at a price less than $5.85 per share.

Additionally, in February 2016, we issued the 2021 Notes. The 2021 Notes are convertible at an initial conversion rate of 58.4454 shares of our common stock per $1,000 principal amount of the 2021 Notes, subject to adjustment under the indenture governing the 2021 Notes, which is equal to an initial conversion price of approximately $17.11 per share of our common stock. Upon conversion, the 2021 Notes will be settled in shares of our common stock, together with a cash payment in lieu of delivering any fractional shares. The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, we will increase the conversion rate for a holder who elects to convert its 2021 Notes in connection with such a corporate event in certain circumstances. Holders who convert on or after the date that is one year after the last date of original issuance of the 2021 Notes may also be entitled to receive, under certain circumstances, an interest make-whole payment payable in shares of common stock. Without regard to this conversion, the 2021 Notes are convertible into 5,040,914 shares of our common stock, assuming a conversion date of December 31, 2017.

If Deerfield or the holders of the 2021 Notes elect to convert the Deerfield Note or the 2021 Notes, your ownership interest will be diluted and the market price of our common stock may be materially and adversely effected.

Pursuant to our equity incentive plan, we may grant equity awards and issue additional shares of our common stock to our employees, directors and consultants, and the number of shares of our common stock reserved for future issuance under this plan will be subject to automatic annual increases in accordance with the terms of the plans. To the extent that new options are granted and exercised, or we issue additional shares of common stock in the future, our stockholders may experience additional dilution, which could cause our stock price to fall.

Additionally, in October 2016, we entered into the ATM Agreement with Cowen under which we may offer and sell, from time to time at our sole discretion, shares of our common stock having an aggregate offering price of up to $50,000,000 through Cowen as our sales agent. Cowen may sell common stock under the ATM Agreement by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415 of the Securities Act, including without limitation sales made by means of ordinary brokers' transactions on The NASDAQ Global Market or otherwise at market prices prevailing at the time of sale, in block transactions, or as otherwise directed by us. Cowen will use commercially reasonable efforts to sell the common stock from time to time, based upon instructions from us (including any price, time or size limits or other customary parameters or conditions we may impose). To the extent that we direct Cowen to make any sales of our common stock under the ATM Agreement, our stockholders may experience additional dilution, which could cause our stock price to fall. As of March 28, 2018, we have sold 446,111 shares of common stock under the ATM Agreement, resulting in gross proceeds of $2.9 million.

***Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business.***

As of December 31, 2017, we had $96.3 million of convertible notes outstanding, consisting of the $10 million Deerfield Note and $86.3 million of 2021 Notes.

The Deerfield Note bears interest at 9.75% per annum. Interest accrued on outstanding debt under the Deerfield Note is due quarterly in arrears. Upon notice to Deerfield, we may choose to have one or more of the first eight of such scheduled interest payments added to the outstanding principal amount of the debt issued under the Deerfield Note, provided that all such interest was due on July 1, 2016. We elected this option on all eight of the scheduled interest payments through June 30, 2016 and paid such interest on July 1, 2016. We must repay one-third of the outstanding principal amount of all debt issued under the Deerfield Note on the fourth and fifth anniversaries of the Deerfield Note. We are then obligated to repay the balance of the outstanding principal amount on February 14, 2020. If we are required to pay additional outstanding amounts due under the Deerfield Note prior to maturity or otherwise incur unanticipated monetary obligations under the Deerfield Note, our cash flow available to invest in the ongoing needs of our business may be limited.

In February 2016, we issued the 2021 Notes. Our ability to make payments on, and to refinance, the 2021 Notes, and to fund planned capital expenditures, sales and marketing efforts, research and development efforts, working capital and other general corporate purposes depends on our ability to generate cash in the future. This, to a certain extent, is subject to general economic, financial, competitive, legislative, regulatory and other factors, some of which are beyond our control. If we do not ever generate sufficient cash flow from operations or if future borrowings are not available to us in an amount sufficient to repay our indebtedness, including any amounts due under the 2021 Notes at their maturity, or to fund our liquidity needs, we may be forced to refinance all or a portion of the 2021 Notes, on or before the maturity thereof, sell assets, reduce or delay capital expenditures, seek to raise additional capital or take other similar actions. We may not be able to affect any of these actions on commercially reasonable terms or at all. Our ability to refinance our indebtedness will depend on our financial condition at the time, the restrictions in the instruments governing our present and potential future indebtedness and other factors, including market conditions. In addition, in the event of a default with respect to the 2021 Notes, the holders of the 2021 Notes and/or the trustee under the indenture governing the 2021 Notes may accelerate the payment of our obligations under 2021 Notes. A default under the indenture governing the 2021 Notes could also lead to a default under agreements governing future indebtedness. Our inability to generate sufficient cash flow to satisfy our debt service obligations, or to refinance or restructure our obligations on commercially reasonable terms or at all, would likely have a material adverse effect on our business, financial condition and results of operations.

***Despite our current debt levels, we may still incur substantially more debt or take other actions which would intensify the risks discussed above.***

Despite our current debt levels, we and our future subsidiaries may incur substantial additional debt in the future, subject to the restrictions contained in our debt instruments, some of which may be secured debt. We are not restricted under the terms of the indenture governing the 2021 Notes from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking a number of other actions that are not limited by the terms of the indenture governing the 2021 Notes that could have the effect of diminishing our ability to make payments on the notes when due. The Deerfield facility restricts our ability to incur additional indebtedness, including secured indebtedness, subject to certain exceptions, but if the facility matures or is repaid, we may not be subject to such restrictions under the terms of any subsequent indebtedness.

***The accounting method for the Deerfield Warrant, Deerfield Note and 2021 Notes could have a material effect on our reported financial results.***

The Deerfield Warrant, Deerfield Note and 2021 Notes contain embedded derivatives, which require mark-to-market accounting treatment and could result in a gain or loss on a quarterly basis with regards to the mark-to-market value of that feature. Such accounting treatment could have a material impact on, and could potentially result in significant volatility in, our quarterly results of operations. Additionally, certain features of the 2021 Notes may result in the yield on the 2021 Notes not being deductible by us for tax purposes.

***Sales of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

Certain holders of shares of our common stock and shares of our common stock issuable upon the exercise of outstanding warrants, including Deerfield, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

***Anti-takeover provisions in our certificate of incorporation and bylaws, as well as provisions of Delaware law and the terms of some or our contracts, might discourage, delay or prevent a change in control of our company or changes in our board of directors or management and, therefore, depress the price of our common stock.***

Our certificate of incorporation and bylaws and Delaware law contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock or transactions that our stockholders might otherwise deem to be in their best interests. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove members of our board of directors or our management. Therefore, these provisions could adversely affect the price of our stock. Our corporate governance documents include provisions:

- establishing a classified board of directors with staggered three-year terms so that not all members of our board of directors are elected at one time;
- providing that directors may be removed by stockholders only for cause;
- preventing the ability of our stockholders to call and bring business before special meetings and to take action by written consent in lieu of a meeting;
- requiring advance notice of stockholder proposals for business to be conducted at meetings of our stockholders and for nominations of candidates for election to our board of directors;
- permitting the board of directors to issue up to 10,000,000 shares of preferred stock with any rights, preferences and privileges they may designate;
- limiting the liability of, and providing indemnification to, our directors and officers;
- providing that vacancies may be filled by remaining directors;
- preventing cumulative voting; and
- providing for a supermajority requirement to amend our bylaws.

As a Delaware corporation, we are also subject to provisions of Delaware law, including Section 203 of the General Corporation Law of the State of Delaware, which prohibits a Delaware corporation from engaging in a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder.

In addition, the provisions of our termination agreement with MonoSol and our agreements with Deerfield and the holders of our 2021 Notes may discourage, delay or prevent a change in control of our company. For example, if we enter into a merger, an asset sale or any other change of control transaction, then MonoSol will be entitled to a percentage in the low teens of the price being paid to us and our stockholders in such transaction which is attributable to the value of KP415 or KP484. Pursuant to the Deerfield facility, we may not enter into any major transaction without the prior approval of Deerfield, including a merger, asset sale or change of control transaction, and pursuant to the Deerfield Note, Deerfield has the option to demand repayment of all outstanding principal, and any unpaid interest accrued thereon, of the Deerfield Note immediately prior to consummation of such event. Further, under the Deerfield Warrant, Deerfield has the right to demand that we redeem the Deerfield Warrant for a cash amount equal to the Black-Scholes value of a portion of the warrant upon the occurrence of specified events, including a merger, an asset sale or any other change of control transaction. Furthermore, the indenture governing the 2021 Notes requires us to repurchase the 2021 Notes for cash if we undergo certain fundamental changes. A takeover of us may trigger the requirement that we repurchase the 2021 Notes, which could make it more costly for a potential acquirer to engage in a business combination transaction with us.

Any provision of our certificate of incorporation, bylaws or Delaware law or any term of our contracts that has the effect of discouraging, delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

***Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.***

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, any action asserting a claim against us arising pursuant to any provisions of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. If a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

***We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.***

We are an "emerging growth company" as defined in the Jump Start Our Business Startups Act, or the JOBS Act, and we take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (2) the date on which we have issued more than $1.00 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***We might not be able to utilize a significant portion of our net operating loss carryforwards, which could adversely affect our profitability.***

As of December 31, 2017, we had federal net operating loss carryforwards of approximately $137.3 million, due to prior period losses, which if not utilized will begin to expire in 2027. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities, which could adversely affect our profitability. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We performed a Section 382 ownership change analysis in 2017 and determined that we experienced an ownership change in 2010, which resulted in a portion of our net operating loss carryforwards being subject to an annual limitation under Section 382 through 2012. No other ownership changes or limitations on our historical net operating loss carryforwards were noted through the year ended December 31, 2017. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including as a result of the conversion of our outstanding convertible debt or as a result of future changes in our stock ownership. If we determine that an ownership change has occurred and our ability to use our historical net operating loss carryforwards is materially limited, it would harm our future operating results by increasing our future tax obligations.

***Comprehensive tax reform bills could adversely affect our business and financial condition.***

On December 22, 2017, and effective January 1, 2018, the U.S. government enacted H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018" (informally titled the Tax Cuts and Jobs Act) which includes significant changes to the taxation of business entities. The Tax Cuts and Jobs Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the Tax Cuts and Jobs Act remains subject to interpretation and further guidance from U.S. taxing authorities and as a result, the overall impact of this tax reform is uncertain and may change due to interpretation changes, and our business and financial condition could be adversely affected. The impact of the Tax Cuts and Jobs Act on holders of our common stock is also uncertain and could be adverse. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our effective tax rates in the future in countries where we have operations and have an adverse effect on our overall tax rate in the future, along with increasing the complexity, burden and cost of tax compliance. We urge our stockholders to consult with their legal and tax advisors with respect to the Tax Cuts and Jobs Act and the potential tax consequences of investing in or holding our common stock.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.***

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. For our fiscal year ending December 31, 2017, we performed system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Annual Report on Form 10-K, as required by Section 404 of the Sarbanes-Oxley Act. We will be required to perform this evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting on an annual basis. This requires that we incur substantial additional professional fees and internal costs and that we expend significant management efforts on an annual basis. We have and will be required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the U.S. Securities and Exchange Commission, or SEC, or other regulatory authorities.

***Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.***

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of the Deerfield facility, and any future debt agreements may, preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

***We incur increased costs and demands upon management as a result of being a public company.***

As a public company listed in the United States, we incur significant additional legal, accounting and other costs, which we estimate to be between $1.0 million and $2.0 million annually, that we did not incur as a private company. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and The NASDAQ Stock Market, may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

Not applicable.

**ITEM 2. PROPERTIES**

We occupy 1,000 square feet of headquarters office and laboratory space in Coralville, Iowa, under a non-cancelable lease agreement that expires in September 2018, and we have the right to extend the term of the lease for successive one-year terms upon expiration. We also occupy approximately 17,000 square feet of office space in Celebration, Florida, comprised of two contiguous office suites, under a non-cancelable lease agreement that expires in August 2025 and February 2026, respectively. We have the right to extend the term of the lease for two successive five-year terms upon expiration. In addition, we occupy leased space in Blacksburg, Virginia. We believe that our facilities are adequate for our current needs.

**ITEM 3. LEGAL PROCEEDINGS**

In December 2016, a class action suit was filed against us in the Iowa District Court in Johnson County by a stockholder alleging that we, certain of our senior executives and directors who signed the registration statement in connection with our initial public offering, and each of the investment banks that acted as underwriters for the offering negligently issued untrue statements of material facts and omitted to state material facts required to be stated in the registration statement and incorporated offering materials that we filed with the SEC in support of the offering. The plaintiff does not quantify any alleged damages in his complaint but, in addition to attorneys' fees and costs, the plaintiff seeks to recover damages and obtain other relief on behalf of himself and all other persons who purchased our common stock pursuant or traceable to the offering and the registration statement and who were allegedly damaged thereby.

In January 2017, the suit was removed to the U.S. District Court for the Southern District of Iowa. The plaintiff subsequently filed a motion to remand the case to the Iowa District Court, and that motion was granted. In January 2018, the Iowa District Court issued an order postponing all deadlines and the setting of any schedule in the case pending a decision by the United States Supreme Court in *Cyan, Inc. v. Beaver County Employees Retirement Fund.* On March 20, 2018, the Supreme Court issued its decision in *Cyan* and held that state courts have subject matter jurisdiction over putative class actions like the one filed against us, which assert claims arising under the Securities Act. Accordingly, the case will proceed in Iowa District Court. The suit against us is still in a preliminary stage and has not yet been set for trial. Accordingly, we are unable to predict the timing or outcome of this litigation as of the date of this report.

From time to time, we may be involved in routine legal proceedings, as well as demands, claims and threatened litigation, which arise in the normal course of our business. As of the date of this report we are unable to predict whether the pending litigation described above could have a material adverse effect on our results of operations or financial condition.

**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

**Price Range of Common Stock**

Our common stock has been listed on The NASDAQ Global Market under the symbol "KMPH" since April 16, 2015. Prior to that date, there was no public trading market for our common stock. The following table sets forth for the periods indicated the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market:

| | Low | High |
|---|---|---|
| **Year Ended December 31, 2016** | | |
| First Quarter | $ 10.16 | $ 19.72 |
| Second Quarter | $ 3.52 | $ 19.75 |
| Third Quarter | $ 3.69 | $ 5.50 |
| Fourth Quarter | $ 2.90 | $ 5.09 |
| **Year Ended December 31, 2017** | | |
| First Quarter | $ 2.95 | $ 5.40 |
| Second Quarter | $ 2.95 | $ 5.00 |
| Third Quarter | $ 2.45 | $ 4.15 |
| Fourth Quarter | $ 3.44 | $ 4.25 |

**Holders of our Common Stock**

As of March 28, 2018, we had 142 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Dividend Policy**

We have never declared or paid any cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future. The terms of the Deerfield facility, limits our ability to pay dividends.

**Securities Authorized for Issuance under Equity Compensation Plans**

The information regarding securities authorized for issuance under equity compensation plans is included in Part III of this report.

**Recent Sales of Unregistered Securities**

Not applicable.

**Issuer Purchases of Equity Securities**

Not applicable.

### ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

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

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes thereto included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a specialty pharmaceutical company focused on the discovery and development of proprietary prodrugs to treat serious medical conditions through our LAT, platform technology. We utilize our proprietary LAT platform technology to generate improved prodrug versions of FDA-approved drugs in the high need areas of ADHD, pain and other CNS disorders. Our co-lead clinical development candidates are KP415 and KP484, both based on a prodrug of methylphenidate, but with differing ER effect profiles for the treatment of ADHD. In addition, we have received FDA approval for APADAZ, and IR combination product of our prodrug, benzhydrocodone, and APAP. We are also advancing KP201/IR, an APAP-free IR formulation of our benzhydrocodone prodrug. Both APADAZ and KP201/IR are intended for the treatment of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

To date, we have not generated any revenue. We have incurred operating losses since our inception and, as of December 31, 2017, had an accumulated deficit of $164.7 million. Our losses from operations for the years ended December 31, 2017, 2016 and 2015 were $33.4 million, $37.5 million and $22.8 million, respectively.

We expect to continue to incur significant expenses and operating losses for the foreseeable future, and those expenses and losses may fluctuate significantly from quarter-to-quarter and year-to-year. We anticipate that our expenses will increase substantially as we:

- continue our ongoing preclinical studies, clinical trials and our product development activities for our pipeline of product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- continue research and preclinical development and initiate clinical trials of our other product candidates;
- seek to discover and develop additional product candidates either internally or in partnership with other pharmaceutical companies;
- potentially establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize APADAZ and any of our other product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- incur additional legal, accounting and other expenses in operating as a public company; and
- add operational systems and personnel, including systems and personnel, if needed, to support any future commercialization efforts.

Our commercial revenue, if any, will be derived from sales of APADAZ or our other prodrug product candidates for which we obtain regulatory approval and we do not currently know when, if ever, APADAZ or our other product candidates will be commercially available. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or debt, the terms of these securities may restrict our ability to operate. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

**Third-Party Agreements**

In November 2009, we entered into a supply agreement, or the Supply Agreement, with Johnson Matthey Inc., or JMI, whereby JMI has agreed to supply us with all the KP201 necessary for clinical trials and commercial sale for a price equal to JMI's manufacturing cost and to provide process optimization and development services for KP201. In exchange, we issued shares of our common stock to JMI, provided that the commercial supply arrangement for KP201 would be exclusive to JMI in the United States and agreed to pay JMI royalties on the net sales of any products that utilize KP201 as the active pharmaceutical ingredient, or API. The percentage royalty rate ranges from the high teens at low volumes to the mid-single digits at higher volumes. Our FDA-approved drug, APADAZ, and product candidate, KP201/IR, both contain KP201.

We are responsible for all costs of any KP201 manufactured during a specified validation process for APADAZ and KP201/IR. After completion of the validation process, but prior to the commercial launch of any products that utilize KP201 as the API, JMI will manufacture batches of KP201 at a price to be negotiated. Failure to agree upon this pricing would result in JMI supplying these batches to us free of charge and we would pay JMI an additional royalty payment on such batches. The percentage royalty rate ranges from the low teens at low volumes to the low single digits at higher volumes and is additive to any minimum royalty we may owe JMI on such batch. JMI will manufacture and supply KP201 at a price equal to JMI's fully allocated manufacturing cost after commercial launch of APADAZ, as well as for KP201/IR should we obtain approval for marketing from the FDA.

We must purchase all our U.S. KP201 needs from JMI and JMI cannot supply KP201 to other companies. After the commercial launch of any product that utilizes KP201 as the API, JMI is required to identify a secondary manufacturing site and qualify and validate that site to produce KP201.

The term of the supply agreement extends as long as we hold a valid and enforceable patent for KP201 or until the tenth anniversary of the commercial launch of any product that utilizes KP201 as the API, whichever date is later. Upon the expiration of such term, the agreement will automatically renew for a period of two years unless either party provides 12 months' prior notice of its intent not to renew.

Under our March 2012 asset purchase agreement with Shire Pharmaceuticals, LLC, or Shire, has a right of first refusal to acquire, license or commercialize KP415 and KP484.

Under our March 2012 termination agreement with MonoSol Rx, LLC, or MonoSol, MonoSol has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415 or KP484, and any product candidates arising therefrom, including royalty payments on any license of KP415 or KP484, the sale of KP415 or KP484 to a third party, the commercialization of KP415 or KP484 and the portion of any consideration that is attributable to the value of KP415 or KP484 and paid to us or our stockholders in a change of control transaction.

**Components of our Results of Operations**

***Revenue***

To date, we have not generated any revenue. We do not currently know when, if ever, we will generate revenue. On February 23, 2018, we announced that the FDA approved our NDA for APADAZ for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. We have not yet determined our strategy for commercializing APADAZ. If we fail to commercialize APADAZ or complete the development of our product candidates in a timely manner or fail to obtain their regulatory approval, our ability to generate future revenue would be compromised.

***Operating Expenses***

We classify our operating expenses into three categories: research and development expenses, general and administrative expenses and severance expense. Salaries and personnel-related costs, including benefits, bonuses and stock-based compensation expense, comprise a significant component of each of these expense categories. We allocate expenses associated with our facilities, information technology costs and depreciation and amortization between research and development expenses and general and administrative expenses based on employee headcount and the nature of work performed by each employee.

***Research and Development Expense***

Research and development expense consists of expenses incurred while performing research and development activities to discover and develop potential product candidates. This includes conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for product candidates. We recognize research and development expenses as they are incurred. Our research and development expense primarily consists of:

- salaries and personnel-related costs, including benefits and any stock-based compensation, for our scientific personnel performing research and development activities;
- costs related to executing preclinical studies and clinical trials;
- fees paid to consultants and other third parties who support our product candidate development;
- other costs in seeking regulatory approval of our products; and
- allocated facility-related costs and overhead.

We typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or external consultant costs to specific product candidates or development programs.

The following table summarizes our research and development costs for the years ended December 31, 2017, 2016 and 2015 (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2017** | **2016** | **2015** |
| Outsourced development costs directly identified to programs: | | | |
| KP415 | $ 10,116 | $ 2,889 | $ 111 |
| KP484 | 153 | — | — |
| APADAZ | 956 | 7,019 | 7,342 |
| KP201/IR | 29 | 18 | — |
| KP511 | 667 | 2,511 | 1,564 |
| KP606 | — | 24 | — |
| Total outsourced development costs directly identified to programs | 11,921 | 12,461 | 9,017 |
| Research and development costs not directly identified to programs: | | | |
| Personnel costs including cash compensation, benefits and stock-based compensation | 6,069 | 5,198 | 3,655 |
| Facilities costs | 456 | 394 | 197 |
| Other costs | 2,147 | 2,419 | 1,062 |
| Total research and development costs not directly identified to programs | 8,672 | 8,011 | 4,914 |
| Total research and development costs | $ 20,593 | $ 20,472 | $ 13,931 |

We plan to increase our research and development expense for the foreseeable future as we continue our efforts to advance the development of our product candidates, subject to the availability of additional funding.

The successful commercialization of APADAZ and our product candidates, if approved, and development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs required to commercialize APADAZ or our product candidates, if approved, and complete the remaining development of any product candidates. This is due to the numerous risks and uncertainties associated with the commercialization and development of products and product candidates.

***General and Administrative Expense***

General and administrative expense consists primarily of salaries and personnel-related costs, including employee benefits and any stock-based compensation, for employees performing functions other than research and development. This includes personnel in executive, finance, human resources and administrative support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expense, professional fees for auditing, tax and legal services, expenses associated with obtaining and maintaining patents, consulting costs and costs of our information systems.

We expect that our general and administrative expense will increase as we continue to operate as a public reporting company and continue to develop our product candidates. We believe that these increases will likely include increased costs related to the hiring of additional personnel and increased fees for outside consultants, lawyers and accountants. We also expect to continue to incur increased costs to comply with corporate governance, internal controls, investor relations, disclosure and similar requirements applicable to public reporting companies.

***Severance Expense***

Severance expense consists primarily of salaries and personnel-related costs, including employee benefits and any stock-based compensation, for employees terminated in the third quarter of 2016 due to the deferral of commercial operations and realignment of financial resources and operational priorities during the period. We had no severance expense in 2017, and at this time, we do not expect to incur significant additional severance expense in future periods.

***Other (Expense) Income***

Other (expense) income consists primarily of non-cash costs associated with fair value adjustments to our derivative and warrant liability and amortization of debt issuance costs and debt discount to interest expense. Other (expense) income also includes interest expense incurred on our outstanding borrowings, as well as, interest and other income consisting primarily of interest earned on investments. Additionally, we recognized a loss on extinguishment of debt, for the year ended December 31, 2016, related to the payment of our term note previously issued to Deerfield. These items are unrelated to our core business and thus are recognized as other (expense) income in our statements of operations.

***Income Tax Benefit (Expense)***

Income tax benefit (expense) consists of refundable state income tax credits. To date, we have not been required to pay U.S. federal or state income taxes because we have not generated taxable income. We have received state income tax credits related to our qualified research activities in Iowa.

**Results of Operations**

***Comparison of the Years Ended December 31, 2017 and 2016 (in thousands):***

| | Year Ended December 31, | | Period-to-Period Change |
|---|---|---|---|
| | 2017 | 2016 | |
| Revenue | $ — | $ — | $ — |
| Operating expenses: | | | |
| Research and development | 20,593 | 20,472 | 121 |
| General and administrative | 12,773 | 14,000 | (1,227) |
| Severance expense | — | 3,010 | (3,010) |
| Total operating expenses | 33,366 | 37,482 | (4,116) |
| Loss from operations | (33,366) | (37,482) | 4,116 |
| Other (expense) income: | | | |
| Loss on extinguishment of debt | — | (4,740) | 4,740 |
| Interest expense related to amortization of debt issuance costs and discount | (1,561) | (1,616) | 55 |
| Interest expense on principal | (5,776) | (5,511) | (265) |
| Fair value adjustment | (3,091) | 32,465 | (35,556) |
| Interest and other income, net | 365 | 353 | 12 |
| Total other (expense) income | (10,063) | 20,951 | (31,014) |
| Loss before income taxes | (43,429) | (16,531) | (26,898) |
| Income tax benefit | 43 | 15 | 28 |
| Net loss | $ (43,386) | $ (16,516) | $ (26,870) |

***Net Loss***

Net loss for the year ended December 31, 2017 was $43.4 million, an increase of $26.9 million compared to net loss for the year ended December 31, 2016 of $16.5 million. The increase was primarily attributable to a period-over-period change of $35.6 million in fair value adjustment related to changes in the derivative and warrant liability for each period resulting in non-cash expense of $3.1 million for the year ended December 31, 2017 compared to non-cash income of $32.5 million for the year ended December 31, 2016. Also contributing to the increase in net loss was an increase in net interest expense and other items of $0.1 million. These increases were partially offset by a decrease in loss from operations of $4.1 million and the non-recurrence in 2017 of a non-cash loss on extinguishment of debt of $4.7 million recognized during the year ended December 31, 2016 related to the payment of the term note previously issued to Deerfield.

***Research and Development***

Research and development expenses increased by $0.1 million, from $20.5 million for the year ended December 31, 2016, to $20.6 million for the year ended December 31, 2017. This increase was primarily attributable to an increase in personnel costs, including stock-based compensation of $0.7 million. This increase was partially offset by decreases in net third-party research and development costs of $0.5 million and other research and development costs related to overhead of $0.1 million.

***General and Administrative***

General and administrative expenses decreased by $1.2 million, from $14.0 million for the year ended December 31, 2016, to $12.8 million for the year ended December 31, 2017. This decrease was primarily attributable to decreases in professional fees and other expenses related to the APADAZ pre-commercialization efforts in 2016 of $0.7 million and personnel costs, including stock-based compensation of $0.9 million. These decreases are partially offset by increases in general and administrative costs related to overhead of $0.4 million in 2017.

***Severance Expense***

We had no severance expense in 2017. Severance expense of $3.0 million was recognized for the year ended December 31, 2016 due to the deferral of commercial operations and realignment of financial resources and operational priorities during the period. Severance expense was comprised of $1.9 million of stock-based compensation expense related to the acceleration of vesting on certain stock options upon employee termination and $1.1 million of personnel and other related charges.

***Other (Expense) Income***

Other (expense) income changed by $31.0 million, from income of $20.9 million for the year ended December 31, 2016, to expense of $10.1 million for the year ended December 31, 2017. This period-to-period change was primarily attributable to the $35.6 million change in the fair value adjustment related to our derivative and warrant liability and an increase in net interest expense and other items of $0.1 million. These changes were partially offset by the non-recurrence in 2017 of a non-cash loss on extinguishment of debt of $4.7 million recognized during the year ended December 31, 2016 related to the payment of the term note previously issued to Deerfield.

***Comparison of the Years Ended December 31, 2016 and 2015 (in thousands):***

| | Year Ended December 31, | | Period-to-Period Change |
|---|---|---|---|
| | 2016 | 2015 | |
| Revenue | $ — | $ — | $ — |
| Operating expenses: | | | |
| Research and development | 20,472 | 13,931 | 6,541 |
| General and administrative | 14,000 | 8,883 | 5,117 |
| Severance expense | 3,010 | — | 3,010 |
| Total operating expenses | 37,482 | 22,814 | 14,668 |
| Loss from operations | (37,482) | (22,814) | (14,668) |
| Other (expense) income: | | | |
| Loss on extinguishment of debt | (4,740) | — | (4,740) |
| Interest expense related to amortization of debt issuance costs and discount | (1,616) | (1,909) | 293 |
| Interest expense on principal | (5,511) | (2,671) | (2,840) |
| Fair value adjustment | 32,465 | (27,276) | 59,741 |
| Interest and other income, net | 353 | 32 | 321 |
| Total other (expense) income | 20,951 | (31,824) | 52,775 |
| Loss before income taxes | (16,531) | (54,638) | 38,107 |
| Income tax benefit (expense) | 15 | (26) | 41 |
| Net loss | $ (16,516) | $ (54,664) | $ 38,148 |

***Net Loss***

Net loss for the year ended December 31, 2016 was $16.5 million, a decrease of $38.2 million compared to net loss for the year ended December 31, 2015 of $54.7 million. The decrease was primarily attributable to a period-over-period change of $59.7 million in fair value adjustment related changes in the derivative and warrant liability for each period resulting in non-cash income of $32.4 million for the year ended December 31, 2016 compared to non-cash expense of $27.3 million for the year ended December 31, 2015. This decrease was partially offset by increases in loss from operations of $14.7 million, net interest expense and other items of $2.1 million and the recognition of a non-cash loss on extinguishment of debt of $4.7 million related to the payment of the term note previously issued to Deerfield.

***Research and Development***

Research and development expenses increased by $6.6 million, from $13.9 million for the year ended December 31, 2015, to $20.5 million for the year ended December 31, 2016. This increase was primarily attributable to a $3.5 million payment to a third-party to license an abuse-deterrent technology, as well as increases in personnel costs, including stock-based compensation of $1.6 million, professional fees and other expenses related to preparation for, and attendance at, the FDA advisory committee meeting held during the second quarter of 2016 of $1.0 million, and an increase in other research and development costs related to overhead of $0.5 million.

***General and Administrative***

General and administrative expenses increased by $5.1 million, from $8.9 million for the year ended December 31, 2015, to $14.0 million for the year ended December 31, 2016. This increase was primarily attributable to increases in personnel costs, including stock-based compensation of $3.1 million, professional fees and other expenses related to APADAZ pre-commercialization efforts in 2016 of $0.7 million, and general and administrative costs of $1.3 million.

***Severance Expense***

Severance expense of $3.0 million was recognized for the year ended December 31, 2016 due to the deferral of commercial operations for APADAZ and realignment of financial resources and operational priorities during the period. Severance expense was comprised of $1.9 million of stock-based compensation expense related to the acceleration of vesting on certain stock options upon employee termination and $1.1 million of personnel and other related charges. We had no severance expense in 2015.

***Other (Expense) Income***

Other (expense) income changed by $52.8 million, from an expense of $31.8 million for the year ended December 31, 2015, to income of $21.0 million for the year ended December 31, 2016. This period-to-period change was primarily attributable to the $59.7 million change in the fair value adjustment related to our derivative and warrant liability. This change was partially offset by an increase in net interest expense and other items of $2.2 million and a non-cash loss on extinguishment of debt of $4.7 million recognized in the first quarter of 2016 related to the payment of the term note previously issued to Deerfield.

**Liquidity and Capital Resources**

***Sources of Liquidity***

Through December 31, 2017, we have funded our research and development and operating activities primarily through the issuance of $115.9 million of debt, $25.3 million of private placements of redeemable convertible preferred stock and the sale of common stock in our IPO. As of December 31, 2017, we had cash and cash equivalents of $10.9 million, restricted cash of $1.1 million, marketable securities of $31.4 million, trade date receivables of $2.0 million and long-term investments of $3.3 million. We completed the initial closing of our IPO in April 2015, with a subsequent closing in May 2015, pursuant to which we received net proceeds, including net proceeds from the underwriters' exercise of their option to purchase additional shares, of $59.9 million, after deducting underwriting discounts and commissions of $4.5 million. In addition, we incurred offering expenses totaling $2.8 million.

We filed a registration statement on Form S-3 covering the sale from time to time of up to $150.0 million of our common stock, preferred stock, debt and/or warrants, which was declared effective by the SEC on October 17, 2016.

On October 3, 2016, we entered into a Common Stock Sales Agreement, or ATM Agreement, with Cowen under which we may offer and sell, from time to time, in our sole discretion, shares of common stock having an aggregate offering price of up to $50,000,000 through Cowen as our sales agent. The registration statement on Form S-3 included a prospectus covering the offering up to $20,000,000 of shares of common stock in accordance with the ATM Agreement. As of March 28, 2018, we have sold 446,111 shares of our common stock under the ATM Agreement resulting in gross proceeds of $2.9 million.

We have incurred operating losses since our inception and, as of December 31, 2017, had an accumulated deficit of $164.7 million. We anticipate that we will continue to incur operating losses for at least the next several years. We expect that our operating expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements.

***Convertible Debt***

As of December 31, 2017, we had $96.3 million of convertible notes outstanding, consisting of a secured convertible note with Deerfield in the principal amount of $10.0 million, or the Deerfield Note, and $86.3 million of principal amount of 5.50% senior convertible notes due 2021, or the 2021 Notes.

*Deerfield Facility*

In June 2014, we entered into the $60.0 million multi-tranche credit facility with Deerfield. At the time we entered into the Deerfield Facility Agreement, we borrowed the first tranche, which consisted of a $15.0 million term note and the $10.0 million convertible note, or the Deerfield Note. We used approximately $18.6 million of the net proceeds from the offering of our 5.50% senior convertible notes due 2021, or the 2021 Notes, to repay in full the $15.0 million original principal amount on the term note issued under the Deerfield Facility Agreement plus all accrued but unpaid interest on the term note, a make whole interest payment on the term note and a prepayment premium on the term note. Deerfield is no longer obligated to provide us any additional disbursements under the Deerfield Facility Agreement.

All loans issued under the Deerfield Facility Agreement, including the Deerfield Note, bear interest at 9.75% per annum. Interest accrued on outstanding debt under the Deerfield Facility Agreement is due quarterly in arrears. Upon notice to Deerfield, we may choose to have one or more of the first eight of such scheduled interest payments added to the outstanding principal amount of the debt issued under the Deerfield facility, provided that all such interest was due on July 1, 2016. We elected this option on all eight of the scheduled interest payments through June 30, 2016, and paid all such interest on July 1, 2016. We must repay one-third of the outstanding principal amount of all debt issued under the Deerfield Facility Agreement on the fourth and fifth anniversaries of the Deerfield Facility Agreement. We are then obligated to repay the balance of the outstanding principal amount on February 14, 2020.

Prepayment of the outstanding balance is not allowed without written consent of Deerfield. However, in connection with our offering of the 2021 Notes, on February 3, 2016, we entered into an amendment to the Deerfield Facility Agreement in which Deerfield consented to the prepayment of its $15.0 million term note and the issuance of the 2021 Notes.

Pursuant to the Deerfield Facility Agreement, we issued to Deerfield 1,923,077 shares of our Series D redeemable convertible preferred stock as consideration for the loans provided to us thereunder. Upon closing of our IPO, these shares of Series D redeemable convertible preferred stock reclassified into 256,410 shares of our common stock.

We also issued to Deerfield a warrant to purchase 14,423,076 shares of our Series D redeemable convertible preferred stock at an initial exercise price of $0.78 per share, or the Deerfield Warrant. Upon closing of our IPO, this warrant converted into a warrant exercisable for 1,923,077 shares of our common stock at an exercise price of $5.85 per share.

Pursuant to the Deerfield Facility Agreement, we may not enter into specified transactions, including a debt financing in the aggregate value of $750,000 or more, a merger, an asset sale or any other change of control transaction or any joint venture, partnership or other profit sharing arrangement, without the prior approval of Deerfield. Additionally, if we were to enter into a major transaction, including a merger, consolidation, sale of substantially all of our assets or other change of control transaction, Deerfield would have the ability to demand that prior to consummation of such transaction we repay all outstanding principal and accrued interest of the Deerfield Note. Deerfield has the right to demand that we redeem the Deerfield Warrant for a cash amount equal to the Black-Scholes value of a portion of the warrant upon the occurrence of specified events, including a merger, an asset sale or any other change of control transaction.

The Deerfield Facility Agreement also includes high yield discount obligation protections that go into effect in June 2019. After this time, if at any interest payment date our outstanding indebtedness under the Deerfield facility would qualify as an "applicable high yield discount obligation" under the Internal Revenue Code, as amended, or the Code, then we are obligated to prepay in cash on each such date the amount necessary to avoid such classification.

*2021 Notes*

In February 2016, we issued the 2021 Notes in aggregate principal amount of $86.3 million. The 2021 Notes were originally issued to Cowen and RBC as representatives of the several initial purchasers, who subsequently resold the 2021 Notes to qualified institutional buyers in reliance on the exemption from registration provided by Rule 144A under the Securities Act.

The 2021 Notes were issued pursuant to an indenture, dated as of February 9, 2016, or the indenture, between the Company and U.S. Bank National Association, as trustee. Interest on the 2021 Notes is payable semi-annually in cash in arrears on February 1 and August 1 of each year, beginning on August 1, 2016, at a rate of 5.50% per year. The 2021 Notes mature on February 1, 2021 unless earlier converted or repurchased.

The 2021 Notes are not redeemable prior to the maturity date, and no sinking fund is provided for the 2021 Notes. The 2021 Notes are convertible at an initial conversion rate of 58.4454 shares of our common stock per $1,000 principal amount of the 2021 Notes, subject to adjustment under the indenture, which is equal to an initial conversion price of approximately $17.11 per share of our common stock. Upon conversion, the 2021 Notes will be settled in shares of our common stock, together with a cash payment in lieu of delivering any fractional shares. The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, we will increase the conversion rate for a holder who elects to convert its 2021 Notes in connection with such a corporate event in certain circumstances. These notes are not considered participating securities.

If we undergo a "fundamental change" (as defined in the indenture), holders may require that we repurchase for cash all or any portion of their 2021 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2021 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

Holders who convert on or after the date that is one year after the last date of original issuance of the 2021 Notes may also be entitled to receive, under certain circumstances, an interest make-whole payment payable in shares of our common stock.

The indenture includes customary terms and covenants, including certain events of default after which the 2021 Notes may be due and payable immediately.

**Cash Flows (in thousands):**

***Comparison of the Years Ended December 31, 2017 and 2016 (in thousands)***

| | Year Ended December 31, | | Period-to-Period |
|---|---|---|---|
| | 2017 | 2016 | Change |
| Net cash used in operating activities | $ (33,100) | $ (29,772) | $ (3,328) |
| Net cash provided by (used in) investing activities | 27,412 | (45,847) | 73,259 |
| Net cash (used in) provided by financing activities | (203) | 61,163 | (61,366) |
| Net decrease in cash, cash equivalents and restricted cash | $ (5,891) | $ (14,456) | $ 8,565 |

***Operating Activities***

For the year ended December 31, 2017, net cash used in operating activities of $33.1 million consisted of a net loss of $43.4 million, primarily attributable to our spending on research and development programs, and $1.6 million in changes in working capital, partially offset by $11.9 million in adjustments for non-cash items. The changes in working capital consisted of $0.9 million related to an increase in prepaid expenses and other assets and $0.8 million related to an increase in accounts payable and accrued expenses, partially offset by $0.1 million related to other liabilities. The adjustments for non-cash items primarily consisted of stock-based compensation expense of $4.6 million, a non-cash loss related to the change in the fair value of our derivative and warrant liabilities of $3.1 million, non-cash interest expense of $2.2 million, amortization of debt issuance costs and debt discount of $1.6 million, and $0.4 million related to depreciation, amortization and other items.

For the year ended December 31, 2016, net cash used in operating activities of $29.8 million consisted of a net loss of $16.5 million, primarily attributable to changes in fair value of our derivative and warrant liabilities and our spending on research and development programs, and $16.6 million in adjustments for non-cash items, partially offset by $3.3 million in changes in working capital. The adjustments for non-cash items primarily consisted of non-cash income related to the change in the fair value of our derivative and warrant liabilities of $32.5 million, partially offset by stock-based compensation expense of $6.6 million, a loss on extinguishment of debt of $4.7 million related to the repayment of the term note issued under the Deerfield Facility Agreement, non-cash interest expense of $2.2 million, amortization of debt issuance costs and debt discount of $1.6 million, and $0.7 million related depreciation, amortization and other items. The changes in working capital consisted of $2.0 million related to a reduction in prepaid expenses and other assets, $1.1 million related to a reduction in accounts payable and accrued expenses and $0.2 million related to other liabilities.

***Investing Activities***

For the year ended December 31, 2017, net cash provided by investing activities was $27.4 million, which was primarily attributable to maturities of marketable securities of $55.0 million, partially offset by purchases of marketable securities and long-term investments of $27.4 million and purchases of property and equipment of $0.2 million.

For the year ended December 31, 2016, net cash used in investing activities was $45.8 million, which was primarily attributable to purchases of marketable securities and long-term investments of $89.8 million and purchases of property and equipment of $0.6 million, partially offset by maturities of marketable securities of $44.6 million.

***Financing Activities***

For the year ended December 31, 2017, net cash used in financing activities was $203,000. Net cash consisted of a repayment of $157,000 of obligations under capital lease arrangements and payment of $50,000 of deferred offering costs; these payments were partially offset by proceeds from exercise of common stock warrants of $4,000.

For the year ended December 31, 2016, net cash provided by financing activities was $61.2 million. Net cash consisted of (i) $82.8 million in proceeds, net of discounts and commissions, from the issuance of the 2021 Notes, of which we used approximately $18.6 million to repay in full the $15.0 million principal amount, accrued but unpaid interest, a make whole interest payment and a prepayment premium all related to the term note issued under the Deerfield Facility Agreement and (ii) $0.1 million in proceeds from the exercise of common stock options and warrants; partially offset by payment of $1.9 million of principal on the Deerfield Note, related to capitalized interest that was added to principal, payment of debt issuance costs of $1.0 million and payment of $0.2 million of deferred offering costs and obligations under a capital lease.

***Comparison of the Years Ended December 31, 2016 and 2015 (in thousands):***

| | Year Ended December 31, | | Period-to-Period |
|---|---|---|---|
| | 2016 | 2015 | Change |
| Net cash used in operating activities | $ (29,772) | $ (20,268) | $ (9,504) |
| Net cash used in investing activities | (45,847) | (19,137) | (26,710) |
| Net cash provided by financing activities | 61,163 | 61,468 | (305) |
| Net (decrease) increase in cash, cash equivalents and restricted cash | $ (14,456) | $ 22,063 | $ (36,519) |

***Operating Activities***

For the year ended December 31, 2016, net cash used in operating activities of $29.8 million consisted of a net loss of $16.5 million, primarily attributable to changes in fair value of our derivative and warrant liabilities and our spending on research and development programs, and $16.6 million in adjustments for non-cash items, partially offset by $3.3 million in changes in working capital. The adjustments for non-cash items primarily consisted of non-cash income related to the change in the fair value of our derivative and warrant liabilities of $32.5 million, partially offset by stock-based compensation expense of $6.6 million, a loss on extinguishment of debt of $4.7 million related to the repayment of the term note issued under the Deerfield Facility Agreement, non-cash interest expense of $2.2 million, amortization of debt issuance costs and debt discount of $1.6 million, and $0.7 million related to depreciation, amortization and other items. The changes in working capital consisted of $2.0 million related to a reduction in prepaid expenses and other assets, $1.1 million related to a reduction in accounts payable and accrued expenses and $0.2 million related to other liabilities.

For the year ended December 31, 2015, net cash used in operating activities of $20.3 million consisted of a net loss of $54.7 million, primarily attributable to changes in fair value of our derivative and warrant liabilities and our spending on research and development programs, partially offset by $34.3 million in adjustments for non-cash items and $0.1 million in changes in working capital. The adjustments for non-cash items primarily consisted of a non-cash loss related to the change in the fair value of our derivative and warrant liabilities of $27.3 million, non-cash interest expense of $2.7 million, stock-based compensation expense of $2.4 million, and amortization of debt issuance costs and debt discount of $1.9 million. The changes in working capital consisted of $1.3 million related to a reduction in prepaid expense and other assets, partially offset by $1.2 million related to an increase in accounts payable and accrued expenses.

***Investing Activities***

For the year ended December 31, 2016, net cash used in investing activities was $45.8 million, which was primarily attributable to purchases of marketable securities and long-term investments of $89.8 million and purchases of property and equipment of $0.6 million, partially offset by maturities of marketable securities of $44.6 million.

For the year ended December 31, 2015, net cash used in investing activities was $19.1 million, which was primarily attributable to the purchases of marketable securities and long-term investments of $19.0 million and purchases of property and equipment of $0.1 million.

***Financing Activities***

For the year ended December 31, 2016, net cash provided by financing activities was $61.2 million. Net cash consisted of (i) $82.8 million in proceeds, net of discounts and commissions, from the issuance of the 2021 Notes, of which we used approximately $18.6 million to repay in full the $15.0 million principal amount, accrued but unpaid interest, a make whole interest payment and a prepayment premium all related to the term note issued under the Deerfield Facility Agreement and (ii) $0.1 million in proceeds from the exercise of common stock options and warrants; partially offset by payment of $1.9 million of principal on the Deerfield Note, related to capitalized interest that was added to principal, payment of debt issuance costs of $1.0 million and payment of $0.2 million of deferred offering costs and obligations under a capital lease.

For the year ended December 31, 2015, net cash provided by financing activities was $61.5 million. Net cash consisted of (i) $59.9 million in proceeds, net of underwriter's discounts, from our IPO, in which we issued and sold 5,090,909 shares of our common stock at a public offering price of $11.00 per share in April 2015, and subsequently sold an additional 763,636 shares of our common stock pursuant to the underwriters' option to purchase additional shares in May 2015, and (ii) proceeds of $4.0 million from the issuance of our Series D-1 convertible redeemable preferred stock in February 2015 and $0.5 million of proceeds related to the exercise of stock options and warrants, partially offset by payment of debt and stock issuance costs of $2.5 million and payment of deferred offering costs and other items of $0.4 million.

***Future Funding Requirements***

To date, we have not generated any revenue. We do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue until we commercialize APADAZ and/or we obtain regulatory approval of and commercialize one of our product candidates. In addition, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, product candidates. We also have not determined our strategy for commercializing APADAZ, and we cannot guarantee that any strategy we adopt will be successful. We also expect to continue to incur additional costs associated with operating as a public company. In addition, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution of APADAZ and our product candidates, subject to obtaining regulatory approval of our product candidates. We anticipate that we will need substantial additional funding in connection with our continuing operations.

The auditor's opnion on our audited financial statements for the year ended December 31, 2017, includes an explanatory paragraph stating that our recurring losses and negative operating cash flows raise substantial doubt about our ability to continue as a going concern. While we believe that we will be able to raise the capital we need to continue our operations, 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.

Based upon our current operating plan, existing resources are not expected to be sufficient to fund operating expense and capital investment requirements through the first quarter of 2019. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. To meet any additional cash requirements, we may seek to sell additional equity, including pursuant to our ATM Agreement, debt financings, including potential convertible securities that may result in dilution to our stockholders, or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements. We cannot guarantee that we will be able to generate sufficient proceeds from sales under our ATM Agreement or otherwise, or be successful in completing other funding transactions, to fund our operating expenses. Because of the numerous risks and uncertainties associated with the development and commercialization of products and product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the commercialization and development of any of our product or product candidates.

Our future capital requirements will depend on many factors, including:

- the progress and results of our preclinical studies, clinical trials and other product development and commercialization activities;
- the ability to obtain differentiated claims in the labels for our product candidates;
- the number and development requirements of product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the efforts necessary to institute post-approval regulatory compliance requirements for APADAZ and our product candidates;
- the costs and timing of commercialization activities, including product manufacturing, marketing, sales and distribution, for APADAZ and any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of APADAZ and our product candidates for which we receive marketing approval, which may be affected by market conditions, including obtaining coverage and adequate reimbursement of APADAZ and our product candidates from third-party payors, including government programs and managed care organizations, and competition within the therapeutic class to which APADAZ and our product candidates are assigned;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products or product candidates and technologies.

Our commercial revenue, if any, will be derived from sales of APADAZ or our prodrug product candidates and we do not currently know when, if ever, APADAZ or our product candidates will be commercially available. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or debt, the terms of these securities or this debt may restrict our ability to operate. The Deerfield Facility Agreement includes, and any future debt financing and equity financing, if available, may involve agreements that include, covenants limiting and restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, entering into profit-sharing or other arrangements or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

**Off-Balance Sheet Arrangements**

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

**Critical Accounting Policies and Significant Judgements and Estimates**

This management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported revenues and expenses during the reported periods. We evaluate these estimates and judgements on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgements about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note B to our audited financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements and understanding and evaluating our reported financial results.

***Accrued Expenses***

We enter into contractual agreements with third-party vendors who provide research and development, manufacturing, and other services in the ordinary course of business. Some of these contracts are subject to milestone-based invoicing and services are completed over an extended period of time. We record liabilities under these contractual commitments when an obligation has been incurred. This accrual process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed and estimating the level of service performed and the associated cost when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include:

- fees paid to contract research organizations, or CROs, in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of our raw materials, drug substance and product candidates; and
- professional fees.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of these costs, our actual expenses could differ from our estimates.

***Stock-Based Compensation***

We record the fair value of stock options issued as of the grant date as compensation expense. We recognize compensation expense over the requisite service period, which is equal to the vesting period. Stock-based compensation expense has been reported in our statements of operations as follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Research and development | $ 1,304 | $ 1,051 | $ 610 |
| General and administrative | 3,258 | 3,639 | 1,759 |
| Severance expense | — | 1,910 | — |
| Total stock-based compensation expense | $ 4,562 | $ 6,600 | $ 2,369 |

***Determination of the Fair Value of Stock-Based Compensation Grants***

We calculate the fair value of stock-based compensation arrangements using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including the expected volatility of our common stock, the assumed dividend yield, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and the fair value of the underlying common stock on the date of grant. In applying these assumptions, we considered the following factors:

- historically we have not had sufficient experience to estimate the volatility of our common stock. As such we calculated the expected volatility based on reported data for selected similar publicly traded companies for which the historical information is available, or peer volatility, and blended it with our historical volatility, or leverage-adjusted peer volatility. For the purpose of identifying peer companies, we consider characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. We utilized this leverage-adjusted peer volatility for grants prior to the IPO, as well as grants within the two-year period immediately following the IPO. For grants after the second anniversary of the IPO we utilized our historical volatility to determine the expected volatility;

- the assumed dividend yield is based on our expectation of not paying dividends for the foreseeable future;

- we determine the average expected life of "plain vanilla" stock options based on the simplified method in accordance with SEC Staff Accounting Bulletin Nos. 107 and 110, as our common stock to date has been publicly traded for a limited amount of time. We expect to use the simplified method until we have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term. For options that are not considered "plain vanilla," such as those with exercise prices in excess of the fair market value of the underlying stock, we use an expected life equal to the contractual term of the option;

- we determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant; and

- we estimate forfeitures based on our historical analysis of actual stock option forfeitures.

We account for stock-based compensation arrangements with directors and consultants that contain only service conditions for vesting using a fair value approach. The fair value of these options is measured using the Black-Scholes option pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option. For consultant and other non-employee options subject to vesting, the compensation costs of these arrangements are subject to re-measurement over the vesting period.

The following summarizes the assumptions used for estimating the fair value of stock options granted to employees for the periods indicated:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Risk-free interest rate | 1.88% - 2.26% | 1.29% - 1.50% | 1.40% - 1.99% |
| Expected term (in years) | 5.12 - 7.00 | 5.50 - 6.25 | 4.33 - 6.25 |
| Expected volatility | 85.35% - 95.08% | 77.38% - 94.78% | 68.79% - 86.84% |
| Expected dividend yield | 0% | 0% | 0% |

Based upon the stock price of $4.05 per share, which is the last sale price of our common stock reported on The NASDAQ Global Market as of December 29, 2017, the aggregate intrinsic value of outstanding options to purchase shares of our common stock as of December 31, 2017 and 2016, was $472,000 and $26,000, respectively, of which $29,000 as of December 31, 2017, and $26,000 as of December 31, 2016, related to vested options and $443,000 as of December 31, 2017, and $0 as of December 31, 2016, related to unvested options.

***Determination of Exercise Price of Stock Options and the Fair Value of Common Stock on Grant Dates Prior to Our IPO***

The following table summarizes by grant date the number of shares of common stock subject to stock options granted between January 1, 2015 and March 2, 2015, as well as the associated per-share exercise price and the estimated fair value per share of our common stock on the grant date:

| Grant Date | Number of Shares Underlying Options Granted | Exercise Price Per Share | Estimated Fair Value Per Share |
|---|---|---|---|
| January 20, 2015 | 8,640 | 8.63 | 8.63 |
| March 2, 2015 | 145,999 | 8.63 | 8.63 |

In setting the exercise price of the stock options at each of the grant dates management and the board of directors considered a third-party valuation in determining the exercise price of the stock options.

We undertook a third-party valuation of the fair value of our common stock as of December 31, 2014, for financial reporting purposes. The estimated fair value per share of our common stock in the table above, as determined by the third-party valuation was used to measure the stock-based compensation expense for options granted.

There is inherent uncertainty in these estimates and, if we had made different assumptions than those described, the fair value of the underlying common stock and amount of our stock-based compensation expense, net loss and net loss per share amounts would have differed.

***Common Stock Valuation Methodology—Third-Party Valuations***

In estimating the fair value of our common stock at December 31, 2014, given the absence of a public trading market for our common stock, and in accordance with the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, management and our third-party valuation specialists utilized the probability weighted expected return method, or PWERM, approach to allocate equity value to our common stock. The PWERM approach employs various market, income or cost approach calculations depending on the likelihood of various liquidation scenarios. For each of the various scenarios, an equity value is estimated and the rights and preferences for each class of stock are then considered to allocate the equity value to common stock. The common stock value is then multiplied by a discount factor reflecting the calculated discount rate and the timing of the event. Lastly, the common share value is multiplied by an estimated probability for each scenario. The probability and timing of each scenario are based on discussions between our board of directors and our management team. Under the PWERM, the value of our common stock was estimated based on four possible future events for our company:

- an earlier or later IPO;
- a strategic merger or sale;
- our remaining a private company; and
- the dissolution of our company.

We used the market approach in determining the equity value of our business for use in the early and late IPO, strategic merger or sale and remaining private scenarios. We used the cost approach to value our net assets available to common stockholders if we were forced to liquidate our assets and dissolve the company. The cost approach involves identifying our significant tangible assets and liabilities, estimating the individual current market values of each and then totaling them to derive the value of the business as a whole.

The market approach estimates the fair value of a company by applying market multiples of comparable publicly traded companies and publicly disclosed data from arm's-length strategic merger or sale transactions involving similar companies in the marketplace. We reviewed recent precedent biopharmaceutical IPOs and merger or sale transactions to develop equity value estimates for application at each measurement date. We gave consideration to differences between us and the selected guideline public companies in terms of size, anticipated profitability, market size and other critical characteristics that generally reflect an investor's assessment of the business and financial risks inherent in our industry. In particular, we gave consideration to the fact that we had only one clinical-stage product candidate under development and that the product candidate is a chemically modified form of an existing approved drug with potential, but as yet unproven, differentiation. We also considered that this product candidate is intended to compete in a large existing market characterized by intense competition, low generic pricing and a challenging third-party reimbursement environment. In addition, we considered the size of the transaction, anticipated debt outstanding at IPO and number of employees as possible valuation proxies when comparing us with the guideline companies.

***Determination of Exercise Price of Stock Options made at Our IPO***

For the grants made on April 15, 2015, management and the board of directors relied on our IPO price to determine the exercise price of the stock options.

***Determination of Exercise Price of Stock Options after Our IPO***

After completion of our IPO, management and the board of directors have relied on the closing sale price of our common stock as reported on The NASDAQ Global Market on the date of grant to determine the exercise price of stock options.

***Fair Value of Financial Instruments***

We have common stock warrants, put options embedded within those warrants, fundamental change and make-whole interest provisions embedded within our convertible notes and put option embedded within the Deerfield Note that meet the definition of derivative financial instruments and are accounted for as derivatives. The fair value of these derivatives is based on Monte Carlo simulation models generated at each reporting period.

The derivative liability for the common stock warrants was $5.1 million and $4.2 million at December 31, 2017 and 2016, respectively. The derivative liability for the put options embedded within the common stock warrants was $0.4 million at December 31, 2017 and 2016, respectively. The derivative liability for the fundamental change and make-whole interest provisions embedded within our convertible notes was $14,000 and $6,000 at December 31, 2017 and 2016. The put option embedded within the Deerfield Note was $2.2 million at December 31, 2017 and had no value as of December 31, 2016. A 10% increase in the enterprise value would result in an increase of $0.6 million in the estimated fair value of the common stock warrants, an increase of $38,000 in the estimated fair value of the put options embedded within the common stock warrants, an increase of $4,000 in the estimated fair value of the fundamental change and make-whole interest provisions embedded within our convertible notes and an increase of $0.4 million in the estimated fair value of the put option embedded within the Deerfield Note at December 31, 2017.

Upon exercise of the warrants, we will adjust the associated derivative liability to fair value with any changes recorded in other (expense) income. At such time, such derivative liability will also be reclassified to additional paid-in capital, and no further revaluations will be necessary.

***Utilization of Net Operating Loss Carryforwards and Research and Development Credits***

As of December 31, 2017, we had federal net operating loss, or NOL, carryforwards of approximately $137.3 million with expiration dates from 2027 to 2037. We also had research and development credit carryforwards of $3.8 million with expiration dates ranging from 2027 to 2037.

In accordance with Section 382 of the Code, a change in equity ownership of greater than 50% within a three-year period results in an annual limitation on a company's ability to utilize its NOL carryforwards created during the tax periods prior to the change in ownership. We performed a Section 382 ownership change analysis in 2017 and determined that we experienced an ownership change in 2010, which resulted in a portion of our net operating loss carryforwards being subject to an annual limitation under Section 382 through 2012. No other ownership changes or limitations on our historical net operating loss carryforwards were noted through the year ended December 31, 2017. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including as a result of the conversion of our outstanding convertible debt or as a result of future changes in our stock ownership. If we determine that an ownership change has occurred and our ability to use our historical net operating loss carryforwards is materially limited, it would harm our future operating results by increasing our future tax obligations.

***Emerging Growth Company Status***

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***Recent Accounting Pronouncements***

On April 5, 2012, President Obama signed the JOBS Act into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an emerging growth company. As an emerging growth company, we may elect to adopt new or revised accounting standards when they become effective for non-public companies, which typically is later than public companies must adopt the standards. We have elected not to take advantage of the extended transition period afforded by the JOBS Act and, as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

In May 2014, the Financial Accounting Standards Board, or FASB, issued guidance codified in Accounting Standards Codification, or ASC, Topic 606, *Revenue Recognition—Revenue from Contracts with Customers,* or ASC 606, which amends the guidance in former ASC 605, *Revenue Recognition*, and becomes effective beginning January 1, 2018. We do not currently expect this standard to have a material effect on our financial statements upon adoption since we are not generating revenue at this time.

In November 2015, the FASB issued Accounting Standards Update, or ASU, 2015-17, *Income Taxes: Balance Sheet Classification of Deferred Taxes (Topic 740)*, or ASU 2015-17, which requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. This update applies to all entities that present a classified statement of financial position. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. The adoption of ASU 2015-17 did not have a material impact on our financial statements and disclosures as we maintain a full valuation allowance over our deferred tax liabilities and assets.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments Overall – Recognition and Measurement of Financial Assets and Liabilities (Topic 825-10),* or ASU 2016-01, which provides several updates related to Topic 825-10. This update applies to all entities that hold financial assets or owe financial liabilities. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. We do not currently expect ASU 2016-01 to have a material effect on our financial statements and disclosures upon adoption.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842),* or ASU 2016-02, which requires lessees to recognize assets and liabilities for operating leases with lease terms greater than twelve months in the balance sheet. The update also requires improved disclosures to help users of financial statements better understand the amount, timing and uncertainty of cash flows arising from leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years, with early adoption permitted. We are currently evaluating the impact of the adoption of ASU 2016-02 on our financial statements and disclosures.

In March 2016, the FASB issued ASU 2016-06, *Derivatives and Hedging (Topic 815), Contingent Put and Call Options in Debt Instruments,* or ASU 2016-06, which clarifies the requirements for assessing whether contingent call and put options that can accelerate the payment of principal on debt instruments are clearly and closely related to their debt hosts. ASU 2016-06 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years, with early adoption permitted. The adoption of ASU 2016-06 did not have a material impact on our financial statements and disclosures.

In March 2016, the FASB issued ASU 2016-09, *Compensation–Stock Compensation (Topic 718), Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09, which simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years, with early adoption permitted. The adoption of ASU 2016-09 did not have a material impact on our financial statements and disclosures.

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows – Classification of Certain Cash Receipts and Cash Payments (Topic 230)*, or ASU 2016-15, which addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice. This update applies to all entities that are required to present a statement of cash flows under Topic 230. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. We do not currently expect ASU 2016-15 to have a material effect on our financial statements and disclosures upon adoption.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash,* or ASU 2016-18, which addresses the treatment of restricted cash and restricted cash equivalents in the statement of cash flows. This update applies to all entities that have restricted cash or restricted cash equivalents and are required to present a statement of cash flows. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. We early adopted ASU 2016-18 in the second quarter of 2017. The adoption of ASU 2016-18 reduced our net cash used in investing activities and net decrease in cash and cash equivalents on the statements of cash flows by $1.1 million for the year ended December 31, 2016, as compared to the net cash used in investing activities and net decrease in cash and cash equivalents on the statements of cash flows if we had not early adopted ASU 2016-18. This reclassification had no effect on the balance sheets, statements of operations or statements of changes in redeemable convertible preferred stock and stockholders' deficit.

In May 2017, the FASB issued ASU 2017-09, *Compensation – Stock Compensation (Topic* 718*) – Scope of Modification Accounting,* or ASU 2017-09, which provides guidance about which changes to the terms or conditions of a stock-based payment award require an entity to apply modification accounting in Topic 718. This update applies to any entity that changes the terms or conditions of a stock-based payment award. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. We do not currently expect ASU 2017-09 to have a material effect on our financial statements and disclosures upon adoption.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic* 260*), Distinguishing Liabilities from Equity (Topic* 480*), Derivatives and Hedging (Topic* 815*) – I. Accounting for Certain Financial Instruments with Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception*, or ASU 2017-11, which addresses the complexity of accounting for certain financial instruments with down round features and addresses the difficulty of navigating Topic 480 because of the existence of extensive pending content in the ASC as a result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. This update applies to all entities that issue financial instruments that include down round features and entities that present earnings per share in accordance with Topic 260. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. If early adopted in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. We are currently evaluating the impact of the adoption of ASU 2017-11 on our financial statements and disclosures.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Not applicable.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

The financial statements required by this item are set forth beginning in Item 15 of this report and are incorporated herein by reference.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

Not applicable.

**ITEM 9A. CONTROLS AND PROCEDURES**

***Evaluation of Disclosure Controls and Procedures***

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our chief executive officer and our chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. Based on the evaluation of our disclosure controls and procedures as of December 31, 2017, our chief executive officer and our chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

***Management's Report on Internal Control over Financial Reporting***

Internal control over financial reporting refers to the process designed by, or under the supervision of, our chief executive officer and chief financial officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that: (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; 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.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(e) under the Exchange Act. Under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled "*Internal Control – Integrated Framework (2013)"* published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2017, the end of our most recent fiscal year.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

***Changes in Internal Control over Financial Reporting***

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the most recent fiscal quarter that materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

***Inherent Limitations on Effectiveness of Controls***

Our management, including our chief executive officer and our chief financial officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

**ITEM 9B. OTHER INFORMATION**

None.

## PART III

**ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this Item 10 will be set forth under the headings "Proposal 1 - Election of Directors," "Executive Officers," "Information Regarding the Board of Directors and Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement for our 2018 annual meeting of stockholders, or the proxy statement, and, is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, applicable to all of our employees, executive officers and directors. The Code of Conduct is available on our website at www.kempharm.com. The nominating and corporate governance committee of our board of directors is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for employees, executive officers and directors. We intend to post any amendments to the Code of Conduct or any waivers of its requirements on our website.

**ITEM 11. EXECUTIVE COMPENSATION**

The information required by this Item 11 will be set forth under the headings "Executive Compensation" and "Information Regarding the Board of Directors and Corporate Governance" in our 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 12 will be set forth under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under the Equity Compensation Plans" in the proxy statement and is incorporated herein by reference.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The information required by this Item 13 will be set forth under the headings "Information Regarding the Board of Directors and Corporate Governance" and "Transactions with Related Persons" in the proxy statement and is incorporated herein by reference.

**ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information required by this Item 14 will be set forth under the headings "Proposal 2 - Ratification of Selection of Independent Registered Public Accounting Firm" in the proxy statement and is incorporated herein by reference.

## PART IV

**ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

(a) The following documents are filed as part of this report:

(1) *Index list to Financial Statements:*



(2) *Financial Statement Schedules*

All other schedules are omitted because they are not required or the required information is included in the financial statements or notes thereto.

(3) *Exhibits*

The exhibits listed in the accompanying Exhibit Index are filed or incorporated by reference as part of this report.

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of KemPharm, Inc.

**Opinion on the Financial Statements**
We have audited the accompanying balance sheet of KemPharm, Inc. (the Company) as of December 31, 2017, the related statements of operations, changes in redeemable convertible preferred stock and stockholders' deficit and cash flows, for the year then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017, and the results of its operations and its cash flows for the year then ended in conformity with accounting principles generally accepted in the United States of America.

**Emphasis of Matter Regarding Going Concern**
The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note A to the financial statements, the Company has recurring losses from operations, negative operating cash flows, and a stockholders' deficit and its existing cash and cash equivalents, restricted cash, marketable securities, trade date receivables and long-term investments are not sufficient to fund the Company's operating expenses and capital expenditure requirements for at least one year from the auditor report date. This raises 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 A. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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

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

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

/s/ RSM US LLP

We have served as the Company's auditor since 2017.

Orlando, Florida
March 30, 2018

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of KemPharm, Inc.

We have audited the accompanying balance sheet of KemPharm, Inc. as of December 31, 2016, and the related statements of operations, changes in redeemable convertible preferred stock and stockholders' deficit and cash flows for each of the two years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of KemPharm, Inc. at December 31, 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
Certified Public Accountants

Tampa, Florida
March 10, 2017

except for the effects of the retrospective adoption of Accounting Standards Update 2016-18 discussed in Note A, *Reclassifications*, as to which the date is

March 30, 2018

**KEMPHARM, INC.**
**BALANCE SHEETS**
**(in thousands, except share and par value amounts)**

| | December 31, | |
|---|---|---|
| | **2017** | **2016** |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 10,871 | $ 16,762 |
| Restricted cash | 1,100 | 1,100 |
| Marketable securities | 31,358 | 51,003 |
| Trade date receivables | 2,005 | 5,003 |
| Prepaid expenses and other current assets | 1,662 | 489 |
| Total current assets | 46,996 | 74,357 |
| Property and equipment, net | 2,004 | 1,970 |
| Long-term investments | 3,250 | 8,200 |
| Other long-term assets | 206 | 360 |
| Total assets | $ 52,456 | $ 84,887 |
| | | |
| **Liabilities and stockholders' deficit** | | |
| Current liabilities: | | |
| Accounts payable and accrued expenses | $ 7,875 | $ 6,444 |
| Current portion of convertible notes | 3,333 | — |
| Current portion of capital lease obligation | 189 | 157 |
| Other current liabilities | 112 | 41 |
| Total current liabilities | 11,509 | 6,642 |
| Convertible notes, less current portion, net | 89,398 | 91,170 |
| Derivative and warrant liability | 7,709 | 4,618 |
| Capital lease obligation, less current portion | 562 | 657 |
| Other long-term liabilities | 794 | 496 |
| Total liabilities | 109,972 | 103,583 |
| | | |
| Commitments and contingencies (Note G) | | |
| | | |
| Stockholders' deficit: | | |
| Common stock, $0.0001 par value, 250,000,000 shares authorized, 14,657,430 shares issued and outstanding as of December 31, 2017; 14,646,982 shares issued and outstanding as of December 31, 2016 | 1 | 1 |
| Additional paid-in capital | 107,209 | 102,643 |
| Preferred stock, $0.0001 par value, 10,000,000 shares authorized, no shares issued or outstanding as of December 31, 2017 or December 31, 2016 | — | — |
| Accumulated deficit | (164,726) | (121,340) |
| Total stockholders' deficit | (57,516) | (18,696) |
| Total liabilities and stockholders' deficit | $ 52,456 | $ 84,887 |

*See accompanying notes to financial statements*

**KEMPHARM, INC.**
**STATEMENTS OF OPERATIONS**
**(in thousands, except share and per share amounts)**

| | Year ended December 31, | | |
|---|---|---|---|
| | **2017** | **2016** | **2015** |
| Revenue | $ — | $ — | $ — |
| Operating expenses: | | | |
| Research and development | 20,593 | 20,472 | 13,931 |
| General and administrative | 12,773 | 14,000 | 8,883 |
| Severance expense | — | 3,010 | — |
| Total operating expenses | 33,366 | 37,482 | 22,814 |
| Loss from operations | (33,366) | (37,482) | (22,814) |
| Other (expense) income: | | | |
| Loss on extinguishment of debt | — | (4,740) | — |
| Interest expense related to amortization of debt issuance costs and discount | (1,561) | (1,616) | (1,909) |
| Interest expense on principal | (5,776) | (5,511) | (2,671) |
| Fair value adjustment related to derivative and warrant liability | (3,091) | 32,465 | (27,276) |
| Interest and other income, net | 365 | 353 | 32 |
| Total other (expense) income | (10,063) | 20,951 | (31,824) |
| Loss before income taxes | (43,429) | (16,531) | (54,638) |
| Income tax benefit (expense) | 43 | 15 | (26) |
| Net loss | $ (43,386) | $ (16,516) | $ (54,664) |
| | | | |
| Net loss per share: | | | |
| Basic and diluted | $ (2.96) | $ (1.13) | $ (7.42) |
| | | | |
| Weighted average number of shares of common stock outstanding: | | | |
| Basic and diluted | 14,652,898 | 14,597,053 | 7,368,681 |

*See accompanying notes to financial statements*

**KEMPHARM, INC.**
**STATEMENTS OF CHANGES IN REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT**
**(in thousands)**

| | Redeemable Convertible Preferred Stock | | | | | | Common Stock | Additional Paid-in Capital | Preferred Stock | Accumulated Deficit | Total Stockholders' Equity |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Series A | Series B | Series C | Series D | Series D-1 | Total | | | | | |
| Balance as of January 1, 2015 | $ 3,343 | $ 3,313 | $ 11,892 | $ 5,659 | $ — | $ 24,207 | $ — | $ 1,652 | $ — | $ (50,160) | $ (48,508) |
| Net loss | — | — | — | — | — | — | — | — | — | (54,664) | (54,664) |
| Stock-based compensation expense | — | — | — | — | — | — | — | 2,369 | — | — | 2,369 |
| Exercise of stock options and warrants | — | — | — | — | — | — | — | 4,749 | — | — | 4,749 |
| Issuance of Series D-1 preferred stock | — | — | — | — | 4,000 | 4,000 | — | — | — | — | — |
| Issuance of common stock in connection with IPO, net of discounts and commissions | — | — | — | — | — | — | 1 | 59,891 | — | — | 59,892 |
| Conversion of 2013 warrants to equity classification | — | — | — | — | — | — | — | 1,110 | — | — | 1,110 |
| Conversion of preferred stock into common stock upon IPO | (3,343) | (3,313) | (11,892) | (5,659) | (4,000) | (28,207) | — | 28,207 | — | — | 28,207 |
| Offering expenses charged to equity | — | — | — | — | — | — | — | (3,276) | — | — | (3,276) |
| Balance as of December 31, 2015 | $ — | $ — | $ — | $ — | $ — | $ — | $ 1 | $ 94,702 | $ — | $ (104,824) | $ (10,121) |
| Net loss | — | — | — | — | — | — | — | — | — | (16,516) | (16,516) |
| Stock-based compensation expense | — | — | — | — | — | — | — | 6,600 | — | — | 6,600 |
| Exercise of stock options and warrants | — | — | — | — | — | — | — | 896 | — | — | 896 |
| Write-off of deferred offering costs | — | — | — | — | — | — | — | 445 | — | — | 445 |
| Balance as of December 31, 2016 | $ — | $ — | $ — | $ — | $ — | $ — | $ 1 | $ 102,643 | $ — | $ (121,340) | $ (18,696) |
| Net loss | — | — | — | — | — | — | — | — | — | (43,386) | (43,386) |
| Stock-based compensation expense | — | — | — | — | — | — | — | 4,562 | — | — | 4,562 |
| Exercise of stock options and warrants | — | — | — | — | — | — | — | 4 | — | — | 4 |
| Balance as of December 31, 2017 | $ — | $ — | $ — | $ — | $ — | $ — | $ 1 | $ 107,209 | $ — | $ (164,726) | $ (57,516) |

*See accompanying notes to financial statements*

**KEMPHARM, INC.**
**STATEMENTS OF CASH FLOWS**
**(in thousands)**

| | Year ended December 31, | | |
|---|---|---|---|
| | **2017** | **2016** | **2015** |
| **Cash flows from operating activities:** | | | |
| Net loss | $ (43,386) | $ (16,516) | $ (54,664) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Loss on extinguishment of debt | — | 4,740 | — |
| Write-off of deferred offering costs | 60 | 445 | — |
| Stock-based compensation expense | 4,562 | 6,600 | 2,369 |
| Non-cash interest expense | 2,222 | 2,222 | 2,671 |
| Amortization of debt issuance costs and debt discount | 1,561 | 1,616 | 1,909 |
| Depreciation and amortization expense | 336 | 175 | 84 |
| Fair value adjustment | 3,091 | (32,465) | 27,276 |
| Loss on sublease and disposal of fixed assets | 104 | 91 | — |
| Change in assets and liabilities: | | | |
| Prepaid expenses and other assets | (926) | 2,018 | (1,228) |
| Accounts payable and accrued expenses | (801) | 1,118 | 1,315 |
| Other liabilities | 77 | 184 | — |
| Net cash used in operating activities | (33,100) | (29,772) | (20,268) |
| | | | |
| **Cash flows from investing activities:** | | | |
| Purchases of property and equipment | (181) | (643) | (135) |
| Purchases of marketable securities and long-term investments | (27,378) | (89,849) | (19,002) |
| Maturities of marketable securities | 54,971 | 44,645 | — |
| Net cash provided by (used in) investing activities | 27,412 | (45,847) | (19,137) |
| | | | |
| **Cash flows from financing activities:** | | | |
| Proceeds from issuance of debt, net of discounts and commissions | — | 82,800 | — |
| Repayment of term notes and related accrued interest | — | (18,621) | — |
| Payment of principal on convertible notes arising from capitalized interest | — | (1,931) | — |
| Payment of deferred offering costs | (50) | (164) | (315) |
| Payment of debt and stock issuance costs | — | (983) | (2,533) |
| Repayment of obligations under capital lease | (157) | (79) | (32) |
| Proceeds from exercise of common stock options and warrants | 4 | 141 | 413 |
| Proceeds from issuance of Series D-1 redeemable convertible preferred stock | — | — | 4,000 |
| Proceeds from initial public offering, net of discounts and commissions | — | — | 59,892 |
| Proceeds from exercise of Series D preferred stock warrants | — | — | 43 |
| Net cash (used in) provided by financing activities | (203) | 61,163 | 61,468 |
| Net (decrease) increase in cash, cash equivalents and restricted cash | (5,891) | (14,456) | 22,063 |
| Cash, cash equivalents and restricted cash, beginning of year | 17,862 | 32,318 | 10,255 |
| Cash, cash equivalents and restricted cash, end of year | $ 11,971 | $ 17,862 | $ 32,318 |
| | | | |
| **Supplemental cash flow information:** | | | |
| Cash paid for interest | $ 5,717 | $ 3,289 | $ — |
| Trade date receivables | 2,005 | 5,003 | — |
| Property and equipment financed under a lease agreement | 284 | 867 | — |
| Transfer of warrants to equity upon exercise | — | 755 | 4,293 |
| Property and equipment included in accounts payable and accrued expenses | 3 | 281 | — |
| Deferred offering costs included in accounts payable and accrued expenses | — | 85 | 428 |
| Conversion of preferred stock into common stock upon initial public offering | — | — | 28,207 |
| Unpaid offering costs charged to equity | — | — | 3,276 |
| Reclassification of 2013 warrants to equity | — | — | 1,110 |

*See accompanying notes to financial statements*

**KEMPHARM, INC.**
**NOTES TO FINANCIAL STATEMENTS**

## A. Description of Business and Basis of Presentation

***Organization***

KemPharm, Inc. (the "Company") is a specialty pharmaceutical company focused on the discovery and development of proprietary prodrugs to treat serious medical conditions through its Ligand Activated Therapy ("LAT") platform technology. The Company utilizes its proprietary LAT platform technology to generate improved prodrug versions of U.S. Food and Drug Administration (the "FDA") approved drugs in the high need areas of attention deficit hyperactivity disorder ("ADHD"), pain and other central nervous system ("CNS") disorders. The Company was formed and incorporated in Iowa on October 30, 2006 and reorganized in Delaware on May 30, 2014.

***Going Concern***

The financial statements have been prepared on a going concern basis which assumes that the Company will be able to realize its assets and discharge its liabilities in the normal course of business for the foreseeable future. The Company has experienced recurring losses from operations, stockholders' deficit and negative operating cash flows due to its ongoing research and development of its product and product candidates. The Company also has an accumulated deficit as of December 31, 2017. Various internal and external factors will affect whether and when product candidates become approved drugs and how significant the market share of those approved products will be. The length of time and cost of developing and commercializing these product and product candidates and/or failure of them at any stage of the drug approval or commercialization process will materially affect the Company's financial condition and future operations.

Management believes these conditions raise substantial doubt about the Company's ability to continue as a going concern within the twelve months after the date these financial statements are issued. The ability to continue as a going concern is dependent upon profitable future operations, positive cash flows and additional financing.

Management intends to finance operating costs over the next twelve months with existing cash and cash equivalents, marketable securities and trade date receivables, as well as, financing through the Company's active registration statement on Form S-3 covering the sale of up to $150.0 million of the Company's common stock, preferred stock, and debt and/or warrants. The registration statement on Form S-3 included a prospectus covering the offering up to $20,000,000 of shares of common stock through an "at-the-market offering."

***Initial Public Offering and Reverse Stock Split***

In April 2015, the Company completed an initial public offering ("IPO") of its common stock. Prior to the commencement of the IPO, the Company effected a 1-for-7.5 reverse stock split of its issued common stock. All applicable share data, per share amounts and related information in the financial statements and notes thereto have been retroactively adjusted to give effect to this reverse stock split. Upon completion of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock were converted or reclassified into shares of common stock and all outstanding warrants to acquire shares of the Company's redeemable convertible preferred stock became warrants to acquire the Company's common stock. In connection with the IPO, the Company amended and restated its Amended and Restated Certificate of Incorporation to change the authorized capital stock to 250,000,000 shares, designated as common stock, and 10,000,000 shares, designated as preferred stock, each with a par value of $0.0001 per share.

***Reclassifications***

Certain prior year amounts have been reclassified to conform with current year presentation.

During the second quarter of 2017, the Company early adopted Accounting Standards Update ("ASU") 2016-18, *Statement of Cash Flows (Topic* 230*): Restricted Cash* ("ASU 2016-18"), which addresses the treatment of restricted cash and restricted cash equivalents in the statement of cash flows. The adoption of ASU 2016-18 reduced the Company's net cash used in investing activities and net decrease in cash and cash equivalents on the statements of cash flows by $1.1 million for the year ended December 31, 2016, as compared to the net cash used in investing activities and net decrease in cash and cash equivalents on the statements of cash flows if the Company had not early adopted ASU 2016-18. This reclassification had no effect on the balance sheets, statements of operations or statements of changes in redeemable convertible preferred stock and stockholders' deficit. The Company did not have restricted cash for the year ended December 31, 2015.

***Entry into ATM Agreement***

On October 3, 2016, the Company entered into a Common Stock Sales Agreement (the "ATM Agreement") with Cowen and Company, LLC ("Cowen") under which the Company may offer and sell, from time to time, in its sole discretion, shares of common stock having an aggregate offering price of up to $50,000,000 through Cowen as the Company's sales agent. The Company's registration statement on Form S-3 contemplated under the ATM Agreement was declared effective by the U.S. Securities and Exchange Commission ("SEC") on October 17, 2016. The registration statement on Form S-3 included a prospectus covering the offering up to $20,000,000 of shares of common stock in accordance with the ATM Agreement.

Cowen may sell common stock under the ATM Agreement by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415 of the Securities Act or 1933, as amended ("Securities Act"), including without limitation sales made by means of ordinary brokers' transactions on The NASDAQ Global Market or otherwise at market prices prevailing at the time of sale, in block transactions, or as otherwise directed by the Company. Cowen will use commercially reasonable efforts to sell the common stock from time to time, based upon instructions from the Company (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company will pay Cowen a commission of up to three percent (3.0%) of the gross sales proceeds of any common stock sold through Cowen under the ATM Agreement, and also has provided Cowen with customary indemnification rights.

The Company is not obligated to make any sales of common stock under the ATM Agreement. The offering of shares of common stock pursuant to the ATM Agreement will terminate upon the earlier of (i) the sale of all common stock subject to the ATM Agreement, or (ii) termination of the ATM Agreement in accordance with its terms. As of December 31, 2017, the Company had deferred offering costs recorded within other long-term assets in the

amount of $0.2 million.

As of March 28, 2018, the Company has sold 446,111 shares of common stock under the ATM Agreement, resulting in gross proceeds of $2.9 million.

**B. Summary of Significant Accounting Policies**

***Use of Estimates***

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

On an ongoing basis, the Company evaluates its estimates, including those related to the useful lives of property and equipment, and assumptions used for purposes of determining stock-based compensation, income taxes, and the fair value of the derivative and warrant liability, among others. The Company bases its estimates on historical experience and on various other assumptions that it believes to be reasonable, the results of which form the basis for making judgments about the carrying value of assets and liabilities.

***Concentration of Credit Risk***

Financial instruments that potentially expose the Company to concentrations of credit risk consist principally of cash on deposit with multiple financial institutions, the balances of which frequently exceed insured limits.

***Cash and Cash Equivalents***

The Company considers any highly liquid investments with an original maturity of three months or less to be cash equivalents.

***Marketable Securities and Long-term Investments***

The Company maintains investment securities that are classified as trading securities. These securities are carried at fair value with unrealized gains and losses included in other (expense) income on the statements of operations. The securities primarily consist of certificates of deposit, U.S. Treasury securities and U.S. government-sponsored agency securities.

***Property and Equipment***

The Company records property and equipment at cost less accumulated depreciation and amortization. Costs of renewals and improvements that extend the useful lives of the assets are capitalized. Maintenance and repairs are expensed as incurred. Depreciation is determined on a straight-line basis over the estimated useful lives of the assets, which generally range from three to ten years. Leasehold improvements are amortized over the shorter of the useful life of the asset or the term of the related lease. Upon retirement or disposition of assets, the costs and related accumulated depreciation and amortization are removed from the accounts with the resulting gains or losses, if any, reflected in the statements of operations.

***Debt Issuance Costs***

Debt issuance costs incurred in connection with financing arrangements are amortized over the life of the respective financing arrangement using the effective interest method.

***Supply Arrangements***

The Company enters into supply arrangements for the supply of components of its product and product candidates. These arrangements also may include a share of future revenue if related product or product candidates reach commercialization. Costs under these supply arrangements, if any, are expensed as incurred (Note H).

***Impairment of Long-Lived Assets***

Long-lived assets to be held and used are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If the undiscounted cash flows are insufficient to recover the carrying values, an impairment loss is recorded for the difference between the carrying values and fair values of the asset. No such impairment occurred for the years ended December 31, 2017, 2016 or 2015.

***Fair Value of Financial Instruments***

The accounting standard for fair value measurements provides a framework for measuring fair value and requires disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date, based on the Company's principal or, in absence of a principal, most advantageous market for the specific asset or liability.

The Company uses a three-tier fair value hierarchy to classify and disclose all assets and liabilities measured at fair value on a recurring basis, as well as assets and liabilities measured at fair value on a non-recurring basis, in periods subsequent to their initial measurement. The hierarchy requires the Company to use observable inputs when available, and to minimize the use of unobservable inputs, when determining fair value. The three tiers are defined as follows:

- Level 1—Observable inputs that reflect quoted market prices (unadjusted) for identical assets or liabilities in active markets;
- Level 2—Observable inputs other than quoted prices in active markets that are observable either directly or indirectly in the marketplace for identical or similar assets and liabilities; and
- Level 3—Unobservable inputs that are supported by little or no market data, which require the Company to develop its own assumptions.

***Research and Development***

Major components of research and development costs include cash compensation, stock-based compensation, depreciation and amortization expense on research and development property and equipment, costs of preclinical studies, clinical trials and related clinical manufacturing, costs of drug development, costs of materials and supplies, facilities cost, overhead costs, regulatory and compliance costs, and fees paid to consultants and other entities that conduct certain research and development activities on the Company's behalf. Costs incurred in research and development are expensed as incurred.

The Company records nonrefundable advance payments it makes for future research and development activities as prepaid expenses. Prepaid expenses are recognized as expense in the statements of operations as the Company receives the related goods or services.

The Company enters into contractual agreements with third-party vendors who provide research and development, manufacturing, and other services in the ordinary course of business. Some of these contracts are subject to milestone-based invoicing and services are completed over an extended period of time. The Company records liabilities under these contractual commitments when an obligation has been incurred. This accrual process involves reviewing open contracts and purchase orders, communicating with the applicable personnel to identify services that have been performed and estimating the level of service performed and the associated cost when the Company has not yet been invoiced or otherwise notified of actual cost. The majority of the service providers invoice the Company monthly in arrears for services performed. The Company makes estimates of the accrued expenses as of each balance sheet date based on the facts and circumstances known. The Company periodically confirms the accuracy of the estimates with the service providers and make adjustments if necessary.

***Patent Costs***

Patent costs, including related legal costs, are expensed as incurred and recorded within general and administrative expenses on the statements of operations.

***Income Taxes***

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial reporting and tax basis of assets and liabilities, as well as for operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using the tax rates that are expected to apply to taxable income for the years in which those tax assets and liabilities are expected to be realized or settled. Valuation allowances are recorded to reduce deferred tax assets to the amount the Company believes is more likely than not to be realized.

Uncertain tax positions are recognized only when the Company believes it is more likely than not that the tax position will be upheld on examination by the taxing authorities based on the merits of the position. The Company recognizes interest and penalties, if any, related to unrecognized income tax uncertainties in income tax expense. The Company did not have any accrued interest or penalties associated with uncertain tax positions as of December 31, 2017 and 2016.

The Company files income tax returns in the United States for federal and various state jurisdictions. With few exceptions, the Company is no longer subject to U.S. federal and state and local income tax examinations for years prior to 2013, although carryforward attributes that were generated prior to 2013 may still be adjusted upon examination by the Internal Revenue Service if used in a future period. No income tax returns are currently under examination by taxing authorities.

***Stock-Based Compensation***

The Company measures and recognizes compensation expense for all stock-based payment awards made to employees, officers and directors based on the estimated fair values of the awards as of the grant date. The Company records the value of the portion of the award that is ultimately expected to vest as expense over the requisite service period. The Company also accounts for equity instruments issued to non-employees using a fair value approach under Accounting Standards Codification ("ASC") subtopic 505-50. The Company values equity instruments and stock options granted using the Black-Scholes option pricing model. The value of non-employee stock-based compensation is subject to periodic adjustments as the underlying equity instruments vest and is recognized as an expense over the term of the related financing or the period over which services are received.

***Basic and Diluted Net Loss per Share of Common Stock***

The Company uses the two-class method to compute net loss per common share because the Company has issued securities, other than common stock, that contractually entitle the holders to participate in dividends and earnings of the Company. The two-class method requires earnings for the period to be allocated between common stock and participating securities based upon their respective rights to receive distributed and undistributed earnings. Holders of each series of the Company's redeemable convertible preferred stock are entitled to participate in distributions, when and if declared by the board of directors, that are made to common stockholders and, as a result, are considered participating securities.

***Segment and Geographic Information***

Operating segments are defined as components of an enterprise (business activity from which it earns revenue and incurs expenses) for which discrete financial information is available and regularly reviewed by the chief operating decision maker ("CODM") in deciding how to allocate resources and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company views its operations and manages its business as a single operating and reporting segment. All assets of the Company were held in the United States as of December 31, 2017 and 2016.

***Application of New or Revised Accounting Standards—Adopted***

From time to time, the Financial Accounting Standards Board (the "FASB") or other standard-setting bodies issue accounting standards that are adopted by the Company as of the specified effective date.

On April 5, 2012, President Obama signed the Jump-Start Our Business Startups Act (the "JOBS Act") into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an emerging growth company. As an emerging growth company, the Company may elect to adopt new or revised accounting standards when they become effective for non-public companies, which typically is later than public companies must adopt the standards. The Company has elected not to take advantage of the extended transition period afforded by the JOBS Act and, as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

In November 2015, the FASB issued ASU 2015-17, *Income Taxes: Balance Sheet Classification of Deferred Taxes (Topic* 740*)* ("ASU 2015-17"), which requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. This update applies to all entities that present a classified statement of financial position. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. The adoption of ASU 2015-17 did not have a material impact on the Company's financial statements and disclosures as the Company maintains a full valuation allowance over its deferred tax liabilities and assets.

In March 2016, the FASB issued ASU 2016-06, *Derivatives and Hedging (Topic* 815*), Contingent Put and Call Options in Debt Instruments* ("ASU 2016-06"), which clarifies the requirements for assessing whether contingent call and put options that can accelerate the payment of principal on debt instruments are clearly and closely related to their debt hosts. ASU 2016-06 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years, with early adoption permitted. The adoption of ASU 2016-06 did not have a material impact on the Company's financial statements and disclosures.

In March 2016, the FASB issued ASU 2016-09, *Compensation–Stock Compensation (Topic* 718*), Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"), which simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years, with early adoption permitted. The adoption of ASU 2016-09 did not have a material impact on the Company's financial statements and disclosures.

In November 2016, the FASB issued ASU 2016-18, which applies to all entities that have restricted cash or restricted cash equivalents and are required to present a statement of cash flows. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The Company early adopted ASU 2016-18 in the second quarter of 2017. Refer to Note A for discussion regarding the impact the adoption of ASU 2016-18 had on the Company's financial statements and disclosures.

***Application of New or Revised Accounting Standards*—Not *Yet Adopted***

In May 2014, the FASB issued guidance codified in ASC Topic 606, *Revenue Recognition—Revenue from Contracts with Customers* ("ASC 606"), which amends the guidance in former ASC 605, *Revenue Recognition*, and becomes effective beginning January 1, 2018. The Company does not currently expect this standard to have a material effect on its financial statements upon adoption since the Company is not generating revenue at this time.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments Overall – Recognition and Measurement of Financial Assets and Liabilities (Topic* 825-10*)* ("ASU 2016-01"), which provides several updates related to Topic 825-10. This update applies to all entities that hold financial assets or owe financial liabilities. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company does not currently expect ASU 2016-01 to have a material effect on its financial statements and disclosures upon adoption.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic* 842*)* ("ASU 2016-02"), which requires lessees to recognize assets and liabilities for operating leases with lease terms greater than twelve months in the balance sheet. The update also requires improved disclosures to help users of financial statements better understand the amount, timing and uncertainty of cash flows arising from leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years, with early adoption permitted. The Company is currently evaluating the impact of the adoption of ASU 2016-02 on its financial statements and disclosures.

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows – Classification of Certain Cash Receipts and Cash Payments (Topic* 230*)* ("ASU 2016-15"), which addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice. This update applies to all entities that are required to present a statement of cash flows under Topic 230. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company does not currently expect ASU 2016-15 to have a material effect on its financial statements and disclosures upon adoption.

In May 2017, the FASB issued ASU 2017-09, *Compensation – Stock Compensation (Topic* 718*) – Scope of Modification Accounting* ("ASU 2017-09"), which provides guidance about which changes to the terms or conditions of a stock-based payment award require an entity to apply modification accounting in Topic 718. This update applies to any entity that changes the terms or conditions of a stock-based payment award. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company does not currently expect ASU 2017-09 to have a material effect on its financial statements and disclosures upon adoption.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic* 260*), Distinguishing Liabilities from Equity (Topic* 480*), Derivatives and Hedging (Topic* 815*) – I. Accounting for Certain Financial Instruments with Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"), which addresses the complexity of accounting for certain financial instruments with down round features and addresses the difficulty of navigating Topic 480 because of the existence of extensive pending content in the ASC as a result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. This update applies to all entities that issue financial instruments that include down round features and entities that present earnings per share in accordance with Topic 260. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. If early adopted in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. The Company is currently evaluating the impact of the adoption of ASU 2017-11 on its financial statements and disclosures.

**C. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consist of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2017 | 2016 |
| Prepaid insurance | $ 202 | $ 333 |
| Other receivables | 76 | 58 |
| Other prepaid expenses and current assets | 1,384 | 98 |
| Total prepaid expenses and other current assets | $ 1,662 | $ 489 |

**D. Property and Equipment**

Property and equipment consists of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2017 | 2016 |
| Laboratory equipment | $ 983 | $ 842 |
| Furniture and office equipment | 655 | 733 |
| Computers and hardware | 292 | 231 |
| Leasehold improvements | 1,003 | 769 |
| Total property and equipment | 2,933 | 2,575 |
| Less: accumulated depreciation and amortization | (929) | (605) |
| Property and equipment, net | $ 2,004 | $ 1,970 |

The Company leases various equipment and leasehold improvements under capital lease agreements. The assets under capital leases are included in property and equipment as follows (in thousands):

| | December 31, | |
|---|---|---|
| | 2017 | 2016 |
| Laboratory equipment | $ 366 | $ 271 |
| Furniture and office equipment | 541 | 537 |
| Leasehold improvements | 59 | 59 |
| Total property and equipment financed under a capital lease agreement | 966 | 867 |
| Less: accumulated depreciation and amortization | (150) | (31) |
| Property and equipment financed under a capital lease agreement, net | $ 816 | $ 836 |

The estimated useful lives of property and equipment are as follows:

| Asset Category | Useful Life (in years) |
|---|---|
| Laboratory equipment | 10 |
| Furniture and office equipment | 5 - 10 |
| Computers and hardware | 3 - 7 |
| Leasehold improvements | 9 |

Depreciation and amortization expense, including amounts pertaining to assets held under capital leases, was approximately $336,000, $175,000 and $84,000 for the years ended December 31, 2017, 2016 and 2015, respectively.

**E. Accounts Payable and Accrued Expenses**

Accounts payable and accrued expenses consist of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2017 | 2016 |
| Accrued interest | $ 2,222 | $ 2,222 |
| Accrued banking fees | 700 | 700 |
| Accrued severance | — | 646 |
| Accrued payroll | 1,118 | 1,024 |
| Accounts payable | 2,177 | 469 |
| Other accrued expenses | 1,658 | 1,383 |
| Total accounts payable and accrued expenses | $ 7,875 | $ 6,444 |

**F. Debt Obligations**

***Deerfield Facility Agreement***

On June 2, 2014, the Company entered into a $60 million facility agreement (the "Deerfield Facility Agreement") with Deerfield Private Design Fund III, LP ("Deerfield"). The first payment to the Company under the terms of the Deerfield Facility Agreement consisted of a term loan of $15 million (the "Term Notes") and a senior secured loan of $10 million (the "Deerfield Convertible Notes"). As of June 30, 2016, Deerfield is no longer obligated to provide the Company any additional disbursements under the Deerfield Facility Agreement. All loans issued under the Deerfield Facility Agreement bear interest at 9.75% per annum. Deerfield may convert any portion of the outstanding principal and any accrued but unpaid interest on the Deerfield Convertible Notes into shares of the Company's common stock at an initial conversion price of $5.85 per share (the "Deerfield Note Put Option").

The Company also issued to Deerfield a warrant to purchase 14,423,076 shares of Series D redeemable convertible preferred stock ("Series D Preferred") at an exercise price of $0.78 per share, which is exercisable until June 2, 2024 (the "Deerfield Warrant"). Upon completion of the IPO, the Deerfield Warrant automatically converted into a warrant to purchase 1,923,077 shares of the Company's common stock at an exercise price of $5.85 per share. This warrant qualifies as a participating security under ASC Topic 260, *Earnings per Share,* and is treated as such in the net loss per share calculation (Note I). If a Major Transaction occurs, as defined below, Deerfield may require the Company to redeem the Deerfield Warrant for a cash amount equal to the Black-Scholes value of the portion of the Deerfield Warrant to be redeemed (the "Warrant Put Option"). A Major Transaction is (i) a consolidation, merger, exchange of shares, recapitalization, reorganization, business combination or other similar event; (ii) the sale or transfer in one transaction or a series of related transactions of all or substantially all of the assets of the Company; (iii) a third-party purchase, tender or exchange offer made to the holders of outstanding shares, such that following such purchase, tender or exchange offer a change of control has occurred; (iv) the liquidation, bankruptcy, insolvency, dissolution or winding-up affecting the Company; (v) the shares of the Company's common stock cease to be listed on any eligible market; and (vi) at any time, the shares of the Company's common stock cease to be registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

In addition, the Company issued to Deerfield 1,923,077 shares of Series D Preferred as consideration for the loans provided to the Company under the Deerfield Facility Agreement. Upon completion of the IPO, these shares automatically reclassified into 256,410 shares of the Company's common stock. The Company recorded the fair value of the shares of Series D Preferred of $1.5 million, to debt issuance costs on the date of issuance. The Company recorded the fair value of the Deerfield Warrant and the embedded Warrant Put Option to debt discount on the date of issuance. The debt issuance costs and debt discount are amortized over the term of the related debt and the expense is recorded as interest expense related to amortization of debt issuance costs and discount in the statements of operations.

Pursuant to the Deerfield Facility Agreement, the Company may not enter into specified transactions, including a debt financing in the aggregate value of $750,000 or more, a merger, an asset sale or any other change of control transaction or any joint venture, partnership or other profit sharing arrangement, without the prior approval of Deerfield. Additionally, if the Company were to enter into a major transaction, including a merger, consolidation, sale of substantially all of its assets or other change of control transaction, Deerfield would have the ability to demand that prior to consummation of such transaction the Company repay all outstanding principal and accrued interest of any notes issued under the Deerfield Facility Agreement. Under each warrant issued pursuant to the Deerfield Facility Agreement, Deerfield has the right to demand that the Company redeem the warrant for a cash amount equal to the Black-Scholes value of a portion of the warrant upon the occurrence of specified events, including a merger, an asset sale or any other change of control transaction.

The Company must repay one-third of the outstanding principal amount of all debt issued under the Deerfield Facility Agreement on the fourth and fifth anniversaries of the Deerfield Facility Agreement. The Company is then also obligated to repay the balance of the outstanding principal amount on February 14, 2020. The Company prepaid all outstanding interest and principal on the Term Notes in February 2016.

Interest accrued on outstanding debt under the Deerfield Facility Agreement is due quarterly in arrears. Upon notice to Deerfield, the Company had the option to have one or more of the first eight of such scheduled interest payments added to the outstanding principal amount of the debt issued under the Deerfield Facility Agreement, provided that all such interest was due on July 1, 2016. The Company elected this option on all eight of the scheduled interest payments through June 30, 2016. The accrued interest added to outstanding principal, was paid to Deerfield on July 1, 2016.

***Second Amendment to Senior Secured Convertible Note and Warrant***

On January 6, 2016, the Company entered into a Second Amendment (the "Second Amendment") to the Deerfield Convertible Notes and Deerfield Warrant, by and between the Company and Deerfield. The Second Amendment, among other things, clarified the calculation of an anti-dilution adjustment of the conversion price and exercise price of the Deerfield Convertible Notes and Deerfield Warrant, respectively, in the event that the Company effects a firm commitment underwritten public offering of its securities. Except as modified by the Second Amendment, the Third Amendment (as described below) and the Fourth Amendment (as described below), all terms and conditions of the Deerfield Convertible Notes and Deerfield Warrant remain in full force and effect.

***Issuance of 5.50% Senior Convertible Notes and Third Amendment to Senior Secured Convertible Note and Warrant***

On February 9, 2016, the Company issued $86.3 million aggregate principal amount of its 5.50% Senior Convertible Notes due 2021 (the "2021 Notes") to Cowen and RBC Capital Markets, LLC., as representatives of the several initial purchasers (the "Initial Purchasers"), who subsequently resold the 2021 Notes to qualified institutional buyers (the "Note Offering") in reliance on the exemption from registration provided by Rule 144A under the Securities Act.

The net proceeds from the Note Offering were approximately $82.8 million, after deducting the Initial Purchasers' discount and estimated offering expenses. Concurrent with the Note Offering, the Company used approximately $18.6 million of the net proceeds from the Note Offering to repay in full the Term Notes, plus all accrued but unpaid interest, a make-whole interest payment and a prepayment premium on the Term Notes. This principal, accrued but unpaid interest, make-whole interest payment and prepayment premium on the Term Notes is reflected as a cash outflow from financing activity in the statements of cash flows.

The 2021 Notes were issued pursuant to an Indenture, dated as of February 9, 2016 (the "Indenture"), between the Company and U.S. Bank National Association, as trustee. Interest on the 2021 Notes is payable semi-annually in cash in arrears on February 1 and August 1 of each year, beginning on August 1, 2016, at a rate of 5.50% per year. The 2021 Notes mature on February 1, 2021 unless earlier converted or repurchased. The 2021 Notes are not redeemable prior to the maturity date, and no sinking fund is provided for the 2021 Notes.

The 2021 Notes are convertible at an initial conversion rate of 58.4454 shares of the Company's common stock per $1,000 principal amount of the 2021 Notes, subject to adjustment under the Indenture, which is equal to an initial conversion price of approximately $17.11 per share of common stock. Upon conversion, the 2021 Notes will be settled in shares of the Company's common stock, together with a cash payment in lieu of delivering any fractional share. The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, the Company will increase the conversion rate for a holder who elects to convert its 2021 Notes in connection with such a corporate event in certain circumstances.

If the Company undergoes a "fundamental change" (as defined in the Indenture), holders may require that the Company repurchase for cash all or any portion of their 2021 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2021 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, holders who convert their 2021 Notes on or after the date that is one year after the last date of original issuance of the 2021 Notes may also be entitled to receive, under certain circumstances, an interest make-whole payment payable in shares of the Company's common stock. The Company is bifurcating the fundamental change and make-whole interest payment provisions as embedded derivatives and marking them to fair value each reporting period (Note L).

The Indenture includes customary terms and covenants, including certain events of default after which the 2021 Notes may be due and payable immediately.

In connection with the Note Offering, on February 3, 2016, the Company entered into a Third Amendment (the "Third Amendment") to the Deerfield Facility Agreement, Deerfield Convertible Notes and Deerfield Warrant with Deerfield. The Third Amendment, among other things, eliminated the Company's ability to require Deerfield to convert the Deerfield Convertible Notes into Company common stock. In addition, pursuant to the Third Amendment, Deerfield consented to the prepayment of the Term Notes and the issuance of the 2021 Notes. Except as modified by the Third Amendment and the Fourth Amendment (as described below), all terms and conditions of the Deerfield Facility Agreement remain in full force and effect.

***Fourth Amendment to Deerfield Convertible Notes and Deerfield Warrant***

In connection with entering into the ATM Agreement, on October 3, 2016, the Company entered into a Fourth Amendment (the "Fourth Amendment") to the Deerfield Convertible Note and the Deerfield Warrant with Deerfield. The Fourth Amendment, among other things, clarifies the calculation of an anti-dilution adjustment of the conversion price and exercise price of the Deerfield Convertible Note and Deerfield Warrant, respectively, in the event that the Company effects an "at the market offering" as defined in Rule 415 of the Securities Act of its common stock.

***Convertible Notes***

Future minimum principal payments under convertible notes as of December 31, 2017, were as follows (in thousands):

| Year Ending December 31, | Convertible Notes |
|---|---|
| 2018 | $ 3,333 |
| 2019 | 3,333 |
| 2020 | 3,334 |
| 2021 | 86,250 |
| Total minimum principal payments | 96,250 |
| Less: debt issuance costs and discount | (3,519) |
| Convertible notes, net | $ 92,731 |

***Line of Credit***

During the second quarter of 2016, the Company opened a line of credit with a total borrowing capacity of $1.1 million with City National Bank

of Florida (the "Line of Credit Agreement") to support several irrevocable letters of credit issued by the bank on behalf of the Company. As of December 31, 2017 and 2016, the Company had unused letters of credit in the amount of $0.4 million. The line of credit had a maturity date of January 31, 2018. On January 31, 2018, the line of credit was renewed for an additional two year term and will now mature on January 31, 2020. As of December 31, 2017 and 2016, the Company had no outstanding balances under the line of credit. The Line of Credit Agreement is collateralized by a restricted money market account, equal to the total amount of the borrowing capacity under the line of credit, held by the same bank institution. The money market account is reported as restricted cash on the balance sheets. The line of credit contains no financial covenants. Borrowings under the Line of Credit Agreement carry interest at a rate equal to the 1-month London Interbank Offered Rate plus 2.00% per annum. The interest rate under the Line of Credit Agreement was 3.36%, as of December 31, 2017.

**G. Commitments and Contingencies**

***Legal Matters***

From time to time, the Company is involved in various legal proceedings arising in the normal course of business. For some matters, a liability is not probable, or the amount cannot be reasonably estimated and, therefore, an accrual has not been made. However, for such matters when it is probable that the Company has incurred a liability and can reasonably estimate the amount, the Company accrues and discloses such estimates. As of December 31, 2017 and 2016, no accruals have been made related to commitments and contingencies.

In 2014, a former financial advisor of the Company filed a request with the Iowa District Court to declare valid a purported right of first refusal to serve as the Company's exclusive financial advisor for specified strategic transactions and to receive fees for the specified strategic transactions irrespective of whether any such specified transaction occurred during or after the term of the financial advisor's service agreement. This filing by the former financial advisor was made in response to an action initiated by the Company in 2013 seeking a declaratory judgement finding that such purported right was invalid and unenforceable. Two former members of the Company's board of directors (the "Board") joined the lawsuit as intervenors based on the former financial advisor's purported assignment of its rights, or a portion thereof, under the agreement to the intervenors. In September 2015, the court granted summary judgement in favor of the Company with respect to the Company's declaratory judgement action and the former financial advisor's counterclaims and the Company separately entered into settlement agreements with each of the intervenors. The settlements reached with the intervenors did not differ from the accrual previously recorded by the Company by a material amount. The former financial advisor subsequently filed a notice of appeal of the court's ruling with the Supreme Court of Iowa. On January 6, 2016, the Company entered into a Settlement Agreement and Mutual Release (the "Settlement Agreement") with the former financial advisor and Donald DeWaay, Jr. pursuant to which, among other things, the former financial advisor agreed, in exchange for the consideration described therein, to dismiss with prejudice its pending appeal. The former financial advisor's appeal was subsequently dismissed by the Supreme Court of Iowa on January 7, 2016. The settlement amount was commensurate with the contingency recorded in the books and records of the Company. The consideration in the Settlement Agreement did not differ from the accrual previously recorded by the Company by a material amount.

In December 2016, a class action suit was filed against the Company in the Iowa District Court in Johnson County by a stockholder alleging that the Company, certain of its senior executives and directors who signed the registration statement in connection with its IPO, and each of the investment banks that acted as underwriters for the offering negligently issued untrue statements of material facts and omitted to state material facts required to be stated in the registration statement and incorporated offering materials that the Company filed with the SEC in support of the offering. The plaintiff does not quantify any alleged damages in his complaint but, in addition to attorneys' fees and costs, the plaintiff seeks to recover damages and obtain other relief on behalf of himself and all other persons who purchased the Company's common stock pursuant or traceable to the offering and the registration statement and who were allegedly damaged thereby.

In January 2017, the class action suit was removed to the U.S. District Court for the Southern District of Iowa. The plaintiff subsequently filed a motion to remand the case to the Iowa District Court, and that motion was granted. In January 2018, the Iowa District Court issued an order postponing all deadlines and the setting of any schedule in the case pending a decision by the United States Supreme Court in *Cyan, Inc. v. Beaver County Employees Retirement Fund.* On March 20, 2018, the Supreme Court issued its decision in *Cyan* and held that state courts have subject matter jurisdiction over putative class actions like the one filed against us, which assert claims arising under the Securities Act. Accordingly, the case will proceed in Iowa District Court. The suit against the Company is still in a preliminary stage and has not yet been set for trial. Accordingly, the Company is unable to predict the timing or outcome of this litigation as of the date of this report.

***Lease Agreements***

***Iowa***

The Company leases office and laboratory facilities in Iowa under a non-cancelable operating lease. The Company's lease for its Iowa facilities expires in September 2018 and includes a renewal option that could extend the lease for successive one-year terms upon expiration.

***Florida***

The Company leases office space in Florida, comprised of two contiguous office suites, under non-cancelable operating leases, which expire in August 2025 and February 2026, as to each space respectively, and include the right to extend the term of the leases for two successive five-year terms upon expiration.

***Virginia***

The Company leases office and laboratory facilities in Virginia under a non-cancelable operating lease. The Company's lease for its Virginia facilities expires in August 2018.

***North Carolina***

The Company leases office space in North Carolina under a non-cancelable operating lease. The expiration date of the Company's lease is May 2020, and includes renewal options that could extend the lease for an additional three years. During the second quarter of 2017, the Company subleased its office space in North Carolina under a non-cancelable operating lease to a third-party tenant. The sublease term with the third-party runs concurrent with the lease term the Company has with the landlord.

***Capital Lease***

The Company leases various laboratory equipment, furniture and office equipment and leasehold improvements that are accounted for as capital leases and that require ongoing payments, including interest expense. The capital leases are financed through various financial institutions and are collateralized by the underlying assets. As of December 31, 2017 and 2016, the interest rates for assets under remaining capital leases range from 7.19% to 8.05%.

Rent expense for non-cancelable operating and capital leases was $0.6 million, $0.6 million and $0.3 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Future minimum lease payments under capital leases and non-cancelable operating leases as of December 31, 2017, were as follows (in thousands):

| Year Ending December 31, | Capital Leases | Operating Leases |
|---|---|---|
| 2018 | $ 242 | $ 688 |
| 2019 | 231 | 604 |
| 2020 | 231 | 499 |
| 2021 | 151 | 449 |
| 2022 | 11 | 461 |
| Thereafter | — | 1,376 |
| Total minimum lease payments | 866 | $ 4,077 |
| Less: amounts representing interest | (115) | |
| Total minimum capital lease principal payments | $ 751 | |

## H. Supply Arrangement

As of December 31, 2017 and 2016, the Company has one manufacturing arrangement that involves potential future expenditures related to research and development.

In November 2009, the Company entered into a supply agreement (the "Supply Agreement") with Johnson Matthey Inc. ("JMI") whereby JMI has agreed to supply the Company with all of the KP201 necessary for clinical trials and commercial sale for a price equal to JMI's manufacturing cost and to provide process optimization and development services for KP201. The Company's FDA-approved drug, APADAZ, and product candidate, KP201/IR, contain KP201. No expense was recorded under this agreement for the years ended December 31, 2017, 2016 and 2015. The Company must purchase all of its U.S. KP201 needs from JMI and JMI cannot supply KP201 to other companies. The term of the Supply Agreement extends as long as the Company holds a valid and enforceable patent for KP201 or until the tenth anniversary of a commercial launch of a FDA-approved drug incorporating KP201, whichever date is later. Upon the expiration of such term, the agreement will automatically renew for a period of two years unless either party provides 12 months prior notice of its intent not to renew. Under the agreement, JMI will receive a tiered-based royalty share on the net sales on the commercial sale of a FDA-approved drug incorporating KP201. No reliable estimate of the future payments can be made at this time.

## I. Preferred Stock and Warrants

***Authorized, Issued, and Outstanding Preferred Stock***

In April 2015, the Company amended and restated its Certificate of Incorporation to decrease the number of its authorized shares of preferred stock to 10,000,000 shares with a par value of $0.0001 per share. As described in Note A, in April 2015, the Company completed an IPO of its common stock. Upon completion of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock were automatically converted or reclassified into an aggregate of 5,980,564 shares of the Company's common stock. As of December 31, 2017, the Company had 10,000,000 shares of authorized and undesignated preferred stock and did not have any preferred stock outstanding.

***Preferred Stock Activity***

The following table summarizes redeemable convertible preferred stock activity for the years ended December 31, 2017, 2016 and 2015:

| | Shares of | | | | | |
|---|---|---|---|---|---|---|
| | Series A Preferred | Series B Preferred | Series C Preferred | Series D Preferred | Series D-1 Preferred | Total |
| Balance as of January 1, 2015 | 9,704,215 | 6,220,000 | 18,557,408 | 7,255,425 | — | 41,737,048 |
| Issuance of Series D-1 preferred stock | — | — | — | — | 3,200,000 | 3,200,000 |
| Exercise of Series D preferred warrants | — | — | — | 3,205 | — | 3,205 |
| Effect of reverse stock split | (8,410,377) | (5,390,766) | (16,083,286) | (6,290,844) | (2,784,416) | (38,959,689) |
| Less: Conversion of preferred stock into common stock upon IPO | (1,293,838) | (829,234) | (2,474,122) | (967,786) | (415,584) | (5,980,564) |
| Balance as of December 31, 2015 | — | — | — | — | — | — |
| Balance as of December 31, 2016 | — | — | — | — | — | — |
| Balance as of December 31, 2017 | — | — | — | — | — | — |

***Series D-1 Redeemable Convertible Preferred Stock***

In February 2015, the Company entered into a stock purchase agreement with Cowen KP Investment LLC in which Cowen KP Investment LLC agreed to purchase and the Company agreed to sell 3,200,000 shares of the Company's Series D-1 redeemable convertible preferred stock for $1.25 per share, or an aggregate of $4.0 million. Upon completion of the IPO, these shares automatically converted into 415,584 shares of the Company's common stock.

***Warrants***

As described in Note A, in April 2015, the Company completed an IPO of its common stock. Upon completion of the IPO, warrants to purchase 15,499,324 shares of Series D preferred stock were reclassified into warrants to purchase 2,066,543 shares of the Company's common stock.

During 2013, the Company issued $3.8 million of convertible notes and the warrants (the "2013 Warrants") to purchase 1,079,453 shares of equity securities in a future financing meeting specified requirements (a "Qualified Financing"). The 2013 Warrants allow the holders to purchase shares of the same class and series of equity securities issued in the Qualified Financing for an exercise price equal to the per share price paid by the purchasers of such equity securities in the Qualified Financing. When the Company entered into the Deerfield Facility Agreement, the 2013 Warrants became warrants to purchase 1,079,453 shares of Series D preferred stock. Upon completion of the IPO, the 2013 Warrants automatically converted into warrants to purchase 143,466 shares of the Company's common stock at an exercise price of $5.85 per share. The 2013 Warrants, if unexercised, expire on the earlier of June 2, 2019, or upon a liquidation event.

On June 2, 2014, pursuant to the terms of the Deerfield Facility Agreement, the Company issued the Deerfield Warrant to purchase 14,423,076 shares of Series D preferred stock (Note F). The Company recorded the fair value of the Deerfield Warrant as a debt discount and a warrant liability. The Deerfield Warrant, if unexercised, expires on the earlier of June 2, 2024, or upon a liquidation event. Upon completion of the IPO, the Deerfield Warrant automatically converted into a warrant to purchase 1,923,077 shares of the Company's common stock at an exercise price of $5.85 per share. The Company is amortizing the debt discount over the term of the Deerfield Convertible Notes and the expense is recorded as interest expense related to amortization of debt issuance costs and discount in the statements of operations

The Company determined that the 2013 Warrants and Deerfield Warrant should be recorded as a liability and stated at fair value at each reporting period upon inception. As stated above, upon completion of the IPO, the 2013 Warrants and the Deerfield Warrant automatically converted into warrants to purchase the Company's common stock. The Company marked the 2013 Warrants to fair value and reclassified them to equity upon closing of the IPO. The Deerfield Warrant remains classified as a liability and is recorded at fair value at each reporting period since it can be settled in cash. Changes to the fair value of the warrant liability are recorded through the statements of operations as a fair value adjustment (Note L).

**J. Common Stock and Warrants**

***Authorized, Issued, and Outstanding Common Shares***

In April 2015, the Company amended and restated its Certificate of Incorporation to increase the number of its authorized shares of common stock to 250,000,000 shares. Of the authorized shares, 14,657,430 and 14,646,982 shares of common stock were issued and outstanding as of December 31, 2017 and 2016, respectively.

As of December 31, 2017 and 2016, the Company had reserved authorized shares of common stock for future issuance as follows:

| | December 31, | |
|---|---|---|
| | **2017** | **2016** |
| Conversion of Deerfield Convertible Notes | 1,751,410 | 1,751,296 |
| Conversion of 2021 Notes | 5,040,914 | 5,040,914 |
| Outstanding awards under equity incentive plans | 2,853,924 | 1,990,260 |
| Outstanding common stock warrants | 2,027,763 | 2,087,477 |
| Possible future issuances under equity incentive plans | 944,700 | 1,244,671 |
| Total common shares reserved for future issuance | 12,618,711 | 12,114,618 |

***Common Stock Activity***

The following table summarizes common stock activity for the years ended December 31, 2017, 2016 and 2015:

| | **Shares of Common Stock** |
|---|---|
| Balance as of January 1, 2015 | 2,381,041 |
| Issuance of common stock in connection with the IPO | 5,854,545 |
| Conversion of preferred stock to common stock in connection with the IPO | 5,980,564 |
| Common stock warrants exercised | 270,038 |
| Common stock options exercised | 4,766 |
| Balance as of December 31, 2015 | 14,490,954 |
| Common stock warrants exercised | 141,095 |
| Common stock options exercised | 14,933 |
| Balance as of December 31, 2016 | 14,646,982 |
| Common stock warrants exercised | 698 |
| Common stock options exercised | 9,750 |
| Balance as of December 31, 2017 | 14,657,430 |

The Company calculates the fair value of common stock warrants using a Monte Carlo simulation. There were warrants exercised for an aggregate of 698, 141,095 and 270,038 shares of common stock during the years ended December 31, 2017, 2016 and 2015, respectively. From 2008 through 2012, the Company issued warrants to purchase 595,920 shares of common stock in its private placement offerings of Series A redeemable convertible preferred stock, Series B redeemable convertible preferred stock and Series C redeemable convertible preferred stock (the "Underwriter Warrants") and for leasing laboratory space. The Company accounted for the Underwriter Warrants as a derivative liability, which is adjusted to fair value at each reporting period, with the change in fair value recorded as fair value adjustment in the statements of operations. The last of the Underwriter Warrants expired on the second anniversary of the Company's IPO in the second quarter of 2017.

As of March 28, 2018, the Company has sold 446,111 shares of common stock under the ATM Agreement, resulting in gross proceeds of $2.9 million.

**K. Stock-Based Compensation**

The Company maintains a stock-based compensation plan (the "Incentive Stock Plan") that governs stock awards made to employees and directors prior to completion of the IPO.

In November 2014, the Board of Directors of the Company ("the Board"), and in April 2015, the Company's stockholders, approved the Company's 2014 Equity Incentive Plan (the "2014 Plan"), which became effective in April 2015. The 2014 Plan provides for the grant of stock options, other forms of equity compensation, and performance cash awards. The maximum number of shares of common stock that may be issued under the 2014 Plan is 3,432,183 as of December 31, 2017. The number of shares of common stock reserved for issuance under the 2014 Plan will automatically increase on January 1 of each year, beginning on January 1, 2016, and ending on and including January 1, 2024, by 4% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the Board. Pursuant to the terms of the 2014 Plan, on January 1, 2018, the common stock reserved for issuance under the 2014 Plan automatically increased by 586,297 shares.

During the years ended December 31, 2017, 2016 and 2015, stock options to acquire 9,750, 14,933 and 4,766 shares of common stock were exercised for approximately $7,000, $71,000 and $28,000 with an intrinsic value of approximately $32,000, $169,000 and $54,000, respectively.

Stock-based compensation expense recorded under the Incentive Stock Plan and the 2014 Plan is included in the following line items in the accompanying statements of operations (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Research and development | $ 1,304 | $ 1,051 | $ 610 |
| General and administrative | 3,258 | 3,639 | 1,759 |
| Severance expense | — | 1,910 | — |
| Total stock-based compensation expense | $ 4,562 | $ 6,600 | $ 2,369 |

***Stock Option Awards***

The Company estimates the fair value of stock options using the Black-Scholes option-pricing model, which requires the use of subjective assumptions, including the expected term of the option, the expected stock price volatility, expected dividend yield and the risk-free interest rate for the expected term of the option. The expected term represents the period of time the stock options are expected to be outstanding. Due to the lack of sufficient historical exercise data to provide a reasonable basis upon which to otherwise estimate the expected term of the stock options, the Company uses the simplified method to estimate the expected term for its "plain vanilla" stock options. Under the simplified method, the expected term of an option is presumed to be the mid-point between the vesting date and the end of the contractual term. Some options, for example those that have exercise prices in excess of the fair value of the underlying stock, are not considered "plain vanilla" stock options. For these options, the Company uses an expected term equal to the contractual term of the option. Expected volatility is based on a blend of historical volatilities for publicly traded stock of comparable companies and the Company over the estimated expected term of the stock options. The Company assumes no dividend yield because dividends are not expected to be paid in the near future, which is consistent with the Company's history of not paying dividends.

The Company recognizes compensation expense related to stock-based payment transactions upon satisfaction of the requisite service or vesting requirements. Forfeitures are estimated at the time of grant and revised based on actual forfeitures, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Using the Black-Scholes option-pricing model, the weighted-average fair value of awards granted during the years ended December 31, 2017, 2016 and 2015, fair value was $2.77, $9.25 and $10.63 per share, respectively. The assumptions used to estimate fair value are as follows:

| | December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Risk-free interest rate | 1.88% - 2.26% | 1.29% - 1.50% | 1.40% - 1.99% |
| Expected term (in years) | 5.12 - 7.00 | 5.50 - 6.26 | 4.33 - 6.25 |
| Expected volatility | 85.35% - 95.08% | 77.38% - 94.78% | 68.79% - 86.84% |
| Expected dividend yield | 0% | 0% | 0% |

The activity under the Incentive Stock Plan and the 2014 Plan for the year ended December 31, 2017, is summarized as follows:

| | Number of Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding balance as of January 1, 2017 | 1,990,260 | $ 13.64 | 8.27 | $ 26,400 |
| Granted | 919,000 | $ 3.59 | | |
| Exercised | (9,750) | $ 0.75 | | |
| Canceled or forfeited | (38,920) | $ 11.35 | | |
| Expired | (6,666) | $ 4.65 | | |
| Outstanding balance as of December 31, 2017 | 2,853,924 | $ 10.50 | 7.90 | $ 471,539 |
| Exercisable as of December 31, 2017 | 1,044,392 | $ 12.38 | 6.78 | $ 29,237 |
| Vested and expected to vest as of December 31, 2017 | 2,760,447 | $ 10.62 | 7.87 | $ 440,178 |

Information regarding currently outstanding and exercisable options as of December 31, 2017, is as follows:

| | Options Outstanding | | Options Exercisable | |
|---|---|---|---|---|
| Exercise Price | Number of Shares | Weighted Average Remaining Contractual Term (in years) | Number of Shares | Weighted Average Remaining Contractual Term (in years) |
| $2.75 to $5.00 | 1,055,244 | 8.69 | 76,244 | 3.75 |
| $5.01 to $10.00 | 366,447 | 5.77 | 345,146 | 5.72 |
| $10.01 to $15.00 | 471,833 | 7.94 | 189,291 | 7.73 |
| $15.01 to $20.00 | 612,600 | 7.89 | 259,811 | 7.76 |
| $20.01 to $22.12 | 347,800 | 7.68 | 173,900 | 7.68 |
| | 2,853,924 | 7.90 | 1,044,392 | 6.78 |

The total fair value of stock options vested during the years ended December 31, 2017, 2016 and 2015, was $4.1 million, $5.4 million and $1.1 million, respectively.

Unvested stock options as of December 31, 2017 and 2016, were as follows:

| | Number of Unvested Shares December 31, | |
|---|---|---|
| Exercise Price | 2017 | 2016 |
| $2.75 to $5.00 | 979,000 | 99,000 |
| $5.01 to $10.00 | 21,301 | 97,480 |
| $10.01 to $15.00 | 282,542 | 378,500 |
| $15.01 to $20.00 | 352,789 | 516,938 |
| $20.01 to $22.12 | 173,900 | 260,850 |
| Total number of unvested shares | 1,809,532 | 1,352,768 |

As of December 31, 2017, there was $8.5 million of total unrecognized compensation cost related to unvested share-based compensation arrangements granted under the Incentive Stock Plan and 2014 Plan. That compensation cost is expected to be recognized over a weighted-average period of 2.06 years.

There was no stock-based compensation expense related to performance-based awards recognized during the year ended December 31, 2017. During the year ended December 31, 2016, the Company recognized $44,000 of stock-based compensation expense related to performance-based awards included in research and development expenses. These awards were in connection with the strategic initiatives set for the award that were achieved in 2016 exercisable for an aggregate of 13,333 shares of common stock during the year ended December 31, 2016. During the year ended December 31, 2015, the Company recognized $0.7 million of stock-based compensation expense related to performance-based awards included in general and administrative expenses and $0.2 million of stock-based compensation expense related to performance-based awards included in research and development expenses. These awards were in connection with the grant of fully vested stock options exercisable for an aggregate of 163,998 shares of common stock during the year ended December 31, 2015.

**L. Fair Value of Financial Instruments**

The carrying amounts of certain financial instruments, including cash and cash equivalents, restricted cash and accounts payable, approximate their respective fair values due to the short-term nature of such instruments.

The fair value of the Deerfield Convertible Notes was $11.0 million and $10.2 million, respectively, as of December 31, 2017 and 2016. The fair value of the 2021 Notes was $51.9 million and $46.3 million, respectively, as of December 31, 2017 and 2016. Both the Deerfield Convertible Notes and 2021 Notes fall within Level 3 of the fair value hierarchy as their value is based on the credit worthiness of the Company, which is an unobservable input. The Company used a Tsiveriotis-Fernandes model to value the Deerfield Convertible Notes and 2021 Notes as of December 31, 2017 and 2016.

***Assets and Liabilities Measured at Fair Value on a Recurring Basis***

The Company evaluates its financial assets and liabilities subject to fair value measurements on a recurring basis to determine the appropriate level in which to classify them for each reporting period. This determination requires significant judgments to be made. The following table summarizes the conclusions reached regarding fair value measurements as of December 31, 2017 and 2016 (in thousands):

| | Balance as of December 31, 2017 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
|---|---|---|---|---|
| Deerfield Warrant liability | $ 5,115 | $ — | $ — | $ 5,115 |
| Embedded Warrant Put Option | 365 | — | — | 365 |
| Fundamental change and make-whole interest provisions embedded in 2021 Notes | 14 | — | — | 14 |
| Embedded Deerfield Note Put Option | 2,215 | — | — | 2.215 |
| Total liabilities | $ 7,709 | $ — | $ — | $ 7,709 |
| Trading securities: | | | | |
| Certificates of deposit | 5,616 | 5,616 | — | — |
| U.S. Treasury securities | 25,988 | 25,988 | — | — |
| U.S. government-sponsored agency securities | 3,004 | — | 3,004 | — |
| Total assets | $ 34,608 | $ 31,604 | $ 3,004 | $ — |

| | Balance as of December 31, 2016 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
|---|---|---|---|---|
| Underwriter Warrant liability | $ 16 | $ — | $ — | $ 16 |
| Deerfield Warrant liability | 4,231 | — | — | 4,231 |
| Embedded Warrant Put Option | 365 | — | — | 365 |
| Fundamental change and make-whole interest provisions embedded in 2021 Notes | 6 | | | 6 |
| Total liabilities | $ 4,618 | $ — | $ — | $ 4,618 |
| Trading securities: | | | | |
| Certificates of deposit | 7,788 | 7,788 | — | — |
| U.S. Treasury securities | 37,066 | 37,066 | — | — |
| U.S. government-sponsored agency securities | 14,349 | — | 14,349 | — |
| Total assets | $ 59,203 | $ 44,854 | $ 14,349 | $ — |

The Company's Underwriter Warrant liability, Deerfield Warrant liability, embedded Warrant Put Option, the fundamental change and the make-whole interest provisions embedded in the 2021 Notes and the embedded Deerfield Note Put Option, as well as the trading securities are measured at fair value on a recurring basis. As of December 31, 2017 and 2016, the Underwriter Warrant liability, Deerfield Warrant liability, embedded Warrant Put Option and the fundamental change and make-whole interest provisions embedded in the 2021 Notes are reported on the balance sheets in derivative and warrant liability, while the trading securities are reported on the balance sheets in marketable securities and long-term investments. As of December 31, 2017, the embedded Deerfield Note Put Option is reported on the balance sheet in derivative and warrant liability. The Company used a Monte Carlo simulation to value the Underwriter Warrant liability, Deerfield Warrant liability, embedded Warrant Put Option and the fundamental change and make-whole interest provisions embedded in the 2021 Notes as of December 31, 2017 and 2016. The Company also used a Monte Carlo simulation to value the embedded Deerfield Note Put Option as of December 31, 2017. Significant unobservable inputs used in measuring the fair value of these financial instruments included the Company's estimated enterprise value, an estimate of the timing of a liquidity or fundamental change event, a present value discount rate and an estimate of the Company's stock volatility using the volatilities of guideline peer companies. Changes in the fair value of the Underwriter Warrant liability, Deerfield Warrant liability, embedded Warrant Put Option, the fundamental change and make-whole interest provisions embedded in the 2021 Notes and the embedded Deerfield Note Put Option are reflected in the statements of operations as a fair value adjustment.

A reconciliation of the beginning and ending balances for the derivative and warrant liability measured at fair value on a recurring basis using significant unobservable inputs (Level 3) is as follows (in thousands):

| | 2017 | 2016 |
|---|---|---|
| Balance as of beginning of period | $ 4,618 | $ 37,839 |
| Exercise of warrants | — | (756) |
| Adjustment to fair value | 3,091 | (32,465) |
| Balance as of end of period | $ 7,709 | $ 4,618 |

**M. Income Taxes**

The Company's financial statements include a total state tax benefit related to research and development credits of $43,000, $15,000 and $15,000 on a loss before income taxes of $43.4 million, $16.5 million and $54.6 million for the years ended December 31, 2017, 2016 and 2015, respectively. A reconciliation of the difference between the benefit for income taxes and income taxes at the statutory U.S. federal income tax rate is as follows (in thousands):

| | Year ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Federal statutory rate | 34.00% | 34.00% | 34.00% |
| Effect of: | | | |
| Change in valuation allowance | 13.38 | (69.31) | (19.25) |
| Return to provision and deferred true-up | 2.18 | (23.83) | — |
| Change in rate | (49.06) | (14.63) | — |
| State tax benefit (net of federal) | 2.71 | 15.64 | 4.06 |
| Warrant liability | (2.42) | 68.44 | (15.28) |
| State research and development credit | 0.10 | 0.09 | 0.03 |
| Federal research and development credit | 1.50 | 5.65 | 0.84 |
| Amortization | (1.22) | (3.15) | — |
| Conversion feature and put option on convertible notes | — | — | (1.68) |
| Stock-based compensation | (1.03) | (12.71) | (1.28) |
| Other | (0.04) | (0.10) | (1.49) |
| Federal income tax benefit (provision) effective rate | 0.10% | 0.09% | (0.05)% |

The components of deferred tax assets and liabilities are as follows (in thousands):

| | December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Deferred tax assets relating to: | | | |
| Net operating loss carryforwards | $ 37,028 | $ 44,984 | $ 26,617 |
| Research and development tax carryforward | 3,788 | 3,166 | 2,254 |
| Other deferred tax assets | 2,409 | 715 | 232 |
| Total gross deferred tax assets | 43,225 | 48,865 | 29,103 |
| Deferred tax liabilities relating to: | | | |
| Property and equipment | 260 | 89 | 80 |
| Total gross deferred tax liabilities | 260 | 89 | 80 |
| Deferred tax assets less liabilities | 42,965 | 48,776 | 29,023 |
| Valuation allowance | (42,965) | (48,776) | (29,023) |
| Net deferred tax asset (liability) | $ — | $ — | $ — |

H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018" (the "2017 Tax Act") was signed into law on December 22, 2017. The 2017 Tax Act significantly revises the U.S. corporate income tax by, among other things, lowering the statutory corporate tax rate from 35% to 21%, eliminating certain deductions, imposing a mandatory one-time tax on accumulated earnings of foreign subsidiaries, introducing new tax regimes, and changing how foreign earnings are subject to U.S. tax. The 2017 Tax Act also enhanced and extended through 2026 the option to claim accelerated depreciation deductions on qualified property.

Also on December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provides guidance on accounting for the tax effects of the 2017 Tax Act. SAB 118 provides a measurement period that should not extend beyond one year from the 2017 Tax Act enactment date for companies to complete the accounting under ASC 740, Income Taxes. As of December 31, 2017, the Company has not completed its accounting related to the enactment of the 2017 Tax Act. However, the Company has made reasonable estimates of the effects on its income tax provision with respect to certain items, primarily the revaluation of its existing U.S. deferred tax balances as described above.

In assessing the realizability of deferred tax assets, management considers 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. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in making this assessment. Based upon the level of historical taxable income and projections for future taxable income over the periods in which the deferred tax assets are deductible, management believes it is more likely than not that the Company will not realize the benefits of these deductible differences in the future.

The Company had the following federal net operating loss carryforward and research activities credits as of December 31, 2017 (in thousands):

| Year Incurred | Net Operating Loss Carryforwards | Research Activities Credit | Expiration |
|---|---|---|---|
| 2007 | $ 454 | $ 30 | 2027 |
| 2008 | 1,178 | 65 | 2028 |
| 2009 | 3,060 | 176 | 2029 |
| 2010 | 3,423 | 149 | 2030 |
| 2011 | 9,929 | 176 | 2031 |
| 2012 | — | 170 | 2032 |
| 2013 | 4,353 | 133 | 2033 |
| 2014 | 16,265 | 894 | 2034 |
| 2015 | 24,126 | 598 | 2035 |
| 2016 | 40,715 | 745 | 2036 |
| 2017 | 33,828 | 652 | 2037 |
| | $ 137,331 | $ 3,788 | |

The Company also has certain state net operating loss carryforwards totaling $134.6 million that expire between 2027 and 2037. Due to potential ownership changes that may have occurred or would occur in the future, Internal Revenue Code Section 382 may place additional limitations on the Company's ability to utilize the net operating loss carryforward.

ASC 740-10, *Accounting for Uncertainty in Income Taxes*, uses the term "more likely than not" to evaluate whether or not a tax position will be sustained upon examination. The Company has not identified any tax positions that do not meet the more likely than not threshold.

**N. Net Loss Per Share**

Under the two-class method, for periods with net income, basic net income per common share is computed by dividing the net income attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period. Net income attributable to common stockholders is computed by subtracting from net income the portion of current year earnings that participating securities would have been entitled to receive pursuant to their dividend rights had all of the year's earnings been distributed. No such adjustment to earnings is made during periods with a net loss as the holders of the participating securities have no obligation to fund losses. Diluted net earnings per common share is computed under the two-class method by using the weighted average number of shares of common stock outstanding plus, for periods with net income attributable to common stockholders, the potential dilutive effects of stock options and warrants. In addition, the Company analyzes the potential dilutive effect of the outstanding participating securities under the if-converted method when calculating diluted earnings per share in which it is assumed that the outstanding participating securities convert into common stock at the beginning of the period. The Company reports the more dilutive of the approaches (two-class or if-converted) as its diluted net earnings per share during the period.

The following table summarizes the computation of basic and diluted net loss and net loss per share of the Company (in thousands, except share and per share amounts):

| | Year ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Net loss - basic and diluted | $ (43,386) | $ (16,516) | $ (54,664) |
| Weighted average number of shares of common stock - basic and diluted | 14,652,898 | 14,597,053 | 7,368,681 |
| Net loss per share - basic and diluted | $ (2.96) | $ (1.13) | $ (7.42) |

Diluted net loss per share is the same as basic net loss per share for all periods presented because the effects of potentially dilutive items were anti-dilutive given the Company's net loss. The following securities, presented on a common stock equivalent basis, have been excluded from the calculation of weighted average number of shares of common stock outstanding because their effect is anti-dilutive:

| | December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Warrants to purchase common stock | 2,027,763 | 2,087,477 | 2,325,383 |
| Awards under equity incentive plans | 2,853,924 | 1,990,260 | 1,397,511 |
| Deerfield Convertible Notes | 1,751,410 | 1,751,296 | 1,991,219 |
| 2021 Notes | 5,040,914 | 5,040,914 | — |
| Total securities excluded from the calculation of weighted average number of shares of common stock outstanding | 11,674,011 | 10,869,947 | 5,714,113 |

**O. Severance Expense**

On September 15, 2016, the Company announced its intention to defer its commercial operations and realign its financial resources and operational priorities towards its product development pipeline. The activities related to the deferral and realignment were completed during the year ended December 31, 2016. As part of these activities, the Company reduced its workforce by three employees. Personnel and other related charges of approximately $1.1 million and stock compensation expense of approximately $1.9 million related to the acceleration of vesting on certain stock options, related to the workforce reduction, were presented as severance expense in the statements of operations for the year ended December 31, 2016.

As of December 31, 2017, the Company had no accrued severance expense recorded within accounts payable and accrued expenses.

**P. Employee Benefit Plan**

The Company has a 401(k) retirement plan (the "401(k) Plan") that covers substantially all employees. The Company may provide a discretionary match with a maximum amount of 4% of the participant's compensation, which vests immediately. The Company made matching contributions under the 401(k) Plan of $207,000, $213,000 and $113,000 for the years ended December 31, 2017, 2016 and 2015, respectively.

The Company has a discretionary profit sharing plan (the "Profit Sharing Plan") that covers all employees. Employees become eligible participants in the Profit Sharing Plan once they have provided three years of service to the Company. The Company made no contributions to the Profit Sharing Plan in 2017, 2016 or 2015.

**Q. Quarterly Results of Operations (unaudited)**

The following tables set forth unaudited quarterly statements of operations data for each of the quarters indicated. The financial statements for each of these quarters have been prepared on the same basis as the audited financial statements included herein and, in the opinion of management, include all adjustments, consisting only of normal recurring adjustments, necessary for the fair statement of the results of operations for these periods. You should read this information together with our financial statements and related notes included herein. These quarterly operating results are not necessarily indicative of the results for any future period.

| | Three-Months Ended | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Dec 31, 2017 | Sep 30, 2017 | Jun 30, 2017 | Mar 31, 2017 | Dec 31, 2016 | Sep 30, 2016 | Jun 30, 2016 | Mar 31, 2016 |
| Revenue | $ — | $ — | $ — | $ — | $ — | $ — | $ — | $ — |
| Operating expenses: | | | | | | | | |
| Research and development | 5,536 | 6,293 | 4,650 | 4,114 | 7,963 | 4,287 | 4,988 | 3,234 |
| General and administrative | 2,614 | 3,319 | 3,574 | 3,266 | 2,873 | 3,104 | 4,287 | 3,736 |
| Severance expense | — | — | — | — | — | 3,010 | — | — |
| Total operating expenses | 8,150 | 9,612 | 8,224 | 7,380 | 10,836 | 10,401 | 9,275 | 6,970 |
| Loss from operations | (8,150) | (9,612) | (8,224) | (7,380) | (10,836) | (10,401) | (9,275) | (6,970) |
| Other (expense) income: | | | | | | | | |
| Loss on extinguishment of debt | — | — | — | — | — | — | — | (4,740) |
| Interest expense related to amortization of debt issuance costs and discount | (390) | (391) | (390) | (390) | (391) | (390) | (393) | (442) |
| Interest expense on principal | (1,444) | (1,448) | (1,443) | (1,441) | (1,445) | (1,441) | (1,475) | (1,150) |
| Fair value adjustment related to derivative and warrant liability | (710) | 1,312 | 3,523 | (7,216) | 2,723 | (1,299) | 20,763 | 10,278 |
| Interest and other income, net | 97 | 154 | 13 | 101 | 9 | 98 | 144 | 102 |
| Total other (expense) income | (2,447) | (373) | 1,703 | (8,946) | 896 | (3,032) | 19,039 | 4,048 |
| (Loss) income before income taxes | (10,597) | (9,985) | (6,521) | (16,326) | (9,940) | (13,433) | 9,764 | (2,922) |
| Income tax benefit (expense) | 31 | 4 | 4 | 4 | 4 | 19 | 4 | (12) |
| Net (loss) income | $ (10,566) | $ (9,981) | $ (6,517) | $ (16,322) | $ (9,936) | $ (13,414) | $ 9,768 | $ (2,934) |
| | | | | | | | | |
| Net (loss) income per share: | | | | | | | | |
| Basic | $ (0.72) | $ (0.68) | $ (0.44) | $ (1.11) | $ (0.68) | $ (0.92) | $ 0.59 | $ (0.20) |
| Diluted | $ (0.72) | $ (0.68) | $ (0.44) | $ (1.11) | $ (0.68) | $ (0.92) | $ (0.58) | $ (0.20) |

**R. Subsequent Events**

On February 23, 2018, the Company announced that the FDA approved its New Drug Application for APADAZ for the short-term ( no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. APADAZ is an immediate-release combination of the Company's prodrug, benzhydrocodone, and acetaminophen. APADAZ was developed from the Company's proprietary LAT platform technology.

## EXHIBIT INDEX

| Exhibit No. | Description |
|---|---|
| 2.1+ | Asset Purchase Agreement, by and between Shire LLC and Travis C. Mickle, Ph.D. and the Registrant, dated as of March 21, 2012 (incorporated herein by reference to the Registrant's Amendment No. 1 to Registration Statement on Form S-1/A (File No. 333-202660) as filed with the SEC on April 3, 2015). |
| 3.1 | Amended and Restated Certificate of Incorporation of KemPharm, Inc. (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on April 21, 2015). |
| 3.2 | Amended and Restated Bylaws, as currently in effect, of KemPharm, Inc. (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on April 21, 2015). |
| 4.1 | Reference is made to Exhibits 3.1 and 3.2 hereof. |
| 4.2 | Specimen stock certificate evidencing shares of Common Stock (incorporated herein by reference to the Registrant's Amendment No. 2 to Registration Statement on Form S-1/A (File No. 333-202660) as filed with the SEC on April 9, 2015). |
| 4.3 | Indenture, by and between the Registrant and U.S. Bank National Association, dated as of February 9, 2016 (incorporated herein by reference to the Registrant's Current Report on Form 8-K filed with the SEC on February 9, 2016). |
| 4.4 | Form of Note representing the Company's 5.50% Senior Convertible Notes due 2021 (included as Exhibit A to the Indenture filed hereto as Exhibit 4.3) (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on February 9, 2016). |
| 10.1+ | Material Supply Agreement, by and between the Registrant and Johnson Matthey, Inc., dated as of November 2, 2009 (incorporated by reference Registrant's Amendment No. 1 to Registration Statement on Form S-1/A (File No. 333-202660) as filed with the SEC on April 3, 2015). |
| 10.2 | Facility Agreement, by and between the Registrant and Deerfield Private Design Fund III, L.P., dated as of June 2, 2014 (incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.2.1 | First Amendment to Facility Agreement, Senior Secured Convertible Note and Warrant, by and between Registrant and Deerfield Private Design Fund III, L.P., dated March 6, 2015 (incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.2.2 | Second Amendment to Facility Agreement by and between Registrant and Deerfield Private Design Fund III, L.P., dated December 17, 2015 (incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-208633) as filed with the SEC on December 18, 2015). |
| 10.2.3 | Third Amendment to Facility Agreement, Senior Secured Convertible Note and Warrant, by and betwee n Registrant and Deerfield Private Design Fund III, L.P., dated February 3, 2016 (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on February 9, 2016). |
| 10.3 | Senior Secured Convertible Note issued to Deerfield Private Design Fund III, L.P., dated as of June 2, 2014 (incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.3.1 | Second Amendment to Senior Secured Convertible Note and Warrant, by and between Registrant and Deerfield Private Design Fund III, L.P., dated January 6, 2016 (incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on January 11, 2016). |
| 10.3.2 | Fourth Amendment to Senior Secured Convertible Note and Warrant, effective as of October 3, 2016, by and between KemPharm, Inc. and Deerfield Private Design Fund III, L.P. (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on October 3, 2016). |
| 10.4 | Amended and Restated Investors' Rights Agreement, dated as of February 19, 2015, by and among the Registrant and certain of its stockholders (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.5 | Warrant to Purchase Shares of Series D Preferred Stock issued to Deerfield Private Design Fund III, L.P., dated as of June 2, 2014 (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.6 | Form of Stock Purchase Warrant to purchase shares of Series D Convertible Preferred Stock issued in bridge financing, along with a schedule of warrantholders (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.7+ | Agreement to Terminate CLA, by and between MonoSol Rx, LLC and the Registrant, dated as of March 20, 2012 (incorporated herein by reference to the Registrant's Amendment No. 1 to Registration Statement on Form S-1/A (File No. 333-202660) as filed with the SEC on April 3, 2015). |
| 10.8# | Incentive Stock Plan, as amended to date (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.9# | Form of Incentive Stock Option Agreement under Incentive Stock Plan (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.10# | Form of Nonqualified Stock Option Agreement under Incentive Stock Plan (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.11# | Form of 2014 Equity Incentive Plan (incorporated herein by reference to Registrant's Amendment No. 1 to Registration Statement on Form S-1/A (File No. 333-202660) as filed with the SEC on April 3, 2015). |
| 10.12# | Form of Stock Option Grant Notice and Stock Option Agreement under 2014 Equity Incentive Plan (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.13# | Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under 2014 Equity Incentive Plan (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.14# | Non-Employee Director Compensation Policy (incorporated herein by reference to the Registrant's Annual Report on Form 10-K as filed with the SEC on March 15, 2016). |
| 10.15# | Form of Indemnification Agreement with the Registrant's directors and executive officers (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.16# | Amended and Restated Employment Agreement by and between the Registrant and R. LaDuane Clifton, dated as of June 25, 2015 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on August 14, 2015). |

**EXHIBIT INDEX**

| Exhibit No. | Description |
|---|---|
| 10.16.1# | Amendment to Amended and Restated Employment Agreement by and between the Registrant and R. LaDuane Clifton, dated as of October 13, 2015 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on November 13, 2015). |
| 10.17# | Employment Agreement by and between the Registrant and Christal M.M. Mickle, dated as of May 30, 2014 (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.17.1# | Amendment to Employment Agreement by and between the Registrant and Christal M.M. Mickle, dated as of October 13, 2015 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the SEC on November 13, 2015). |
| 10.18# | Amended and Restated Employment Agreement by and between the Registrant and Gordon K. Johnson, dated as of June 25, 2015 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on August 14, 2015). |
| 10.18.1# | Amendment to Amended and Restated Employment Agreement by and between the Registrant and Gordon K. Johnson, dated as of October 13, 2015 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on November 13, 2015). |
| 10.19# | Employment Agreement by and between the Registrant and Travis C. Mickle, Ph.D., dated as of May 30, 2014 (incorporated herein by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-202660) as filed with the SEC on March 11, 2015). |
| 10.19.1# | Amendment to Employment Agreement by and between the Registrant and Travis C. Mickle, Ph.D., dated as of October 13, 2015 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q filed with the SEC on November 13, 2015). |
| 10.20# | Employment Agreement by and between the Registrant and Daniel L. Cohen, dated as of April 13, 2016 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on May 13, 2016). |
| 10.21# | Amended and Restated Employment Agreement by and between the Registrant and Sven Guenther, dated as of April 13, 2016 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on May 13, 2016). |
| 10.22 | Common Stock Sales Agreement, dated October 3, 2016, by and between KemPharm, Inc. and Cowen and Company, LLC (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on October 3, 2016). |
| 10.23 | Lease Agreement, by and between KemPharm, Inc. and BRE/COH FL LLC, dated as of November 3, 2014 (incorporated herein by reference to the Registrant's Annual Report on Form 10-K as filed with the SEC on March 10, 2017). |
| 10.24 | First Amendment to the Lease Agreement, by and between KemPharm, Inc. and BRE/COH FL LLC, dated as of April 21, 2015 (incorporated herein by reference to the Registrant's Annual Report on Form 10-K as filed with the SEC on March 10, 2017). |
| 10.25 | Second Amendment to the Lease Agreement, by and between KemPharm, Inc. and BRE/COH FL LLC, dated as of December 22, 2015 (incorporated herein by reference to the Registrant's Annual Report on Form 10-K as filed with the SEC on March 10, 2017). |
| 10.26 | Third Amendment to the Lease Agreement, by and between KemPharm, Inc. and BRE/COH FL LLC, dated as of July 15, 2016 (incorporated herein by reference to the Registrant's Annual Report on Form 10-K as filed with the SEC on March 10, 2017). |
| 10.27* | Lease Agreement, by and between KemPharm, Inc. and the Board of Regents, State of Iowa for the Use and Benefit of the University of Iowa, dated as of September 5, 2017. |
| 23.1* | Consent of RSM US LLP, Independent Registered Public Accounting Firm. |
| 23.2* | Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm. |
| 24.1* | Power of Attorney (included on signature page). |
| 31.1* | Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended. |
| 31.2* | Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended. |
| 32.1* | Certification of the Principal Executive Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. (1) |
| 32.2* | Certification of the Principal Financial Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. (1) |
| 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. |

| | |
|---|---|
| * | Filed herewith |
| ** | Attached as Exhibit 101 to this Annual Report on Form 10-K for the year ended December 31, 2017, formatted in XBRL (Extensible Business Reporting Language): (i) Balance Sheets, (ii) Statements of Operations, (iii) Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Deficit, (iv) Statements of Cash Flows, and (v) Notes to Financial Statements, tagged as blocks of text and including detailed tags. |
| # | Indicates management contract or compensatory plan. |
| + | Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a grant for confidential treatment and have been separately filed with the Securities and Exchange Commission. |
| (1) | This certification accompanies the Annual Report on Form 10-K to which it relates, is not deemed filed with the SEC and is not to be incorporated by reference into any filing of the Registrant under the Securities Act or the Exchange Act (whether made before or after the date of the Annual Report on Form 10-K), irrespective of any general incorporation language contained in such filing. |

**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.

KemPharm, Inc.

Dated: March 30, 2018

By: /s/ Travis C. Mickle
Travis C. Mickle, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 30, 2018

By: /s/ R. LaDuane Clifton
R. LaDuane Clifton, CPA
Chief Financial Officer, Secretary and Treasurer
(Principal Financial Officer)

**POWER OF ATTORNEY**

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below hereby constitute and appoint Travis C. Mickle and R. LaDuane Clifton, and each of them (with full power to each of them to act alone), as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments to this report, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

| Signature | Title | Date |
|---|---|---|
| /s/ Travis C. Mickle<br>Travis C. Mickle, Ph.D. | President, Chief Executive Officer and Chairman of the Board of Directors<br>(Principal Executive Officer) | March 30, 2018 |
| /s/ R. LaDuane Clifton<br>R. LaDuane Clifton, CPA | Chief Financial Officer, Secretary and Treasurer<br>(Principal Financial Officer) | March 30, 2018 |
| /s/ Timothy J. Sangiovanni<br>Timothy J. Sangiovanni, CPA | Vice President, Corporate Controller<br>(Principal Accounting Officer) | March 30, 2018 |
| /s/ Danny L. Thompson<br>Danny L. Thompson | Director | March 30, 2018 |
| /s/ Matthew R. Plooster<br>Matthew R. Plooster | Director | March 30, 2018 |
| /s/ Richard W. Pascoe<br>Richard W. Pascoe | Director | March 30, 2018 |
| /s/ Joseph B. Saluri<br>Joseph B. Saluri | Director | March 30, 2018 |
| /s/ David S. Tierney<br>David S. Tierney | Director | March 30, 2018 |

**Exhibit 10.14**

**KemPharm, Inc.**
**Amended and Restated Non-Employee Director Compensation Policy**

Each member of the board of director (the "***Board***") of KemPharm, Inc. (the "***Company***") who is not also an employee of the Company or any subsidiary of the Company shall be entitled to the following compensation for service on the Board and its committees:

Cash Compensation

Cash compensation shall be paid in the following annual amounts. Payments shall be made in quarterly installments in arrears on the last day of each calendar quarter in which service occurred, and shall be *prorated* as appropriated for a director who does not serve for the full quarter.

1. Annual Board Service Retainer:

    a. All non-employee directors: $35,000
    b. Chairman of the Board, if not an employee, or lead independent director, if any (in addition to the retainer for all non-employee directors): $15,000

2. Annual Committee Member Service Retainer:

    a. Member of the Audit Committee: $7,500
    b. Member of the Compensation Committee: $5,000
    c. Member of the Nominating and Corporate Governance Committee: $5,000

3. Annual Committee Chair Service Retainer (in addition to Committee Member Service Retainer):

    a. Chairman of the Audit Committee: $15,000
    b. Chairman of the Compensation Committee: $10,000
    c. Chairman of the Nominating and Corporate Governance Committee: $7,500

Equity Compensation

The equity compensation set forth below will be granted under the Company's 2014 Equity Incentive Plan (the "***Plan***"). All stock options granted under this policy will be nonqualified stock options using the Company's standard form of Nonqualified Stock Option Agreement under the Plan, with an exercise price per share equal to the last reported sale price of the Company's common stock on the NASDAQ Capital Market on the date of grant or, if such grant date is not a trading date, on the last trading date prior to the grant date, and with a term of ten years from the date of grant (subject to earlier termination in connection with a termination of service as provided in the Plan).

Annual Grant: On the date of each annual stockholders meeting of the Company, each director who continues to serve as a non-employee member of the Board following such stockholders meeting will be automatically, and without further action by the Board or the Compensation Committee of the Board, be granted a stock option for 15,000 shares of common stock. The stock options will vest and become exercisable in full on the earlier of (1) the first anniversary of the grant date, (2) the day before the first annual stockholders meeting occurring after the grant date or (3) immediately prior to a "Change in Control" as defined in the Plan, subject in each case to the director's continued service on such vesting date.

**Exhibit 10.27**

LEASE DOCUMENT FOR THE UNIVERSITY OF IOWA BIOVENTURES CENTER

THE LEASE MADE AND ENTERED INTO THIS, 5th of September, 2017, by and between Board of Regents, State of Iowa, for the use and benefit of the University of Iowa, hereinafter referred to as LESSOR, and KemPharm, Inc., hereinafter referred to as the LESSEE. LESSOR and LESSEE are jointly referred to as the "parties".

1. PREMISES: The premises that are the subject of this lease are described in Exhibit A to this lease, which is hereby incorporated into this agreement by reference.

2. LEASE PERIOD:

A. The term of this lease shall be a period of one (1) year, commencing October 1, 2017, and ending September 30, 2018. It is mutually agreed that this lease may be terminated by either party upon 30 days' written notice to the other party.

B. Notwithstanding any other provision in this Agreement to the contrary, the parties acknowledge that LESSOR is presently a subtenant in the building where the premises are located. LESSOR is entering into the present agreement consistent with the authority granted in LESSOR's own multi-year lease and purchase option. The parties agree that the present lease will terminate prior to the end of the lease term described in 2(A) above upon termination of the LESSOR' s own lease of the property, unless the LESSOR's own lease terminates due to the LESSOR's purchase of the building and premises.

3. RENT: Rent and other charges, including late charges, relating to this lease are described in Exhibit B to this lease, which is hereby incorporated into this agreement by reference.

4. RENEWAL: This lease may be renewed for successive terms of one (l) year periods at a rental rate to be agreed upon 45 days prior to the expiration of the existing lease term. If no agreement is reached, the lease shall expire at the end of that term.

5. POSSESSION: LESSEE shall be entitled to possession on the first day of the term of this lease, and shall yield possession to LESSOR at the time and date of the close of the lease term. LESSEE shall receive an electronic key to enter the building, and a physical key to enter the premises. All keys and other property of the LESSOR shall be returned by LESSEE at that time.

6. USE AND MODIFICATION OF PROPERTY:

A. This property shall be used by LESSEE for the purpose of conducting a business to discover and develop new, safer therapies for the treatment of Attention Deficit/Hyperactivity Disorder, pain and various forms of cancer.

B. LESSEE shall submit in writing any proposed plan for changes, modifications or additions to the building or premises and will not proceed with same without LESSOR's written approval, which shall not be umeasonably withheld. At LESSOR's sole discretion, such written approval may include a requirement that any or all such changes, modifications or additions be returned to the original condition of the building or premises upon the expiration or termination of this agreement or a renewal or extension thereof. Any such changes, modifications, or additions that require work to be performed outside the premises or on any of the heating, ventilating, air-conditioning, mechanical, elevator, plumbing, electrical, fire protection, life safety, or security systems in the building shall also require prior approval of BBQ TOO, LLC, or any successor to the interest of BBQ TOO, LLC in the building in question.

Any such changes, modifications, or additions to the building or premises shall be completed by LESSOR, unless agreed in writing by LESSOR and LESSEE that such changes, modifications or additions shall be completed by LESSEE. In the event changes, modifications, or additions to the building or premises are completed by LESSEE, LESSEE shall ensure that any such changes, modifications, or additions to the building or premises are performed in accordance with applicable law (including, but not limited to, the Americans with Disabilities Act), utilizing the appropriate permits and governmental approvals, and done in a good and workmanlike manner. LESSEE shall keep the premises and the building free and clear of all liens in any way related to work performed, materials furnished, or obligations incurred by LESSEE.

C. Unless agreed to in writing beforehand by the parties, any such changes, modifications, or additions to the building or premises shall be completed at LESSEE's sole cost and expense. At LESSOR's sole discretion, LESSOR may agree to assume the up-front costs of changes, modifications, or additions and then modify the rent amount of LESSEE in this agreement to reflect the costs of such changes, modifications, or additions. Any such changes, modifications or additions to the building or premises shall become the property of LESSOR, including without limitation furniture and fixtures, laboratory casework and the like that are affixed to the floor, walls or ceiling. When providing approval in writing, LESSOR may require that LESSEE restore the changed, modified or added to building or premises to their original condition upon the expiration or termination of this agreement or renewals or extensions thereof.

7. CARE OF PREMISES: LESSEE shall keep the premises neat and orderly, and shall surrender the premises at the end of the lease term in the same condition as when it took possession, normal wear and tear excepted. LESSEE shall ensure that its operation shall not create unreasonable noise, interference or disruption for any other LESSEE or for the University. Pursuant to Section 15 herein, LESSOR and Ryan Companies US reserve the right to enter the premises to exercise safety or security measures and to make necessary alterations, repairs, additions or improvements.

8. UTILITIES AND SERVICES: General purpose water, heat, light, trash removal, maintenance, sidewalk maintenance including snow removal and general care of hallways and public areas will be provided by LESSOR or BBQ TOO, LLC. Should LESSEE's operations result in excessive and inordinate utility consumption as determined in the sole discretion of the LESSOR, the LESSOR reserves the right to charge a reasonable fee for such consumption. LESSEE is responsible for telephone and data services and charges. LESSEE will have equal access to conference rooms, the equipment room, equipment, a break room, restrooms, showers, and parking at no additional charge.

9. INSURANCE: LESSOR and LESSEE shall each be responsible to protect its respective property interests.

LESSEE shall purchase and maintain liability insurance with a minimum limit of not less than One Million Dollars ($1,000,000) per occurrence and Two Million Dollars ($2,000,000) annual aggregate. This policy shall be endorsed to include the State of Iowa; University of Iowa; and Board of Regents, State of Iowa as an additional insured. Policy shall contain a severability of interests provision.

Applicable Workers Compensation insurance to cover liability imposed by State statutes. Employer's Liability insurance of no less than $100,000 each employee and $100,000 each accident.

LESSEE shall provide to LESSOR a certificate of insurance evidencing above insurance with the signed Lease and annually.

All required insurance policies shall be issued by insurance companies authorized to engage in the insurance business in the State of Iowa, with an A.M. Best's rating of A-, VII or better. These policies shall be primary coverage.

10. LIABILITY: LESSEE agrees to indemnify, defend and hold hannless the University of Iowa, the State of Iowa, the Iowa Board of Regents, the University of Iowa Research Park Corporation, and their board members, officers, employees, and agents (hereinafter the "Released Parties") from and against any and all liability, loss, costs, damage and expenses occasioned by, arising out of, or relating in any way to LESSEE's business operations, products or services, debts or obligations, or any action of LESSEE, its employees, agents and others.

11. HOLDING OVER: Continued possession beyond the expiration date of the term of this lease by the LESSEE shall constitute a month-to-month extension of this lease at the rate of One Hundred Twenty Percent (120%) of the lease amount set forth on Exhibit B to this agreement. Nothing in this provision limits the right of LESSOR to exercise its right to remove LESSEE from the premises following expiration of this agreement or to exercise any other rights that LESSOR may have in law or in equity.

12. RULES: LESSEE understands and acknowledges that it and its officers, employees, agents, visitors and guests shall observe all operating policies of the LESSOR, including, but not limited to, rules procedures and traffic and parking regulations. Such policies shall be provided in writing by LESSOR.

13. REPRESENTATIONS: LESSEE agrees that it will not represent itself as acting on behalf of or as part of, the University of Iowa.

14. ASSIGNMENT: LESSEE shall not assign or sublet this lease or its rights hereunder to any other party without the prior written approval of LESSOR.

15. INSPECTION: LESSEE shall allow LESSOR to enter the leased premises a t reasonable times, and with reasonable notice considering the circumstances, for the purposes of inspection, repairs or improvements, to exercise safety or security measures, or t o show the premises to prospective Lessees.

16. REMEDIES: If LESSEE fails to comply with the tenns of this lease, and refuses to correct such non-compliance within thirty (30) calendar days following written notice, LESSOR may terminate this lease and proceed to remove LESSEE from the premise, or take such other action as is provided by law. LESSEE and LESSOR agree that the remedies for default set forth above are not exclusive, but shall be cumulative and shall be in addition to any other remedies now or hereinafter allowed by law. Any breach or default by LESSEE shall not be waived or released other than by writing signed by LESSOR. Failure by LESSOR at any time to require performance by LESSEE or to claim a breach of any provision of the agreement shall not be construed as affecting the right to require performance or to claim a breach.

17. CHANGES IN WRITING: Any and all changes, additions or deletions to the terms of this lease shall be in writing, executed by both parties.

18. COMMON AREAS: LESSEE shall have reasonable use of common areas of the building for normal business purposes, within the policy guidelines of the University of Iowa.

19. SECURITY: LESSEE is responsible for securing all windows and doors within and on its leased space and shall exert diligence in keeping building entrances and openings locked after normal business hours. LESSEE shall be solely responsible for any and all losses, damages, claims, or causes of action that may arise that relate in any way from LESSEE's failure or alleged failure to perform the obligations under this provision. LESSEE further agrees to defend, hold harmless, and indemnify LESSOR for any violation of the obligations under this provision.

20. RELOCATION: LESSOR reserves the right to relocate LESSEE to a comparable space at LESSOR's discretion. LESSOR will provide 30 days notice prior to relocation.

21. HAZARDOUS WASTE: LESSEE is required to enter into a Hazardous Waste Agreement with the University of Iowa, which is attached as Exhibit C to this lease and hereby incorporated into this agreement by reference.

22. BUILDING RULES, AND UNIVERSITY AND REGENT POLICIES: LESSEE agrees to abide by all building rules of BBQ TOO, LLC and LESSOR, and all policies and regulations of the University of Iowa and the Iowa Board of Regents, that may be applicable to the use of University-controlled buildings in general and these premises in particular.

23. APPLICABILITY TO THIRD PARTIES AND SUCCESSORS IN INTEREST. There are no third party beneficiaries to this agreement. The tenns, provisions, and conditions of the agreement shall be binding upon and inure to the benefit of LESSOR and LESSEE and their respective successors, assigns, and legal representatives.

24. COUNTERPARTS AND FACIMILE SIGNATURES. The parties agree that this agreement has been or may be executed in several counterparts, each of which shall be deemed an original and all such counterparts shall together constitute one and the same instrument. The parties further agree that the signatures on this Agreement or any amendment or schedule may be manual or a facsimile signature of the person authorized to sign the appropriate document. All authorized facsimile signatures shall have the same force and effect as if manually signed.

25. SEVERABILITY. If any provision of this agreement is determined by a court of competent jurisdiction to be invalid or unenforceable, the invalid portion shall be severed from this agreement. Such a determination shall not affect the validity or enforceability of other parts o r provisions of the agreement.

26. INTEGRATION. This agreement, including all the exhibits and documents incorporated by reference, represents the entire agreement between the parties and neither LESSOR nor LESSEE is relying on any representation that may have been made which is not included in this agreement. This agreement supersedes all prior agreements between LESSOR and LESSEE regarding the premises and the subject matter of this agreement.

27. NO ENDORSEMENT BY LESSOR. LESSEE understands and agrees that neither this agreement nor LESSEE's use of the premises constitutes an endorsement by LESSOR or the University of Iowa of the products or services provided by LESSOR. Neither LESSOR nor the University of Iowa will make any endorsement of LESSOR's products or services. Except in the mailing address, LESSOR shall not use the name of the LESSOR or the University of Iowa in connection with LESSEE's products or services. LESSOR, the University of Iowa, and the State of Iowa will not be responsible for any past, present, or future debts of LESSEE

28. FORCE MAJEURE. Neither LESSOR nor LESSEE shall be liable to the other for any delay or failure of performance of this agreement and no delay or failure of performance shall constitute a default or give rise to any liability for damages if, and only to the extent that, such delay or failure is caused by a "force majeure". As used in this agreement, "force majeure" includes acts of God, war, civil disturbance and any other similar causes which are beyond the control and anticipation of the party affected and which, by the exercise of reasonable diligence, the party was unable to anticipate or prevent. Business downturns or difficulties by LESSEE shall not be considered a force majeure event.

29. CHOICE OF LAW AND FORUM. The laws of the State of Iowa shall govern and determine all matters arising out of or in connection with this agreement. In the event that any procedding of a quasi-judicial or judicial nature is commenced relating in any way to this agreement, the exclusive jurisdiction for the proceeding is the Johnson County District Court, Iowa City, Iowa, or the United States District Court for the Southern District of Iowa, wherever jurisdiction is appropriate. This provision shall not be construed as waiving any immunity to suit or liability, including without limitation sovereign immunity or Eleventh Amendment immunity, which may be available to the University of Iowa, the Iowa Board of Regents, or the State of Iowa.

30. PAYMENTS: Rent payments and other payments due to LESSOR shall be paid at the following address or such other address as may be communicated to LESSEE from time to time in writing:

UI BioVentures Center
2500 Crosspark Rd. El56
Coralville, IA 52241

| | |
|---|---|
| LESSOR: Board of Regents, State of Iowa, for the Use and Benefit of the University of Iowa | LESSEE: KemPharm, Inc. |
| BY: /s/ David Kieft | BY: /s/ R. LaDuane Clifton |
| David Kieft<br>Business Manager,<br>University of Iowa, On Behalf of the Board of Regents,<br>State of Iowa | TITLE: CFO |
| DATE: 9/22/17 | DATE: 5 SEP 2017 |

**EXHIBIT A—DESCRIPTION OF PREMISES**

Premises include the following wet laboratory rooms located in the building at 2500 Crosspark Road, Coralville, Iowa: EI27

The premises also include the following office rooms located in the building at 2500 Crosspark Road, Coralville, Iowa: EI26

**EXHIBIT B--RENTAL CHARGES**

Base Rent includes **Two Thousand Six Hundred and Twenty Dollars ($2620.00)** per month for each of the following wet laboratory rooms: E127

Base Rent also includes **Six Hundred Seventy Dollars ($670.00)** per month for the following office suites: El26,

Based on the foregoing, Total Base Rent is **Three Thousand Two Hundred and Ninety Dollars ($3,290.00)** per month.

Additional rent includes lease of chemical fume hood(s) as follows:
Two chemical fume hood installed in Room E127

Standard hood at **Two Hundred Dollars ($200.00)** per month.

Low flow chemical hood specially installed at **Four Hundred Seventy Seven Dollars ($477.00)** per month.

| | |
|---|---|
| Base Rent | |
| Wet Laboratory | $2620.00 per month |
| Office Suite | $670.00 per month |
| Additional Rent | $677.00 per month |
| **Total Rent** | **$3,490.00 per month** |

**Other Provisions:**

Rent payments are due and payable on the first day of the month. Rents received later than the 10th day of the month are subject to a late payment fee ofone and one-half percent (1.5%) of the outstanding balance of rent due and payable.

**EXHIBIT C—HAZARDOUS WASTE AGREEMENT**

[Attach the UI's standard agreement here.]

**Exhibit 23.1**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the Registration Statement (No. 333-213926) on Form S-3 and Registration Statement (No. 333-203703, No. 333-210369 and No. 333-216858) on Form S-8 of KemPharm, Inc. of our report dated March 30, 2018, relating to the financial statements of KemPharm, Inc., appearing in this Annual Report on Form 10-K of KemPharm, Inc. for the year ended December 31, 2017.

/s/ RSM US LLP

Orlando, Florida
March 30, 2018

**Exhibit 23.2**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-216858) pertaining to the 2014 Equity Incentive Plan of KemPharm, Inc.,
(2) Registration Statement (Form S-3 No. 333-213926) of KemPharm, Inc.,
(3) Registration Statement (Form S-8 No. 333-210369) pertaining to the 2014 Equity Incentive Plan of KemPharm, Inc., and
(4) Registration Statement (Form S-8 No. 333-203703) pertaining to the Incentive Stock Plan, as amended, and the 2014 Equity Incentive Plan of KemPharm, Inc.

of our report dated March 10, 2017 (except for the effects of the retrospective adoption of Accounting Standards Update 2016-18 discussed in Note A, *Reclassifications*, as to which the date is March 30, 2018), with respect to the financial statements of KemPharm, Inc. included in this Annual Report (Form 10-K) of KemPharm, Inc. for the year ended December 31, 2017.

/s/ Ernst & Young LLP
Certified Public Accountants

Tampa, Florida
March 30, 2018

**Exhibit 31.1**

CERTIFICATIONS

I, Travis C. Mickle, certify that:

1. I have reviewed this Annual Report on Form 10-K of KemPharm, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 30, 2018

/s/ Travis C. Mickle
Name: Travis C. Mickle, Ph.D.
Title: President and Chief Executive Officer
(Principal Executive Officer)

**Exhibit 31.2**

CERTIFICATIONS

I, R. LaDuane Clifton, certify that:

1. I have reviewed this Annual Report on Form 10-K of KemPharm, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 30, 2018

/s/ R. LaDuane Clifton
Name: R. LaDuane Clifton, CPA
Title: Chief Financial Officer, Secretary and Treasurer
(Principal Financial Officer)

**Exhibit 32.1**

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of KemPharm, Inc., (the "Company") for the fiscal year ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Travis C. Mickle, Principal Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

March 30, 2018

/s/ Travis C. Mickle
Name: Travis C. Mickle, Ph.D.
Title: President and Chief Executive Officer
(Principal Executive Officer)

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350, is not being "filed" by the Company as part of the Report or as a separate disclosure document and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

**Exhibit 32.2**

CERTIFICATION OF THE PRINCIPAL FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of KemPharm, Inc., (the "Company") for the fiscal year ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, R. LaDuane Clifton, Principal Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

March 30, 2018

/s/ R. LaDuane Clifton
Name: R. LaDuane Clifton, CPA
Title: Chief Financial Officer, Secretary and Treasurer
(Principal Financial Officer)

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350, is not being "filed" by the Company as part of the Report or as a separate disclosure document and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.