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, 2018

☐ **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.)**
1180 Celebration Boulevard, Suite 103, Celebration, FL 34747	**(321) 939-3416**
(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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 ☒

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, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $71,917,131, 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 4,840,972 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 February 28, 2019, the registrant had 26,455,352 shares of common stock outstanding.

Documents Incorporated by Reference

Portions of the registrant's definitive proxy statement for its 2019 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, 2018. 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 expected amount of expenses associated with our research, development and commercialization activities;*
- *our ability to raise additional funds on commercially reasonable terms, or at all, in order to support our continued operations;*
- *the sufficiency of our cash resources to fund our operating expenses and capital investment requirements for any period;*
- *the expected timing of our clinical trials for our product candidates and the availability of data and results of those trials;*
- *our expectations regarding federal, state and foreign regulatory requirements;*
- *the potential therapeutic benefits and effectiveness of our product candidates and partnered asset;*
- *the size and characteristics of the markets that may be addressed by our product candidates and partnered asset;*
- *our intention to seek to establish or the potential outcome of any strategic collaborations or partnerships for the development or sale of our product candidates and partnered asset;*
- *our expectations as to future financial performance, expense levels and liquidity sources;*
- *the timing of commercializing our product candidates and partnered asset; 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 2018. SHS expressly reserves all rights, including rights of copying, distribution and republication.

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 proprietary Ligand Activated Therapy, or LAT™, technology. We utilize our proprietary LAT technology to generate improved prodrug versions of drugs approved by the U.S. Food and Drug Administration, or FDA, as well as to generate prodrug versions of existing compounds that may have applications for new disease indications. Our product candidate pipeline is focused on the high need areas of attention deficit hyperactivity disorder, or ADHD, and stimulant use disorder, or SUD. Our co-lead clinical development candidates, KP415 and KP484, are both based on a prodrug of d-methylphenidate, but with differing extended-release, or ER, effect profiles, and are intended for the treatment of ADHD. In addition, we recently announced our commercial partnership with KVK Tech, Inc., or KVK, of APADAZ®, an FDA approved immediate-release, or IR, combination product of benzhydrocodone, our prodrug of hydrocodone, and acetaminophen, or APAP, 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.

In October 2018, we entered into a collaboration and license agreement, or the License Agreement, with KVK pursuant to which we granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States.

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 $3.5 billion in sales in 2018.

We employ our proprietary LAT 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 the active form of the drug 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 and SUD, and we anticipate submitting a new drug application, or NDA, to the FDA for KP415 in the second quarter of 2019. In addition, we anticipate KVK's commercial launch of APADAZ in the second half of 2019. We also anticipate reporting pivotal efficacy trial data and submitting an NDA for KP484 in 2020. We plan to employ our LAT 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, 2018, our patent portfolio consisted of 155 granted patents and 128 pending patent applications worldwide. Within that patent portfolio, we have received granted U.S. composition-of-matter patents covering benzhydrocodone, our prodrug of hydrocodone, benzhydrocodone-related compositions-of-matter and a composition-of-matter patent that generally covers KP484 and at least one component of KP415.

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 proprietary LAT technology to improve the attributes of widely-prescribed, FDA-approved drugs***. We plan to employ our proprietary LAT technology to discover and develop prodrugs that can improve one or more of the attributes of FDA-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 KP484 in 2020. We also plan to submit an NDA for KP415 in 2019 and an NDA for KP484 in 2020. In addition, we are developing KP879, our prodrug of d-methylphenidate, for the treatment of SUD.

- ***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.

- ***Continue to evaluate potential partnering opportunities for our ADHD product candidates***. We intend to continue to actively evaluate and seek potential partnering opportunities for our ADHD assets.

- ***Commercialize APADAZ.*** In October 2018, we entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States. We anticipate that KVK's commercialization strategy will target outreach to pharmacy benefit managers, managed care organizations and integrated delivery networks for the exclusive utilization of APADAZ as an alternative to currently available hydrocodone/acetaminophen products. We anticipate that KVK may initiate regional pilot launches of APADAZ sales as early as the second half of 2019. We may also license the international commercial rights to APADAZ to one or more collaborators.

Our Proprietary LAT Technology

We employ our proprietary LAT 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 proprietary LAT 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 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 proprietary LAT 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 FDA-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.

Our Product Candidates and Partnered Asset

We have employed our proprietary LAT technology to create a portfolio of product candidates that we believe will offer significant improvements over FDA-approved and widely-prescribed drugs.

In February 2018, we announced that the FDA approved the 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.

In July 2018, we announced top line results from our pivotal efficacy and safety clinical trial of KP415. The trial, also known as KP415.E01 was a multicenter, randomized, parallel, double-blind, placebo-controlled analog laboratory classroom clinical trial in 150 children aged 6-12 years old with a diagnosis of ADHD to assess the efficacy and safety of KP415. Subjects who received KP415 met the trial's primary and secondary efficacy endpoint, showing statistically significant improvement on both the Swanson, Kotkin, Agler, M-Flynn, and Pelham, or SKAMP, Scale and the Permanent Product Measure of Performance, or PERMP, scale.

In September 2018, we announced top line results from our oral HAP clinical trial of serdexmethylphenidate, or SDX, a prodrug of d-methylphenidate, the major active pharmaceutical ingredient, or API, in KP415. Results from this oral HAP trial, suggest that the prodrug component of KP415 may have lower abuse potential compared to FOCALIN XR (d-methylphenidate extended release capsules), a schedule II controlled substance approved for the treatment of ADHD, even when SDX is administered at oral doses up to 1.5 times higher than FOCALIN XR on a molar basis. On September 17, 2018, we announced top line results from our intranasal HAP clinical trial of SDX. In this intranasal HAP trial, SDX produced significantly lower scores on the primary endpoint, maximal Drug Liking, and other abuse-related endpoints, compared to intranasal d-methylphenidate hydrochloride, indicating that SDX is not efficiently converted to active d-methylphenidate when snorted.

In October 2018, we entered into the License Agreement with KVK pursuant to which we have granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States. Under the terms of the License Agreement we are eligible to receive milestone payments of up to $53.0 million and royalties based on the net profits of APADAZ sales in the United States. We anticipate that KVK's commercialization strategy will target outreach to pharmacy benefit managers, managed care organizations and integrated delivery networks for the exclusive utilization of APADAZ as an alternative to currently available hydrocodone/acetaminophen products. We anticipate that KVK may initiate regional pilot launches of APADAZ sales as early as the second half of 2019. In support of this anticipated commercial launch, we have begun the technology transfer process outlined under the License Agreement. As part of this process, in February 2019 we completed the transfer of the NDA for APADAZ to KVK.

We have also developed a number of product candidates focused on the treatment of pain, in addition to our partnered asset, APADAZ. As of the date of this report, we have chosen to redirect our development efforts to focus on our ADHD and SUD programs, and do not anticipate engaging in substantial development efforts on our pain program during the fiscal year ended December 31, 2019.

Our pipeline of product candidates and our partnered asset are summarized in the table below:

Selected KemPharm Product Candidates

Indication / Parent Drug	Product Candidate	Development Status	Key Milestone
ADHD			
Methylphenidate (ER)	KP415	Clinical	NDA Submission - Q2 2019
Methylphenidate (ER)	KP484	Clinical	NDA Submission - 2020 Pivotal Efficacy Trial Data - 2020
SUD			
Methylphenidate (ER)	KP879	Preclinical	

KemPharm Partnered Asset

Product Name	Key Milestone
APADAZ	Commercial Launch - 2H 2019

KP415 and KP484

Overview

The prodrug in KP415 and KP484 is SDX, 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 extended-duration 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 submitting a 505(b)(2) NDA for KP415 in the second quarter of 2019 and reporting additional pharmacokinetic, or PK, and pivotal efficacy trial data and submitting a 505(b)(2) NDA for KP484 in 2020.

We are actively evaluating and seeking potential commercial partnership opportunities for KP415 and KP484.

We have granted Shire, LLC, or 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 or KP484. In early 2019, Shire was acquired by Takeda Pharmaceutical, or Takeda, and Takeda now holds the right of first refusal.

We are also party to an agreement with Aquestive Therapeutics (formerly known as MonoSol Rx, LLC), or Aquestive, pursuant to which Aquestive has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415, KP484 or KP879, and any product candidates arising therefrom, including royalty payments on any license of KP415, KP484 or KP879, the sale of KP415, KP484 or KP879 to a third party or the commercialization of KP415, KP484 or KP879.

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 may provide a new treatment option in this large market segment. While methylphenidate is available as a generic product, the branded formulations, including, among others, CONCERTA, FOCALIN XR, QUILLICHEW XR and COTEMPLA XR-ODT, accounted for sales of $1.2 billion in 2018.

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 July 2018, we announced top line results from our pivotal efficacy and safety clinical trial of KP415. KP415.E01 was a laboratory classroom clinical trial in children aged 6-12 years old with a diagnosis of ADHD to assess the efficacy and safety of KP415. Subjects who received KP415 met the trial's primary and secondary efficacy endpoint, showing statistically significant improvement on both the SKAMP and PERMP scales.

- ***Reduced abuse potential***. In order to evaluate the potential for reduced abuse of SDX, our prodrug of d-methylphenidate and major component of KP415, we conducted preclinical and clinical studies to compare the exposure to d-methylphenidate following oral, intranasal and intravenous, or IV, administration of the prodrug as compared to oral, intranasal and IV administration of d-methylphenidate hydrochloride. We observed significantly lower concentrations of d-methylphenidate following oral, intranasal and IV administration of the prodrug compared to oral, intranasal and IV administered d-methylphenidate hydrochloride. Consistent with this lower exposure, in human abuse potential studies, we also observed significantly lower abuse-related pharmacodynamic effects compared to d-methylphenidate comparators. Our prodrug of d-methylphenidate incorporates our proprietary LAT technology and, based on our preclinical and clinical studies, we believe it may have lower abuse potential compared to d-methylphenidate.

- ***Once-daily dosing***. PK data from our preclinical studies suggest that the time to maximum plasma concentration of d-methylphenidate after oral administration of KP415 is approximately three times longer than that after oral administration of currently marketed IR d-methylphenidate. We believe our PK studies in human subjects also demonstrate that KP415 affords d-methylphenidate concentrations that are consistent with a once-daily, extended-duration product.

- ***Amenable to patient-friendly formulations***. Our preclinical and clinical data show that KP415 could ultimately be used in a variety of patient-friendly dosage forms such as oral thin film and orally dissolving tablets 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, 2018, we have composition-of-matter patents in over 50 countries, including in Canada, China, Europe, Malaysia, Mexico, Indonesia, Israel, Japan, New Zealand, Philippines, Russia, Singapore, South Africa, South Korea and Vietnam, 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 was given a new chemical name, serdexmethylphenidate, by the U.S. Adopted Names Council, or USAN, which means that there may 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 and clinical studies of SDX, the prodrug of d-methylphenidate, discussed above in the KP415 "Reduced Abuse Potential" subsection are being used by us for the abuse potential evaluation of the KP484 product candidate. Accordingly, we believe serdexmethylphenidate may have attributes that disincentivize certain forms of abuse, as observed in these preclinical and clinical studies.

- ***Once-daily dosing***. PK data from our clinical studies suggest that under fasted conditions, the time to maximum plasma concentration of d-methylphenidate after oral administration of KP484 is potentially five to seven times longer compared to oral administration of currently marketed IR d-methylphenidate. We believe this extended-duration 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 and orally dissolving tablets 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, 2018, we have composition-of-matter patents generally protecting the major component of KP484 in New Zealand and South Africa.

- ***No generic equivalent product***. KP484 contains a prodrug that was given a new chemical name, serdexmethylphenidate, by the USAN, which means that there may be no generic equivalent product for KP484 in most states, making drug-equivalent substitution potentially difficult at the pharmacy.

KP879

KP879, a prodrug of d-methylphenidate using our proprietary LAT technology, is our product candidate for the treatment of SUD including, for example, abuse or misuse of cocaine, methamphetamine and prescription stimulants. Currently there are no approved drugs in the United States for SUD.

APADAZ

Overview

In February 2018, we announced that the FDA approved 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 technology. In October 2018, we entered into the License Agreement with KVK pursuant to which we have granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States. We anticipate that KVK's commercialization strategy will target outreach to pharmacy benefit managers, managed care organizations and integrated delivery networks for the exclusive utilization of APADAZ as an alternative to currently available hydrocodone/acetaminophen products. We may also license the international commercial rights to APADAZ to one or more collaborators.

Market Opportunity

Symphony Health estimates that in 2018, IR hydrocodone/APAP combination products represented the most frequently prescribed opioid product in the United States, accounting for 63 million U.S. prescriptions, representing 4.0 billion tablets. Typically, patients are instructed to take 4-6 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.

Key Product Features of APADAZ

We believe APADAZ has many valuable product features and may provide 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 benzhydrocodone, 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, 2018, benzhydrocodone had received granted, issued or allowed patent status in 21 foreign jurisdictions and patent applications covering benzhydrocodone were pending in an additional 12 foreign jurisdictions.

- ***No generic equivalent product***. Benzhydrocodone, 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 benzhydrocodone 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 PK trial, APADAZ can be administered without regard to food and, accordingly, APADAZ will be as convenient as existing IR hydrocodone/APAP combination products.

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 proprietary LAT 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 proprietary LAT 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, 2018, we have been granted 30 issued patents within the United States, and an additional 87 foreign patents covering our prodrugs or product candidates. The terms of the 30 issued U.S. patents extend to various dates ranging, for example, between 2030 and 2035. 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 2035, if pending patent applications in each of our patent families issue as patents. As of December 31, 2018, we had filed 23 pending patent applications under active prosecution in the United States, and an additional 105 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.

We have received composition-of-matter patents and also additionally filed composition-of-matter patent applications related to the KP415 and KP484 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.

In 2013, the United States Patent and Trademark Office, or the USPTO, issued a composition-of-matter patent covering benzhydrocodone, 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 benzhydrocodone in Australia, Belarus, Canada, Chile, China, Colombia, Cuba, India, Indonesia, Israel, Japan, Kazakhstan, Malaysia, Mexico, New Zealand, Philippines, Russia, Singapore, South Africa and Ukraine. In addition, five U.S. patent applications covering benzhydrocodone-related compositions-of-matter were pending as of December 31, 2018, and patent applications covering benzhydrocodone were pending as of December 31, 2018, in the Belarus, Brazil, Costa Rica, Egypt, Europe, Hong Kong, Israel, Oman, South Korea, Thailand, United Arab Emirates and Vietnam.

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 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

In February 2018, we announced that the FDA approved 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.

In October 2018, we entered into the License Agreement with KVK pursuant to which we have granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States. Under the terms of the License Agreement we are eligible to receive milestone payments of up to $53.0 million and royalties based on the net profits of APADAZ sales in the United States. We anticipate that KVK's commercialization strategy will target outreach to pharmacy benefit managers, managed care organizations and integrated delivery networks for the exclusive utilization of APADAZ as an alternative to currently available hydrocodone/acetaminophen products. We anticipate that KVK may initiate regional pilot launches of APADAZ sales as early as the second half of 2019. In support of this anticipated commercial launch, we have begun the technology transfer process outlined under the License Agreement. As part of this process, in February 2019 we completed the transfer of our NDA for APADAZ to KVK. We may also license the international commercial rights to APADAZ to one or more collaborators in the future.

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 candidates. For the years ended December 31, 2018 and 2017, we recorded $41.8 million and $20.6 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 Janssen's CONCERTA, Novartis AG's RITALIN, Tris' QUILLIVANT, QUILLIVANT XR and QULLICHEW, Novartis' FOCALIN and FOCALIN XR, UCB S.A.'s METADATE CD, Noven Pharmaceuticals' DAYTRANA and Neos Therapeutics' CONTEMPLA XR-ODT, 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.

Currently, there are no approved drugs in the United States for the treatment of SUD. If approved, KP879 will face potential competition from any products for the treatment of SUD that are currently in or which may enter into clinical development.

APADAZ 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 will face potential competition from any IR or hydrocodone/APAP combination products for the short-term management of acute pain that are currently in or may enter into clinical development.

Manufacturing

Our manufacturing strategy is to rely on contract manufacturers to produce our 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 benzhydrocodone required to manufacture APADAZ under a supply agreement. 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 APADAZ, 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 benzhydrocodone necessary for clinical trials and commercial sale for a price equal to JMI's manufacturing cost and to provide process development services for benzhydrocodone. In exchange, we issued shares of our common stock to JMI, provided that the commercial supply arrangement for benzhydrocodone 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 benzhydrocodone as the API. 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 benzhydrocodone as the API, and stability testing for those batches is in process.

Under the Supply Agreement, we retain sole ownership of benzhydrocodone and are required to use commercially reasonable efforts to develop and to pursue FDA marketing approval of any products which utilize benzhydrocodone 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 benzhydrocodone as the API are subject to a U.S. Drug Enforcement Agency, or DEA, scheduling quota, then each year, both we and JMI are responsible for using commercially reasonable efforts to obtain a quota from the DEA for the production of benzhydrocodone for use with any products that utilize benzhydrocodone as an API.

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

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

The term of the Supply Agreement extends as long as we hold a valid and enforceable patent for benzhydrocodone or until the tenth anniversary of the commercial launch of any product that utilizes benzhydrocodone 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. In early 2019, Shire was acquired by Takeda, and Takeda now holds this right of first refusal.

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, 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, 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.

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 boxed 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.

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 human prescription drug program fee requirements for approved products. 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 any opioid product candidates we may choose to develop in the future, if approved, may be subject to a REMS. Accordingly, we expect to have to take prescribed measures to ensure the safe use of these product candidates, if any, that may be approved. For example, in September 2018, the FDA approved the Opioid Analgesic REMS for extended-release, long-acting, or ER/LA, and IR opioids as one strategy among multiple national and state efforts to reduce the risk of abuse, misuse, addiction, overdose and deaths due to prescription opioid analgesics which APADAZ is subject to. In accordance with the License Agreement, KVK is responsible for regulatory activities for APADAZ in the United States, including, the REMS program.

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. 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.

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 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 substances 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.

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, 2018, we employed 33 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, 2018 and 2017.

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 1180 Celebration Boulevard, Suite 103, Celebration, FL 34747 and our telephone number is (321) 939-3416.

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, 2018, had an accumulated deficit of $221.2 million. Our loss from operations for the years ended December 31, 2018 and 2017, were $55.9 million and $33.4 million, respectively. We have financed our operations to date with funds raised in private placements of redeemable convertible preferred stock, in the issuance of convertible promissory notes and term debt, our initial public offering, sales under our common stock sales agreement with Cowen and Company, LLC, or Cowen and an underwritten public offering in October 2018. In February 2019, we also entered into a purchase agreement, or the Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which provides that, upon the terms and subject to the conditions and limitations set forth therein, we may sell to Lincoln Park up to $15.0 million of shares of our common stock, from time to time over the 36-month term of the Purchase Agreement, and we shall issue an additional 120,200 shares of our common stock to Lincoln Park as commitment shares under the Purchase Agreement. Concurrently with entering into the Purchase Agreement, we also entered into a registration rights agreement with Lincoln Park, or the Registration Rights Agreement, pursuant to which we agreed to register the sale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to our existing shelf registration statement on Form S-3 or a new registration statement. We have yet to make any sales under the Purchase Agreement, but are obligated to issue 120,200 commitment shares to Lincoln Park upon satisfaction of the closing conditions contained in the Purchase Agreement.

Our recurring operating losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. We have no current source of revenues to sustain our present activities, and we do not expect to generate revenues until, and unless, the FDA or other regulatory agencies approve our product candidates and we successfully commercialize any such product candidates. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations. The perception of our inability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees. 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 product, 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 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 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 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 our product candidates and we cannot guarantee that any strategy we adopt will be successful. For instance, in October 2018, we entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to commercialize APADAZ in the United States. We cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. 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, 2018, included in this annual report on Form 10-K, contains an explanatory paragraph relating to our ability to continue as a going concern.

The auditor's opinion on our audited financial statements for the year ended December 31, 2018 includes an explanatory paragraph stating that our 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, we would need to significantly reduce our operating plans and curtail some or all of our product development, commercialization and strategic plans. Accordingly, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited consolidated financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding on commercially reasonable terms or at all.

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, our existing resources are expected to be sufficient to fund operating expense and capital investment requirements into, but not through, the third quarter of 2019. Because of this, the auditor's opinion on our audited financial statements for the year ended December 31, 2018 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 do not currently have sufficient funds to finance our continuing operations beyond the short-term or to further advance any or our product candidates further into clinical development. In order to continue to advance development of our product candidates, we will need to obtain substantial additional funding in connection with our continuing operations from one or more equity offerings, including pursuant to our Purchase Agreement with Lincoln Park, our Common Stock Sales Agreement, or the Second ATM Agreement, with RBC Capital Markets, LLC, or RBCCM, debt financings or the License Agreement 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 Purchase Agreement, Second ATM Agreement or the License Agreement, or be successful in completing other transactions, that will fund our operating expenses. If we are delayed in obtaining additional funding or are unable to complete a strategic transaction, we may discontinue our development activities on our product candidates or discontinue our operations. Even if we are able to fund continued development and any of our other product candidates is approved, we expect that we will need to complete a strategic transaction or raise substantial additional funding through public or private debt or equity securities to successfully commercialize any other product candidate. 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 any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of APADAZ, under our License Agreement or sales of 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 cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. 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. 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. Additionally, in February 2016, we issued 5.50% senior convertible notes due 2021, or the 2021 Notes, in the aggregate principal amount of $86.3 million. 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.

We may be unable to issue securities under our shelf registration statement, which may have an adverse effect on our liquidity.

We have filed a shelf registration statement on Form S-3 with the SEC. After we file this Annual Report on Form 10-K, in order to issue securities under this registration statement, we must rely on Instruction I.B.6. of Form S-3, which imposes a limitation on the maximum amount of securities that we may sell pursuant to the registration statement during any twelve-month period. At the time we sell securities pursuant to the registration statement, the amount of securities to be sold plus the amount of any securities we have sold during the prior twelve months in reliance on Instruction I.B.6. may not exceed one-third of the aggregate market value of our outstanding common stock held by non-affiliates as of a day during the 60 days immediately preceding such sale, as computed in accordance with Instruction I.B.6. This calculation will be updated immediately after we file this Annual Report on Form 10-K and we expect that the amount of securities we will be able to sell under the registration statement on Form S-3 thereafter will be approximately $18.5 million, of which we anticipate filing prospectus supplements to register (i) approximately $15.3 million for sales under the Purchase Agreement, and (ii) approximately $3.2 million for sales under our Second ATM Agreement. Based on this calculation, we expect that we will be unable to sell additional securities pursuant to our effective registration statement on Form S-3 for a period of twelve months, unless and until the market value of our outstanding common stock held by non-affiliates increases significantly. If we cannot sell securities under our shelf registration statement, we may be required to utilize more costly and time-consuming means of accessing the capital markets, which could materially adversely affect our liquidity and cash position.

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 one product approved by the FDA, 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. Further, we cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. 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 proprietary LAT 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 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 Complete Response Letter, or CRL, from the FDA for the APADAZ NDA. Following a Formal Dispute Resolution Request, or FDRR, process and detailed discussions with the FDA, we responded to the CRL by submitting an amended NDA for APADAZ. In February 2018, we announced that the FDA approved the NDA for APADAZ. If APADAZ is not successfully commercialized under our License Agreement and we do not successfully develop and commercialize our product candidates based upon our proprietary LAT 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. In February 2018, we announced that the FDA approved the 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 the APADAZ NDA. Following a FDRR process and detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended 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. In February 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 commercialization of APADAZ or our product candidates is not successful, or we experience significant delays in commercialization, 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, while we have entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to commercialize APADAZ, we cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. We have invested substantially all our efforts and financial resources in the development of our proprietary LAT technology, the identification of potential product candidates and the development of our product candidates. Our ability to generate revenue from APADAZ under the License Agreement and generate revenue from 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 under the License Agreement and for our other 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 DEA of the controlled substance schedule for 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 cGMPs;
- launching commercial sales of APADAZ under the License Agreement and launching commercial sales of 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 in February 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 KVK could experience an inability to successfully commercialize APADAZ or we could experience an inability to successfully commercialize our product candidates approved for marketing in the future, if any, which would harm our business.

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. 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.

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 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 boxed 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 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 boxed warning for at least some of our product candidates, including APADAZ.

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 the 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. Following a FDRR process and detailed discussions with the FDA, we responded to the CRL we received in June 2016 by submitting an amended NDA for APADAZ. In February 2018, we announced that the FDA approved the 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. Despite this, the final approved product labeling for APADAZ concluded that the overall results of the clinical program did not demonstrate abuse-deterrence by current measurement standards.

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 have 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 that any other opioid analgesic product candidates that we may choose to develop in the future, 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 opioid analgesic 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. In September 2018, the FDA approved the Opioid Analgesic REMS for ER/LA and IR opioids as one strategy among multiple national and state efforts to reduce the risk of abuse, misuse, addiction, overdose and deaths due to prescription opioid analgesics. The Opioid Analgesic REMS affects more than 60 companies that manufacture these products. Under this REMS, companies are required to make training available to all healthcare providers who are involved in the management of patients with pain, including nurses and pharmacists. To meet this requirement, drug companies with approved opioid analgesics will provide unrestricted grants to accredited continuing education providers for the development of education courses for healthcare providers based on the FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain. The REMS program 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 this REMS, and we anticipate that any other opioid product candidates we may choose to develop in the future, if approved by the FDA, are likely to also be subject to a REMS requirement. 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. In October 2018, we entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to commercialize APADAZ in the United States. As part of this agreement KVK has assumed most regulatory and commercialization costs, including this REMS requirement.

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 product candidates, including, KP415, KP484 and KP879, 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 other applicable 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 the ability to commercialize APADAZ under the License Agreement or our other applicable product candidates. Aggressive enforcement and unfavorable publicity regarding, for example, the use or misuse of opioid drugs and stimulants, 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 other applicable 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 other applicable 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. These changes have reduced the number of prescriptions for opioids written by physicians and could negatively impact the potential market for APADAZ or our other applicable 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 previously 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 other applicable 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 partnered product and product candidates that utilize benzhydrocodone and SDX as the API used in our clinical trials and with a sole source supplier for the manufacture of bulk quantities of benzhydrocodone and SDX used in the partnered product 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 benzhydrocodone and SDX, 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, APADAZ and KP879 from sole-source, third-party manufacturers and the partnered product and product candidates that utilize these moieties as the API used in our clinical trials and commercialization efforts 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 of 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 benzhydrocodone, SDX, other bulk drug substances or our partnered product 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.

We do not, other than through our contractual arrangements, control the manufacturing process of APADAZ or our product candidates, and we 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.

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 or KP879 bulk drug substance. If our current contract manufacturer for KP415, KP484 or KP879 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 have entered into a collaboration with KVK for the commercialization of APADAZ in the United States and may seek collaborations with third parties for the development or commercialization of 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 entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to commercialize APADAZ in the United States. We cannot guarantee that our collaboration with KVK will be successful or that we will ever receive any payments under the License Agreement. For instance, if the initial adoption milestone under the License Agreement is not achieved, KVK may terminate the License Agreement without making any payments to us. Further, even if this initial adoption milestone under the License Agreement is achieved, we cannot guarantee that we will receive any additional milestone or royalty payments under the License Agreement. Further, under the License Agreement, we have limited control over the amount and timing of resources that KVK will dedicate to the commercialization of APADAZ, and we may not always agree with KVK's commercialization efforts. Our ability to generate revenue under the License Agreement will depend on KVK's ability to successfully perform the functions assigned to it under the License Agreement, and even if KVK does successfully perform its functions under the License Agreement, we cannot guarantee that there will be sufficient market demand for APADAZ for us to receive any revenue under the License Agreement.

We may also seek additional third-party collaborators for the commercialization of APADAZ outside of the United States or for the development or commercialization of KP415, KP484 or our other product candidates. In such cases, our likely collaborators would include large and mid-size pharmaceutical companies, regional, national and international pharmaceutical companies and biotechnology companies. If we do enter into any such 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 outside of the United States 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.

Our collaboration with KVK poses the following risks to us:

- KVK has significant discretion in determining the efforts and resources that they will apply to this collaboration;
- KVK may not perform their obligations as expected;
- KVK may not pursue commercialization of APADAZ or may elect not to continue or renew commercialization programs based on post-approval clinical trial results, changes in KVK's strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- KVK could independently develop, or develop with third parties, products that compete directly or indirectly with APADAZ if KVK believes that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- APADAZ may be viewed by KVK as competitive with its own product candidates or products, which may cause KVK to cease to devote resources to the commercialization of APADAZ;
- KVK may not commit sufficient resources to the marketing and distribution of APADAZ;
- disagreements with KVK, including disagreements over proprietary rights, contract interpretation or the preferred course of commercialization, might cause delays or termination of the commercialization of APADAZ, might lead to additional responsibilities for us with respect to APADAZ, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- KVK may not properly maintain or defend our or its intellectual property rights or may use our or its 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;
- KVK may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- the License Agreement may be terminated by KVK under specified circumstances and, if terminated, we could be required to raise additional capital to pursue further commercialization of APADAZ.

If we enter into any future collaborations we will face similar risks with any future collaborators as well.

The License Agreement and any other collaboration agreement we may enter into may not lead to commercialization of APADAZ or development or commercialization of our product candidates in the most efficient manner or at all. If KVK or a 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 for our product candidates, we may have to alter our development and commercialization plans.

Our prodrug development programs and the potential commercialization of our product candidates, if approved, will require substantial additional capital. For some of our product candidates, we may need to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we are currently evaluating potential commercial partners for our ADHD assets.

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 the subject product candidate, the costs and complexities of manufacturing and delivering 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 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 our product candidates or reduce the scope of any sales or marketing activities of our product candidates, or increase our expenditures and undertake development or commercialization activities at our own expense of 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 our product candidates to market and generate product revenue.

Provisions in our agreements with Takeda and Aquestive may inhibit our ability to enter into future collaborations with third parties.

We have granted Takeda a right of first refusal to acquire, license or commercialize KP415 and KP484. The right of first refusal may be exercised by Takeda for a period of 30 business days following Takeda'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 Aquestive that may limit the value of any sale, license or commercialization of KP415, KP484 or KP879. Under this termination agreement, Aquestive has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415, KP484 or KP879, and any product candidates arising therefrom, including royalty payments on any license of KP415, KP484 or KP879, the sale of KP415, KP484 or KP879 to a third party or the commercialization of KP415, KP484 or KP879.

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 Agreement, 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 of our product candidates. For instance, Deerfield consented to our entry into the License Agreement, but we cannot guarantee that Deerfield will consent to any future collaboration agreement for commercialization of APADAZ outside of the United States or for the development or commercialization of any of 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 proprietary LAT 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. As part of the License Agreement, KVK obtained from us an exclusive license to certain patents that cover APADAZ.

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 and/or from 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 proprietary LAT 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 proprietary LAT 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.

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 or copyrights 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 registered trademarks for APADAZ and KemPharm. In addition, we have solicited and applied for trademarks for the KemPharm Logo, LAT and several potential tradenames and logos for KP415. 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 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 Partnered Product and Product Candidates

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, if approved, we may not be successful in commercializing 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 any product candidate for which 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. While we entered into the License Agreement to establish a collaboration for the commercialization of APADAZ, we may not choose to enter into a collaboration for any future approved product. 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 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 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 any product candidates that we develop, ourselves. For instance, under the License Agreement, we and KVK will share the quarterly net profits of APADAZ by KVK in the United States at specified tiered percentages, with the portion we receive ranging from 30% to 50% of net profits. As a result, we will be entitled to a smaller portion of the net profits of any sales of APADAZ in the United States than if we had decided to sell, market and distribute APADAZ ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates in the future, or may be unable to do so on terms that are favorable to us, including as a result of restrictions in the Deerfield Facility Agreement. We likely will have little control over such third parties, including KVK, 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, including KVK, 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, they may not generate significant product revenue and we may not become profitable. For instance, under the License Agreement, we are entitled to milestone and royalty payments only if APADAZ sales in the United States are above specified levels. If APADAZ does not achieve an adequate level of market acceptance, it is unlikely that sales will satisfy these thresholds and we may not be entitled to any payments under the License Agreement. 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.

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 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 or our collaborators 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.

The successful commercialization of APADAZ and any of our product candidates 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 under the License Agreement, or commercialize 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 the ability to sell APADAZ under the License Agreement, or our ability to sell any of 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 APADAZ, and any prodrug products that may be approved in the future, are commercialized. This includes the risk that our products may be misused. For example, APADAZ does, and we anticipate that any other opioid product candidates we may choose to develop in the future, 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 our product candidates or products caused injuries, we will incur substantial liabilities on behalf of ourselves. 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 successfully 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 upon commencement of commercialization of any 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 or our collaborators fail to comply with regulatory requirements or if we or our collaborators 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. Under the License Agreement, KVK will be responsible for these regulatory activities going forward, and we cannot guarantee they will be complied with. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, payment of substantial annual product program 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. For example, in September 2018, the FDA approved the Opioid Analgesic REMS for ER/LA and IR opioids as one strategy among multiple national and state efforts to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics. APADAZ is subject to this REMS, and we anticipate that any of our other opioid product candidates that we may choose to develop in the future, if approved by the FDA, are likely to also be subject to a REMS requirement.

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 boxed 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 boxed 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 products 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;

- the Health Insurance Portability and Accountability Act, or 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 the Health Information Technology for Economic and Clinical Health Act of 2009 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 Affordable Care Act, or 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 increase the cost to commercialize APADAZ and any of our product candidates that may be approved in the future and affect the prices thereof.

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 the ability to profitably sell APADAZ under the License Agreement and our ability to profitably sell 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 70% commencing 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 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 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. 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, and Sven Guenther, Ph.D., our executive vice president research and development, 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 candidate 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 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.

If we implement sales, marketing and distribution capabilities, we may encounter difficulties in managing our growth, which could disrupt our operations.

If we implement sales, marketing and distribution capabilities to support any future approved product, we would experience growth in the number of our employees and the scope of our operations. To manage such potential future growth, we would need to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel.

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, if any, 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 $1.72 to $26.15 through February 28, 2019. 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. In June 2018, the case was dismissed without prejudice to members of the putative class. Further 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. In September 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 our 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.

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 Convertible 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 Convertible Note became convertible into shares of our common stock at a conversion price of $5.85 per share. The Deerfield Warrant and Deerfield Convertible 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 Convertible 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 and seventh amendments to the Deerfield Warrant and Deerfield Convertible 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 Convertible 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, provided that this anti-dilution adjustment will not apply to any sales made under the Purchase Agreement or Second ATM Agreement.

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.

We previously issued to Deerfield the Deerfield Convertible Note in the original principal amount of $10.0 million. The Deerfield Convertible 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 Convertible Note into shares of our common stock at a conversion price of $5.85 per share. For instance, in June 2018, $3,333,333 of the principal amount, plus $168,287 of accrued interest, of the Deerfield Convertible Note was converted into 598,568 shares of our common stock.

According to the terms of the Deerfield Convertible Note, as amended, in no event may Deerfield convert the Deerfield Convertible Note to the extent such conversion would result in Deerfield beneficially owning more than 4.985% 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 Convertible Note into a limited number of shares due to this conversion limitation, the Deerfield Convertible 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 Convertible Note is convertible into 1,167,607 shares of our common stock, assuming a conversion date of December 31, 2018. The conversion price of the Deerfield Convertible 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 Convertible 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 Convertible 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, provided that this anti-dilution adjustment will not apply to any sales made under the Purchase Agreement or Second ATM Agreement.

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. In November 2018, we entered into a supplemental indenture with U.S. Bank National Association, as trustee, to that certain Indenture, dated as of February 9, 2016, relating to our 2021 Notes. Pursuant to the supplemental indenture, the Indenture was amended to allow each Holder, as defined in the Indenture, or any beneficial holder of any 2021 Notes to, at its option, elect a limit on beneficial ownership as to such Holder or beneficial owner, but not as to any other Holder or beneficial owner, that is less than or equal to the 9.985% Cap, as defined in the Indenture, or any other limit previously elected and then applicable to such Holder or beneficial owner upon written notice delivered to us at least three business days prior to the date of effectiveness of such beneficial ownership limit, or such shorter period as may be agreed upon by the us, specifying the percentage of shares of our common stock outstanding for the beneficial ownership limit that shall apply to such Holder or beneficial owner. Without regard to this conversion limitation, the 2021 Notes are convertible into 4,481,182 shares of our common stock, assuming a conversion date of December 31, 2018.

In October 2018, we entered into the Exchange Agreement with Deerfield and Deerfield Special Situations Fund, L.P. Under the Exchange Agreement, Deerfield and Deerfield Special Situations Fund, L.P. exchanged an aggregate of $9,577,000 principal amount of our 2021 Notes for an aggregate of 9,577 shares of our Series A Preferred Stock. Each share of Series A Preferred Stock has an aggregate stated value of $1,000 and is convertible into shares of our common stock at a price equal to $3.00 per share (subject to adjustment to reflect stock splits and similar events). Immediately following the exchange, an aggregate of 3,192,334 shares of common stock were issuable upon conversion of the Series A Preferred Stock. The Series A Preferred Stock is convertible at any time at the option of the holders thereof, provided that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such holder (together with certain affiliates and “group” members) would beneficially own more than 4.985% of the total number of shares of common stock then issued and outstanding. As of February 28, 2019, 6,240 shares of Series A Preferred Stock have been converted into 2,080,000 shares of common stock.

If Deerfield, the holders of the 2021 Notes or the holders of Series A Preferred Stock elect to convert more of the Deerfield Convertible Note, the 2021 Notes or additional shares of Series A Preferred Stock, 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.

In September 2018, we entered into the Second ATM Agreement with RBCCM 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 RBCCM as our sales agent. RBCCM may sell common stock under the Second 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. RBCCM 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 RBCCM to make any sales of our common stock under the Second ATM Agreement, our stockholders may experience additional dilution, which could cause our stock price to fall. As of February 28, 2019, we have not sold any shares of common stock under the Second ATM Agreement.

In February 2019, we entered into the Purchase Agreement with Lincoln Park which provides that, upon the terms and subject to the conditions and limitations set forth therein, we may sell to Lincoln Park up to $15.0 million of shares of our common stock, from time to time over the 36-month term of the Purchase Agreement, and we shall issue an additional 120,200 shares of our common stock to Lincoln Park as commitment shares under the Purchase Agreement. Concurrently with entering into the Purchase Agreement, we also entered into the Registration Rights Agreement, pursuant to which we agreed to register the sale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to our existing shelf registration statement on Form S-3 or a new registration statement. We have yet to make any sales under the Purchase Agreement, but are obligated to issue 120,200 commitment shares to Lincoln Park upon satisfaction of the closing conditions contained in the Purchase Agreement.

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

As of December 31, 2018, we had $83.4 million of convertible notes outstanding, consisting of the $6.7 million of the Deerfield Convertible Note and $76.7 million of the 2021 Notes.

The Deerfield Convertible Note bears interest at 9.75% per annum. Interest accrued on outstanding debt under the Deerfield Convertible 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 Convertible 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 Convertible Note on the fourth and fifth anniversaries of the Deerfield Convertible Note. We are then obligated to repay the balance of the outstanding principal amount of the on February 14, 2020. The payment due June 2, 2018 was paid via the conversion of $3,333,333 of the principal amount, plus $168,288 of accrued interest, of the Deerfield Convertible Note into 598,568 shares of our common stock. We cannot guarantee that Deerfield will agree to convert any future principal amount owed under the Deerfield Convertible Note into shares of our common stock. If we are required to pay additional outstanding amounts due under the Deerfield Convertible Note prior to or at maturity or otherwise incur unanticipated monetary obligations under the Deerfield Convertible 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. In October 2018, we entered into the Exchange Agreement pursuant to which Deerfield and Deerfield Special Situations Fund, L.P. exchanged an aggregate of $9,577,000 principal amount of the 2021 Notes for an aggregate of 9,577 shares of Series A Preferred Stock. Following the effectiveness of such exchange, the outstanding principal amount of the 2021 Notes is $76.7 million. 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 Agreement 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 Convertible Note, 2021 Notes and the warrant we issued to KVK under the License Agreement could have a material effect on our reported financial results.

The Deerfield Warrant, Deerfield Convertible Note, 2021 Notes and the warrant we issued to KVK under the License Agreement 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.

Deerfield has the right, subject to some conditions, to require us to file one or more registration statements covering its shares of our common stock, including shares issues or issuable upon conversion or exercise of the Deerfield Convertible Note and Deerfield Warrant, as applicable, or to include such 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 Aquestive and our agreements with Deerfield, the holders of our 2021 Notes and the holders of our Series A Preferred Stock 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 Aquestive 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, KP484 or KP879. Pursuant to the Deerfield Facility Agreement, 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 Convertible Note, Deerfield has the option to demand repayment of all outstanding principal, and any unpaid interest accrued thereon, of the Deerfield Convertible 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. Finally, in the event of a sale of the Company the holders of Series A Preferred Stock will share ratably in any distribution of our assets or other proceeds with holders of common stock on an as-converted basis without giving effect to any limitation on conversion of the Series A Preferred Stock. This would in turn reduce the distribution to the holders of our common stock in such change of control.

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 IPO, (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, 2018, we had federal net operating loss carryforwards of approximately $138.1 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. On December 22, 2017, 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). Under the Tax Cuts and Jobs Act, U.S. federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. To the extent that we continue to generate taxable losses in the United States, unused losses will carry forward to offset future taxable income (subject to any applicable limitations), if any. In addition, under Section 382 and Section 383 of the Code, 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.

The Tax Cuts and Jobs Act 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. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. 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, 2018, 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 Agreement, 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 approximately 17,000 square feet of headquarters 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 laboratory space in Coralville, Iowa and Blacksburg, Virginia. We believe that our facilities are adequate for our current needs.

ITEM 3. LEGAL PROCEEDINGS

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. We believe there is no litigation pending that would reasonably be expected to, individually or in the aggregate, 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

Common Stock Listing

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.

Holders of our Common Stock

As of February 28, 2019, we had 137 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 Agreement 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 proprietary LAT technology. We utilize our proprietary LAT technology to generate improved prodrug versions of drugs approved by the FDA, as well as to generate prodrug compounds of existing compounds that may have applications for new disease indications. Our product candidate pipeline is focused on the high need areas of ADHD and SUD. Our co-lead clinical development candidates, KP415 and KP484, are both based on a prodrug of d-methylphenidate, but with differing ER effect profiles for the treatment of ADHD. In addition, we have received FDA approval for APADAZ, an IR combination product of benzhydrocodone, our prodrug of hydrocodone, and APAP, 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.

To date, we have not generated any revenue. We have incurred operating losses since our inception and, as of December 31, 2018, had an accumulated deficit of $221.2 million. Our losses from operations for the years ended December 31, 2018 and 2017 were $55.9 million and $33.4 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 any of our product candidates for which we may obtain future 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 any other product candidates for which we obtain regulatory approval. In October 2018, we entered into the License Agreement with KVK pursuant to which we granted an exclusive license to KVK to commercialize APADAZ in the United States, we cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. We also do not know when, if ever, any other product candidate will be commercially available or if we will be successful in finding any commercial partners for our ADHD assets.

Our recurring operating losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. We have no current source of revenues to sustain our present activities. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations. The perception of our inability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees. 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

License Agreement

In October 2018, we entered into the License Agreement with KVK pursuant to which we have granted an exclusive license to KVK to conduct regulatory activities for, manufacture and commercialize APADAZ in the United States.

Pursuant to the License Agreement, KVK has agreed to pay us pre-launch payments and cost reimbursements of an estimated $3.4 million, which includes a pre-launch payment of $2.0 million within 10 days of the achievement of a specified milestone related to the initial formulary adoption of APADAZ, or the Initial Adoption Milestone. In addition, KVK has agreed to make additional payments to us upon the achievement of specified sales milestones of up to $53.0 million in the aggregate. Further, we and KVK will share the quarterly net profits of APADAZ by KVK in the United States at specified tiered percentages, ranging from us receiving 30% to 50% of net profits, based on the amount of net sales on a rolling four quarter basis. We are responsible for a portion of commercialization and regulatory expenses for APADAZ until the Initial Adoption Milestone is achieved, after which KVK will be responsible for all expenses incurred in connection with commercialization and maintaining regulatory approval in the United States.

The License Agreement will terminate on the later of the date that all of the patent rights for APADAZ have expired in the United States or KVK's cessation of commercialization of APADAZ in the United States. KVK may terminate the License Agreement upon 90 days written notice if a regulatory authority in the United States orders KVK to stop sales of APADAZ due to a safety concern. In addition, after the third anniversary of the License Agreement, KVK may terminate the Agreement without cause upon 18 months prior written notice. We may terminate the License Agreement if KVK stops conducting regulatory activities for or commercializing APADAZ in the United States for a period of six months, subject to specified exceptions, or if KVK or its affiliates challenge the validity, enforceability or scope of any licensed patent under the License Agreement. Both parties may terminate the License Agreement (i) upon a material breach of the License Agreement, subject to a 30-day cure period, (ii) the other party encounters bankruptcy or insolvency or (iii) if the Initial Adoption Milestone is not achieved. Upon termination, all licenses and other rights granted by us to KVK pursuant to the License Agreement would revert to us.

The License Agreement also establishes a joint steering committee, which will monitor progress in the development and commercialization of APADAZ.

JMI Agreement

In November 2009, we entered into the Supply Agreement with JMI, whereby JMI has agreed to supply us with all the benzhydrocodone 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 benzhydrocodone. In exchange, we issued shares of our common stock to JMI, provided that the commercial supply arrangement for benzhydrocodone would be exclusive to JMI in the United States and agreed to pay JMI royalties on the net sales of any products that utilize benzhydrocodone 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 contains benzhydrocodone.

We are responsible for all costs of any benzhydrocodone manufactured during a specified validation process for APADAZ. After completion of the validation process, but prior to the commercial launch of any products that utilize benzhydrocodone as the API, JMI will manufacture batches of benzhydrocodone 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 benzhydrocodone at a price equal to JMI's fully allocated manufacturing cost after commercial launch of APADAZ.

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

The term of the supply agreement extends as long as we hold a valid and enforceable patent for benzhydrocodone or until the tenth anniversary of the commercial launch of any product that utilizes benzhydrocodone 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.

Other Third-Party Agreements

Under our March 2012 asset purchase agreement with Shire, Shire has a right of first refusal to acquire, license or commercialize KP415 and KP484. In early 2019, Shire was acquired by Takeda and now holds this right of first refusal.

Under our March 2012 termination agreement with Aquestive, Aquestive has the right to receive an amount equal to a percentage in the low teens of any value generated by KP415, KP484 or KP879, and any product candidates arising therefrom, including royalty payments on any license of KP415, KP484 or KP879, the sale of KP415, KP484 or KP879 to a third party, the commercialization of KP415, KP484 or KP879 and the portion of any consideration that is attributable to the value of KP415, KP484 or KP879 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. Our commercial revenue, if any, will be derived from sales of APADAZ or any other product candidates for which we obtain regulatory approval. In October 2018, we entered into the License Agreement, with KVK, pursuant to which we granted an exclusive license to KVK to commercialize APADAZ in the United States. We cannot guarantee that KVK will be able to successfully commercialize APADAZ or that we will ever receive any payments under the License Agreement from commercial sales of APADAZ. We also do not know when, if ever, any other product candidate will be commercially available. If KVK fails to successfully commercialize APADAZ or if we are unable to 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, 2018 and 2017 (in thousands):

	Year Ended December 31,	
	2018	**2017**
Outsourced development costs directly identified to programs:		
KP415	$ 28,798	$ 10,116
KP484	195	153
APADAZ	4,150	956
Total outsourced development costs directly identified to programs	33,143	11,225
Research and development costs not directly identified to programs:		
Personnel costs including cash compensation, benefits and stock-based compensation	6,244	6,069
Facilities costs	473	456
Other costs	1,899	2,843
Total research and development costs not directly identified to programs	8,616	9,368
Total research and development costs	$ 41,759	$ 20,593

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 consisted of severance payments and stock-based compensation paid to our former executive vice president, government and public relations who resigned in August 2018. 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 gain on extinguishment of debt for the year ended December 31, 2018, related to the exchange of $9.6 million of principal on the 2021 Notes for Series A Preferred Stock in October 2018. These items are unrelated to our core business and thus are recognized as other (expense) income in our statements of operations.

Income Tax Benefit

Income tax benefit 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, 2018 and 2017 (in thousands):

	Year Ended December 31,		Period-to-Period Change
	2018	2017	
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	41,759	20,593	21,166
General and administrative	12,508	12,773	(265)
Severance expense	1,636	—	1,636
Total operating expenses	55,903	33,366	22,537
Loss from operations	(55,903)	(33,366)	(22,537)
Other (expense) income:			
Gain on extinguishment of debt	2	—	2
Interest expense related to amortization of debt issuance costs and discount	(1,618)	(1,561)	(57)
Interest expense on principal	(5,469)	(5,776)	307
Fair value adjustment related to derivative and warrant liability	5,976	(3,091)	9,067
Interest and other income, net	420	365	55
Total other (expense) income	(689)	(10,063)	9,374
Loss before income taxes	(56,592)	(43,429)	(13,163)
Income tax benefit	126	43	83
Net loss	$ (56,466)	$ (43,386)	$ (13,080)

Net Loss

Net loss for the year ended December 31, 2018 was $56.5 million, an increase of $13.1 million compared to net loss for the year ended December 31, 2017 of $43.4 million. The increase was primarily attributable to an increase in loss from operations of $22.5 million, partially offset by a change in fair value adjustment of $9.1 million, from non-cash expense in prior period to non-cash income in current period, related changes in the derivative and warrant liability and an increase in net interest expense and other items of $0.4 million.

Research and Development

Research and development expenses increased by $21.2 million, from $20.6 million for the year ended December 31, 2017, to $41.8 million for the year ended December 31, 2018. This increase was primarily attributable to an increase in net third-party research and development costs primarily related to our clinical trials for KP415 and validation costs for APADAZ.

General and Administrative

General and administrative expenses decreased by $0.3 million, from $12.8 million for the year ended December 31, 2017, to $12.5 million for the year ended December 31, 2018. This decrease was primarily attributable to a decrease in general and administrative costs related to overhead.

Severance Expense

Severance expense of $1.6 million was recognized for the year ended December 31, 2018 due to the resignation of our executive vice president, government and public relations in August 2018. Severance expense is comprised of $0.4 million of severance payments and $1.2 million of stock compensation expense related to the acceleration of vesting on certain stock options upon termination. We had no severance expense for the year ended December 31, 2017.

Other (Expense) Income

Other (expense) income decreased by $9.4 million, from expense of $10.1 million for the year ended December 31, 2017, to expense of $0.7 million for the year ended December 31, 2018. This period-to-period decrease in expense was primarily attributable to the change in the fair value adjustment from non-cash expense to non-cash income related to our derivative and warrant liability.

Liquidity and Capital Resources

Sources of Liquidity

Through December 31, 2018, we have funded our research and development and operating activities primarily through the issuance of debt, private placements of redeemable convertible preferred stock and the sale of common stock in our IPO, at-the-market offering and underwritten public offerings. As of December 31, 2018, we had cash and cash equivalents of $18.4 million, restricted cash of $0.7 million and marketable securities of $3.3 million. We completed our IPO in 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.

In October 2016, we entered into a Common Stock Sales Agreement, or First ATM Agreement, with Cowen. In September 2018, we terminated the First ATM Agreement. Prior to termination of the First ATM Agreement, we sold an aggregate of 762,338 shares of our common stock under the First ATM Agreement resulting in gross proceeds of $4.9 million.

In September 2018, we entered into the Second ATM Agreement with RBCCM 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 RBCCM as our sales agent. The registration statement on Form S-3 contemplated under the Second ATM Agreement includes a prospectus supplement covering the offering of up to $50,000,000 of shares of common stock in accordance with the Second ATM Agreement. As of February 28, 2019, we have not sold any shares of common stock under the Second ATM Agreement.

In October 2018, we entered into an underwriting agreement with RBCCM pursuant to which we sold 8,333,334 shares of our common stock in an underwritten public offering pursuant to our registration statement on Form S-3. Our net proceeds from the offering were approximately $23.1 million after deducting underwriting discounts and commissions and estimated offering expenses.

In February 2019, we entered into the Purchase Agreement with Lincoln Park which provides that, upon the terms and subject to the conditions and limitations set forth therein, we may sell to Lincoln Park up to $15.0 million of shares of our common stock from time to time over the 36-month term of the Purchase Agreement, and we shall issue an additional 120,200 shares of our common stock to Lincoln Park as commitment shares under the Purchase Agreement. Concurrently with entering into the Purchase Agreement, we also entered into the Registration Rights Agreement, pursuant to which we agreed to register the sale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to our existing shelf registration statement on Form S-3 or a new registration statement.

We have filed a shelf registration statement on Form S-3 with the SEC. After we file this Annual Report on Form 10-K, in order to issue securities under this registration statement, we must rely on Instruction I.B.6. of Form S-3, which imposes a limitation on the maximum amount of securities that we may sell pursuant to the registration statement during any twelve-month period. At the time we sell securities pursuant to the registration statement, the amount of securities to be sold plus the amount of any securities we have sold during the prior twelve months in reliance on Instruction I.B.6. may not exceed one-third of the aggregate market value of our outstanding common stock held by non-affiliates as of a day during the 60 days immediately preceding such sale, as computed in accordance with Instruction I.B.6. This calculation will be updated immediately after we file this Annual Report on Form 10-K and we expect that the amount of securities we will be able to sell under the registration statement on Form S-3 thereafter will be approximately $18.5 million, of which we anticipate filing prospectus supplements to register (i) approximately $15.3 million for sales under the Purchase Agreement; and (ii) approximately $3.2 million for sales under our Second ATM Agreement. Based on this calculation, we expect that we will be unable to sell additional securities pursuant to our effective registration statement on Form S-3 for a period of twelve months, unless and until the market value of our outstanding common stock held by non-affiliates increases significantly.

We have incurred operating losses since our inception and, as of December 31, 2018, had an accumulated deficit of $221.2 million. We anticipate that we will continue to incur operating losses for at least the next several years. Our recurring operating losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. We have no current source of revenues to sustain our present activities. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations. The perception of our inability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees. 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.

Convertible Debt

As of December 31, 2018, we had $83.4 million of convertible notes outstanding, consisting of the Deerfield Convertible Note, in the principal amount of $6.7 million and the 2021 Notes, in the aggregate principal amount of $76.7 million.

Deerfield Facility Agreement

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. We used approximately $18.6 million of the net proceeds from the offering of 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 Convertible 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 Agreement, 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.

In June 2018, we entered into an amendment to the Deerfield Convertible Note with Deerfield, which, among other things, provided that (i) $3,333,333 of the principal amount, plus $168,288 of accrued interest, of the Deerfield Convertible Note was converted into 598,568 shares of our common stock, with such principal conversion amount being applied against and in full satisfaction of the amortization payment due June 2, 2018; (ii) Deerfield waived specified rights under the Deerfield Facility Agreement with regards to such principal and interest amount; and (iii) specified provisions of the Deerfield Convertible Note were amended as they relate to the delivery of shares of our common stock in connection with any conversion of the Deerfield Convertible Note.

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, or Series D Preferred, as consideration for the loans provided to us thereunder. Upon closing of our IPO, these shares of Series D Preferred 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 Preferred 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 Convertible 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 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 RBCCM 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.

2021 Note Exchange

In October 2018, we entered into an exchange agreement, or the Exchange Agreement, with Deerfield and Deerfield Special Situations Fund, L.P. Under the Exchange Agreement, Deerfield and Deerfield Special Situations Fund, L.P. exchanged an aggregate of $9,577,000 principal amount of our 2021 Notes for an aggregate of 9,577 shares of our Series A Convertible Preferred Stock, par value $0.0001, or the Series A Preferred Stock.

As a condition to closing of the Exchange Agreement, we filed a Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock, or the Certificate of Designation, with the Secretary of State of the State Delaware, setting forth the preferences, rights and limitations of the Series A Preferred Stock.

Each share of Series A Preferred Stock has an aggregate stated value of $1,000 and is convertible into shares of our common stock at a price equal to $3.00 per share (subject to adjustment to reflect stock splits and similar events). Immediately following the exchange, an aggregate of 3,192,334 shares of common stock were issuable upon conversion of the Series A Preferred Stock. The Series A Preferred Stock is convertible at any time at the option of the holders thereof, provided that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such holder (together with certain affiliates and “group” members) would beneficially own more than 4.985% of the total number of shares of common stock then issued and outstanding. The Series A Preferred Stock is not redeemable. In the event of our liquidation, dissolution or winding up, the holders of Series A Preferred Stock will receive an amount equal to $0.0001 per share, plus any declared but unpaid dividends, and thereafter will share ratably in any distribution of our assets with holders of common stock on an as-converted basis. With respect to rights upon liquidation, the Series A Preferred Stock ranks senior to the common stock and junior to existing and future indebtedness. Except as otherwise required by law (or with respect to approval of certain actions involving our organizational documents that materially and adversely affect the holders of Series A Preferred Stock), the Series A Preferred Stock does not have voting rights. The Series A Preferred Stock is not subject to any price-based anti-dilution protections and does not provide for any accruing dividends, but provides that holders of Series A Preferred Stock will participate in any dividends on the common stock on an as-converted basis (without giving effect to the limitation on conversion described above). The Certificate of Designation also provides for partial liquidated damages in the event that we fail to timely convert shares of Series A Preferred Stock into common stock in accordance with the Certificate of Designation.

As of February 28, 2019, 6,240 shares of Series A Preferred Stock have been converted into 2,080,000 shares of common stock.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31,	
	2018	2017
Net cash used in operating activities	$ (54,203)	$ (33,100)
Net cash provided by investing activities	33,332	27,412
Net cash provided by (used in) financing activities	28,019	(203)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 7,148	$ (5,891)

Operating Activities

For the year ended December 31, 2018, net cash used in operating activities of $54.2 million consisted of a net loss of $56.5 million, primarily attributable to our spending on research and development programs, and $2.3 million in changes in working capital, partially offset by $4.5 million in adjustments for non-cash items. The changes in working capital consisted of $1.6 million related to an increase in accounts payable and accrued expenses, $0.5 million related to an increase in prepaid expenses and other assets and $0.1 million related to other liabilities. The adjustments for non-cash items primarily consisted of stock-based compensation expense of $6.5 million, non-cash interest expense of $2.1 million, amortization of debt issuance costs and debt discount of $1.6 million and $0.3 million related to depreciation, amortization and other items, partially offset by non-cash income related to the change in the fair value of our derivative and warrant liabilities of $6.0 million.

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.

Investing Activities

For the year ended December 31, 2018, net cash provided by investing activities was $33.3 million, which was primarily attributable to maturities of marketable securities of $33.4 million, partially offset by purchases of property and equipment of $0.1 million.

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

Financing Activities

For the year ended December 31, 2018, net cash provided by financing activities was $28.0 million. This consisted of proceeds from the issuance of common stock under the underwritten public offering in October 2018, net of commissions, of $23.5 million, proceeds from the issuance of common stock under the First ATM agreement, net of commissions, of $4.8 million and proceeds from the exercise of common stock options of $0.1 million, partially offset by repayment of $0.2 million of obligations under capital lease arrangements and payment of $0.2 million of deferred offering costs.

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.

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 unless our License Agreement with KVK produces such revenue and/or we obtain regulatory approval of and commercialize one of our product candidates. While we have entered into the License Agreement to commercialize APADAZ in the United States, we cannot guarantee that this, or any commercialization strategy we adopt in the future, 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 our product candidates that achieve regulatory approval. We anticipate that we will need substantial additional funding in connection with our continuing operations.

The auditor's opinion on our audited financial statements for the year ended December 31, 2018, includes an explanatory paragraph stating that our recurring losses, negative operating cash flows and stockholders' deficit raise substantial doubt about our ability to continue as a going concern. We have no current source of revenues to sustain our present activities. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations. The perception of our inability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees. 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.

Based upon our current operating plan, existing cash resources as of December 31, 2018 are expected to be sufficient to fund operating expense and capital investment requirements into, but not through, the third 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 and we cannot guarantee that we will be able to generate sufficient proceeds from the License Agreement, sales under our Purchase Agreement or Second ATM Agreement or other funding transactions to fund our operating expenses. To meet any additional cash requirements, we may seek to sell additional equity or convertible securities that may result in dilution to our stockholders, issue additional debt or seek other third-party funding, including potential strategic transactions, such as licensing or collaboration arrangements. 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.

We have filed a shelf registration statement on Form S-3 with the SEC. After we file this Annual Report on Form 10-K, in order to issue securities under this registration statement, we must rely on Instruction I.B.6. of Form S-3, which imposes a limitation on the maximum amount of securities that we may sell pursuant to the registration statement during any twelve-month period. At the time we sell securities pursuant to the registration statement, the amount of securities to be sold plus the amount of any securities we have sold during the prior twelve months in reliance on Instruction I.B.6. may not exceed one-third of the aggregate market value of our outstanding common stock held by non-affiliates as of a day during the 60 days immediately preceding such sale, as computed in accordance with Instruction I.B.6. This calculation will be updated immediately after we file this Annual Report on Form 10-K and we expect that the amount of securities we will be able to sell under the registration statement on Form S-3 thereafter will be approximately $18.5 million, of which we have we anticipate filing prospectus supplements to register (i) approximately $15.3 million for sales under the Purchase Agreement; and (ii) approximately $3.2 million for sales under our Second ATM Agreement. Based on this calculation, we expect that we will be unable to sell additional securities pursuant to our effective registration statement on Form S-3 for a period of twelve months, unless and until the market value of our outstanding common stock held by non-affiliates increases significantly.

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 our product candidates;
- the costs and timing of commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of APADAZ under the License Agreement and commercial sales of any other 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 for which we receive payment under the License Agreement or other sales of our 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 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,	
	2018	**2017**
Research and development	$ 1,608	$ 1,304
General and administrative	3,651	3,258
Severance expense	1,236	—
Total stock-based compensation expense	$ 6,495	$ 4,562

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 grant date 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,	
	2018	**2017**
Risk-free interest rate	2.43% - 2.91%	1.88% - 2.26%
Expected term (in years)	5.50 - 6.79	5.12 - 7.00
Expected volatility	83.10% - 85.05%	85.35% - 95.08%
Expected dividend yield	0%	0%

Based upon the stock price of $1.78 per share, which is the last sale price of our common stock reported on The Nasdaq Global Market as of December 31, 2018 outstanding options to purchase shares of our common stock as of December 31, 2018 had no intrinsic value; and the aggregate intrinsic value of outstanding options to purchase shares of our common stock as of December 31, 2017, was $472,000, of which $29,000 related to vested options and $443,000 related to unvested 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 issued to Deerfield, put options embedded within those Deerfield warrants, fundamental change and make-whole interest provisions embedded within our convertible notes, a conversion feature within the Deerfield Convertible Note and a common stock warrant issued to KVK that meet the definition of derivative financial instruments and are accounted for as derivatives. The fair value of the common stock warrants issued to Deerfield, put options embedded within those Deerfield warrants, fundamental change and make-whole interest provisions embedded within our convertible notes and the conversion feature within the Deerfield Convertible Note are based on Monte Carlo simulations, while the common stock warrant issued to KVK is valued using a probability-weighted Black-Scholes option pricing model. These derivatives are fair valued at each reporting period.

The derivative liability for the Deerfield common stock warrants was $1.6 million and $5.1 million at December 31, 2018 and 2017, respectively. The derivative liability for the put options embedded within the Deerfield common stock warrants was $0.2 million and $0.4 million at December 31, 2018 and 2017, respectively. The derivative liability for the fundamental change and make-whole interest provisions embedded within our convertible notes had no value and was $14,000 at December 31, 2018 and 2017, respectively. The conversion feature within the Deerfield Convertible Note was $0.1 million and $2.2 million at December 31, 2018 and 2017, respectively. The derivative liability for the KVK common stock warrant was $0.3 million at December 31, 2018 and had no value as of December 31, 2017 since the KVK common stock warrant was issued in October 2018. A 10% increase in the enterprise value would result in an increase of $0.2 million in the estimated fair value of the Deerfield common stock warrants, an increase of $19,000 in the estimated fair value of the put options embedded within the Deerfield common stock warrants, no change in the estimated fair value of the fundamental change and make-whole interest provisions embedded within our convertible notes, an increase of $29,000 million in the estimated fair value of the conversion feature within the Deerfield Convertible Note and an increase of $37,000 in the estimated fair value of the KVK common stock warrant at December 31, 2018.

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, 2018, we had federal net operating loss, or NOL, carryforwards of approximately $138.1 million with expiration dates from 2027 to 2037 and $56.1 million with no expiration. We also had research and development credit carryforwards of $3.8 million with expiration dates ranging from 2027 to 2037 and $1.9 million with no expiration.

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 amended the guidance in former ASC 605, *Revenue Recognition*, and became effective January 1, 2018. This guidance did not have a material impact on our financial statements and disclosures upon adoption since we were are not generating revenue at this time.

In January 2016, the FASB issued Accounting Standards Update, or 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 was effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The adoption of ASU 2016-01 did not have a material impact on our financial statements and disclosures.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic* 842*)*, or ASU 2016-02, which requires lessees to recognize operating and finance lease liabilities and corresponding right-of-use assets on the balance sheet and to provide enhanced disclosures surrounding the amount, timing and uncertainty of cash flows arising from leases. We lease office space and laboratory facilities under non-cancelable operating leases. In addition, we lease various laboratory equipment, furniture and office equipment and leasehold improvements that are accounted for as capital leases. We will adopt the new standard effective January 1, 2019 on a modified retrospective basis and will not restate comparative periods. We will elect the package of practical expedients permitted under the transition guidance, which allows us to carryforward our historical lease classification and our assessment on whether a contract is or contains a lease for any leases that exist prior to adoption of the new standard. We will also elect to combine lease and non-lease components and to keep leases with an initial term of 12 months or less off the balance sheet and recognize the associated lease payments in the statements of operations on a straight-line basis over the lease term. We estimate the adoption of this new standard to result in the recognition of total right-of-use assets and total lease liabilities of approximately $3.0 million on our balance sheet as of January 1, 2019.

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. The adoption of ASU 2016-15 did not have a material impact on our financial statements and disclosures.

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. The adoption of ASU 2017-09 did not have a material impact on our financial statements and disclosures.

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. ASU 2017-11 will not material effect on our financial statements and disclosures upon adoption.

In June 2018, the FASB issued ASU 2018-07, *Compensation – Stock Compensation (Topic 820) – Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07, which simplifies several aspects of the accounting for nonemployee share-based payment transactions resulting from expanding the scope of Topic 718, Compensation—Stock Compensation, to include share-based payment transactions for acquiring goods and services from nonemployees. This update applies to all entities that enter into share-based payment transactions for acquiring goods and services from nonemployees. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. The amendments in this ASU expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost (that is, the period of time over which share-based payment awards vest and the pattern of cost recognition over that period). The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. We do not currently expect the adoption of ASU 2018-07 to have a material impact on our financial statements and disclosures

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820) – Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, or ASU 2018-13, which modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, based on the concepts in the FASB Concepts Statement, *Conceptual Framework for Financial Reporting—Chapter 8: Notes to Financial Statements*, which the FASB finalized on August 28, 2018, including the consideration of costs and benefits. This update applies to all entities that are required, under existing U.S. generally accepted accounting principles, to make disclosures about recurring or nonrecurring fair value measurements. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted. An entity is permitted to early adopt any removed or modified disclosures and delay adoption of the additional disclosures until their effective date. We are currently evaluating the impact of the adoption of ASU 2018-13 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, 2018. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, 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, 2018, 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 2019 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 proposal with the heading “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 sheets of KemPharm, Inc. (the Company) as of December 31, 2018 and 2017, the related statements of operations, changes in stockholders' deficit and cash flows, for the years 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, 2018 and 2017, and the results of its operations and its cash flows for the years 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 and marketable securities are not sufficient to fund the Company's operating expenses and capital expenditure requirements for at least one year from the date these financial statements are issued. 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 audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

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

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

/s/ RSM US LLP

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

Orlando, Florida
March 1, 2019

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

	December 31,	
	2018	**2017**
Assets		
Current assets:		
Cash and cash equivalents	$ 18,409	$ 10,871
Marketable securities	3,260	31,358
Trade date receivables	—	2,005
Prepaid expenses and other current assets	2,052	1,662
Total current assets	23,721	45,896
Property and equipment, net	1,753	2,004
Long-term investments	—	3,250
Restricted cash	710	1,100
Other long-term assets	562	206
Total assets	$ 26,746	$ 52,456
Liabilities and stockholders' deficit		
Current liabilities:		
Accounts payable and accrued expenses	$ 8,342	$ 7,875
Current portion of convertible notes	3,333	3,333
Current portion of capital lease obligation	214	189
Other current liabilities	115	112
Total current liabilities	12,004	11,509
Convertible notes, less current portion, net	78,105	89,398
Derivative and warrant liability	2,118	7,709
Capital lease obligation, less current portion	396	562
Other long-term liabilities	689	794
Total liabilities	93,312	109,972
Commitments and contingencies (Note G)		
Stockholders' deficit:		
Preferred stock:		
Series A convertible preferred stock, $0.0001 par value, 9,578 shares authorized, 9,577 shares issued and 3,337 shares outstanding as of December 31, 2018; no shares authorized, issued or outstanding as of December 31, 2017	—	—
Undesignated preferred stock, $0.0001 par value, 9,990,422 shares authorized, no shares issued or outstanding as of December 31, 2018; 10,000,000 shares authorized, no shares issued or outstanding as of December 31, 2017	—	—
Common stock, $0.0001 par value, 250,000,000 shares authorized, 26,455,352 shares issued and outstanding as of December 31, 2018; 14,657,430 shares issued and outstanding as of December 31, 2017	3	1
Additional paid-in capital	154,623	107,209
Accumulated deficit	(221,192)	(164,726)
Total stockholders' deficit	(66,566)	(57,516)
Total liabilities and stockholders' deficit	$ 26,746	$ 52,456

See accompanying notes to financial statements

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

	Year ended December 31,	
	2018	**2017**
Revenue	$ —	$ —
Operating expenses:		
Research and development	41,759	20,593
General and administrative	12,508	12,773
Severance expense	1,636	—
Total operating expenses	55,903	33,366
Loss from operations	(55,903)	(33,366)
Other (expense) income:		
Gain on extinguishment of debt	2	—
Interest expense related to amortization of debt issuance costs and discount	(1,618)	(1,561)
Interest expense on principal	(5,469)	(5,776)
Fair value adjustment related to derivative and warrant liability	5,976	(3,091)
Interest and other income, net	420	365
Total other (expense) income	(689)	(10,063)
Loss before income taxes	(56,592)	(43,429)
Income tax benefit	126	43
Net loss	$ (56,466)	$ (43,386)
Net loss per share:		
Basic and diluted	$ (3.15)	$ (2.96)
Weighted average number of shares of common stock outstanding:		
Basic and diluted	17,930,023	14,652,898

See accompanying notes to financial statements

KEMPHARM, INC.
STATEMENTS OF CHANGES IN STOCKHOLDERS' DEFICIT
(in thousands)

	Preferred Stock					
	Series A Convertible Preferred Stock	Undesignated Preferred Stock	Common Stock	Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
Balance as of January 1, 2017	$ —	$ —	$ 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)
Net loss	—	—	—	—	(56,466)	(56,466)
Stock-based compensation expense	—	—	—	6,495	—	6,495
Issuance of common stock in connection with ATM, net of commissions	—	—	1	4,827	—	4,828
Offering expenses charged to equity	—	—	—	(554)	—	(554)
Conversion of principal and interest on Deerfield Convertible Note	—	—	—	3,502	—	3,502
Exercise of stock options	—	—	—	68	—	68
Issuance of common stock in connection with underwritten public offering, net of commissions	—	—	1	23,499	—	23,500
Conversion of principal on 2021 Notes	—	—	—	9,577	—	9,577
Balance as of December 31, 2018	$ —	$ —	$ 3	$ 154,623	$ (221,192)	$ (66,566)

See accompanying notes to financial statements

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

	Year ended December 31,	
	2018	**2017**
Cash flows from operating activities:		
Net loss	$ (56,466)	$ (43,386)
Adjustments to reconcile net loss to net cash used in operating activities:		
Gain on extinguishment of debt	(2)	—
Write-off of deferred offering costs	—	60
Stock-based compensation expense	6,495	4,562
Non-cash interest expense	2,089	2,222
Amortization of debt issuance costs and debt discount	1,618	1,561
Depreciation and amortization expense	324	336
Fair value adjustment related to derivative and warrant liability	(5,976)	3,091
Loss on sublease and disposal of fixed assets	—	104
Change in assets and liabilities:		
Prepaid expenses and other assets	(548)	(926)
Accounts payable and accrued expenses	(1,635)	(801)
Other liabilities	(102)	77
Net cash used in operating activities	(54,203)	(33,100)
Cash flows from investing activities:		
Purchases of property and equipment	(21)	(181)
Purchases of marketable securities and long-term investments	—	(27,378)
Maturities and sales of marketable securities	33,353	54,971
Net cash provided by investing activities	33,332	27,412
Cash flows from financing activities:		
Proceeds from underwritten public offering, net of commissions	23,500	—
Proceeds from at-the-market offering, net of commissions	4,828	—
Repayment of obligations under capital lease	(193)	(157)
Payment of deferred offering costs	(184)	(50)
Proceeds from exercise of common stock options and warrants	68	4
Net cash provided by (used in) financing activities	28,019	(203)
Net increase (decrease) in cash, cash equivalents and restricted cash	7,148	(5,891)
Cash, cash equivalents and restricted cash, beginning of year	11,971	17,862
Cash, cash equivalents and restricted cash, end of year	$ 19,119	$ 11,971
Supplemental cash flow information:		
Cash paid for interest	$ 5,593	$ 5,717
Trade date receivables	—	2,005
Deerfield Convertible Note principal and interest converted to common stock	3,502	—
2021 Notes principal converted to preferred stock	9,577	—
Property and equipment financed under a lease agreement	52	284
Property and equipment included in accounts payable and accrued expenses	—	3
Deferred offering costs included in accounts payable and accrued expenses	181	—

See accompanying 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 proprietary Ligand Activated Therapy ("LAT") technology. The Company utilizes its proprietary LAT technology to generate improved prodrug versions of U.S. Food and Drug Administration (the "FDA") approved drugs as well as to generate prodrug versions of existing compounds that may have applications for new disease indications. The Company's product candidate pipeline is focused on the high need areas of attention deficit hyperactivity disorder ("ADHD") and stimulant use disorder ("SUD"). 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, negative operating cash flows and has a stockholders' deficit and its existing cash and cash equivalents, restricted cash and marketable securities are not sufficient to fund the Company’s operating expenses and capital expenditure requirements for at least one year from date these financial statements are issued. The Company also has an accumulated deficit as of December 31, 2018. 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. The Company's ability to continue as a going concern may require additional financing to fund operations. The perception of the Company's inability to continue as a going concern may make it more difficult to obtain financing for the continuation of operations and could result in the loss of confidence by investors, suppliers and employees. Adequate additional financing may not be available to the Company on acceptable terms, or at all.

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 and marketable securities, 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. As of December 31, 2018, the Company had approximately $120.1 million available under its Form S-3 registration statement, of which, $50.0 million was covered under a prospectus supplement related to Second ATM Agreement (as defined below). After the Company files its Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (the “Annual Report”), in order to issue securities under registration statement, it must rely on Instruction I.B.6. of Form S-3, which imposes a limitation on the maximum amount of securities that it may sell pursuant to the registration statement during any twelve-month period. At the time it sells securities pursuant to the registration statement, the amount of securities to be sold plus the amount of any securities it has sold during the prior twelve months in reliance on Instruction I.B.6. may not exceed one-third of the aggregate market value of its outstanding common stock held by non-affiliates as of a day during the 60 days immediately preceding such sale, as computed in accordance with Instruction I.B.6. This calculation will be updated immediately after the Company’s files the Annual Report and the Company expects that the amount of securities it will be able to sell under the registration statement on Form S-3 thereafter will be approximately $18.5 million, of which it anticipates filing prospectus supplements to register (i) approximately $15.3 million for sales under the Purchase Agreement (as defined below); and (ii) approximately $3.2 million for sales under our Second ATM Agreement (as defined below). Based on this calculation, the Company expects it will be unable to sell additional securities pursuant to its effective registration statement on Form S-3 for a period of twelve months, unless and until the market value of its outstanding common stock held by non-affiliates increases significantly.

As discussed below, the Company sold shares of its common stock through an at-the-market offering and an underwritten public offering which resulted in gross proceeds of $4.9 million and $25.0 million, respectively.

Entry into First ATM Agreement

On October 3, 2016, the Company entered into a Common Stock Sales Agreement (the "First ATM Agreement") with Cowen and Company, LLC ("Cowen"). The First ATM Agreement was terminated on September 14, 2018. Prior to termination of the First ATM Agreement, the Company sold an aggregate of 762,338 shares of common stock under the First ATM Agreement resulting in gross proceeds to the Company of $4.9 million. The Company paid Cowen a commission of up to three percent (3.0%) of the gross sales proceeds for such sales of common stock. Pursuant to the terms of the First ATM Agreement, specified obligations of the parties, including the Company's indemnification obligations to Cowen, survive the termination of the First ATM Agreement.

Entry into Second ATM Agreement

On September 4, 2018, the Company entered into a Common Stock Sales Agreement (the "Second ATM Agreement") with RBC Capital Markets, LLC ("RBCCM") 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 RBCCM as its sales agent. The Company's registration statement on Form S-3 contemplated under the Second ATM Agreement was declared effective by the SEC on October 17, 2016. The registration statement on Form S-3 includes a prospectus supplement covering the offering of up to $50,000,000 of shares of common stock in accordance with the Second ATM Agreement, but as noted above the Company anticipates that due to the limitations of Instruction I.B.6 of Form S-3 it will file a prospectus supplement reducing this offering to approximately $3.2 million.

RBCCM may sell common stock under the Second 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 of 1933, as amended (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 the Company. RBCCM 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 RBCCM a commission of up to three percent (3.0%) of the gross sales proceeds of any common stock sold through RBCCM under the Second ATM Agreement, and also has provided RBCCM with customary indemnification rights.

The Company is not obligated to make any sales of common stock under the Second ATM Agreement. The offering of shares of common stock pursuant to the Second ATM Agreement will terminate upon the earlier of (i) the sale of all common stock subject to the Second ATM Agreement, or (ii) termination of the Second ATM Agreement in accordance with its terms. As of December 31, 2018, the Company has not sold any shares of common stock under the Second ATM Agreement.

Underwritten Public Offering

On October 5, 2018, the Company entered into an underwriting agreement (the "Underwriting Agreement") with RBCCM, pursuant to which, on October 10, 2018, the Company sold 8,333,334 shares of common stock of the Company in an underwritten public offering pursuant to the Company's registration statement on Form S-3, filed with the SEC on October 17, 2016, and a related prospectus and prospectus supplement, filed with the SEC on October 17, 2016 and October 5, 2018, respectively. The offering price to the public was $3.00 per share. The Company's net proceeds from the offering were approximately $23.1 million, after deducting underwriting discounts and commissions and estimated offering expenses.

Entry into Purchase Agreement

On February 28, 2019, the Company entered into a purchase agreement (the "Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park") which provides that, upon the terms and subject to the conditions and limitations set forth therein, the Company may sell to Lincoln Park up to $15.0 million of shares of common stock from time to time over the 36-month term of the Purchase Agreement, and the Company shall issue an additional 120,200 shares of common stock to Lincoln Park as commitment shares under the Purchase Agreement. Concurrently with entering into the Purchase Agreement, the Company also entered into a registration rights agreement with Lincoln Park (the "Registration Rights Agreement") pursuant to which the Company agreed to register the sale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to the Company's existing shelf registration statement on Form S-3 or a new registration statement.

The Company is not obligated to make any future sales of common stock under the Purchase Agreement, and while it has yet to make any sales under the Purchase Agreement, it is obligated to issue 120,200 commitment shares to Lincoln Park upon satisfaction of the closing conditions contained in the Purchase Agreement.

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, 2018 or 2017.

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, 2018 and 2017.

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 2014, although carryforward attributes that were generated prior to 2014 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 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, 2018 and 2017.

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 May 2014, the FASB issued guidance codified in ASC Topic 606, *Revenue Recognition—Revenue from Contracts with Customers* ("ASC 606"), which amended the guidance in former ASC 605, *Revenue Recognition*, and became effective January 1, 2018. This guidance did not have a material impact on the Company's financial statements and disclosures 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 adoption of ASU 2016-01 did not have a material impact on the Company's 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 adoption of ASU 2016-15 did not have a material impact on the Company's financial statements and disclosures.

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 adoption of ASU 2017-09 did not have a material impact on the Company's financial statements and disclosures.

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

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic* 842*)* ("ASU 2016-02"), which requires lessees to recognize operating and finance lease liabilities and corresponding right-of-use assets on the balance sheet and to provide enhanced disclosures surrounding the amount, timing and uncertainty of cash flows arising from leases. The Company leases office space and laboratory facilities under non-cancelable operating leases. In addition, the Company leases various laboratory equipment, furniture and office equipment and leasehold improvements that are accounted for as capital leases. The Company will adopt the new standard effective January 1, 2019 on a modified retrospective basis and will not restate comparative periods. The Company will elect the package of practical expedients permitted under the transition guidance, which allows the Company to carryforward its historical lease classification and its assessment on whether a contract is or contains a lease for any leases that exist prior to adoption of the new standard. The Company will also elect to combine lease and non-lease components and to keep leases with an initial term of 12 months or less off the balance sheet and recognize the associated lease payments in the statements of operations on a straight-line basis over the lease term. The Company estimates the adoption of this new standard to result in the recognition of total right-of-use assets and total lease liabilities of approximately $3.0 million on the balance sheet as of January 1, 2019.

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 does not expect the adoption of ASU 2017-11 to have a material impact on the Company's financial statements and disclosures.

In June 2018, the FASB issued ASU 2018-07, *Compensation – Stock Compensation (Topic 820) – Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), which simplifies several aspects of the accounting for nonemployee share-based payment transactions resulting from expanding the scope of Topic 718, Compensation—Stock Compensation, to include share-based payment transactions for acquiring goods and services from nonemployees. This update applies to all entities that enter into share-based payment transactions for acquiring goods and services from nonemployees. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. The amendments in this ASU expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost (that is, the period of time over which share-based payment awards vest and the pattern of cost recognition over that period). The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Company does not expect the adoption of ASU 2018-07 to have a material impact on the Company's financial statements and disclosures.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820) – Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, based on the concepts in the FASB Concepts Statement, *Conceptual Framework for Financial Reporting—Chapter 8: Notes to Financial Statements*, which the FASB finalized on August 28, 2018, including the consideration of costs and benefits. This update applies to all entities that are required, under existing GAAP, to make disclosures about recurring or nonrecurring fair value measurements. This guidance is effective for financial statements issued for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted. An entity is permitted to early adopt any removed or modified disclosures and delay adoption of the additional disclosures until their effective date. The Company is currently evaluating the impact of the adoption of ASU 2018-13 on the Company's 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,	
	2018	**2017**
Prepaid insurance	$ 224	$ 202
Other receivables	140	76
Other prepaid expenses and current assets	1,688	1,384
Total prepaid expenses and other current assets	$ 2,052	$ 1,662

D. Property and Equipment

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

	December 31,	
	2018	2017
Laboratory equipment	$ 1,035	$ 983
Furniture and office equipment	655	655
Computers and hardware	299	292
Leasehold improvements	1,017	1,003
Total property and equipment	3,006	2,933
Less: accumulated depreciation and amortization	(1,253)	(929)
Property and equipment, net	$ 1,753	$ 2,004

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,	
	2018	2017
Laboratory equipment	$ 418	$ 366
Furniture and office equipment	541	541
Leasehold improvements	59	59
Total property and equipment financed under a capital lease agreement	1,018	966
Less: accumulated depreciation and amortization	(272)	(150)
Property and equipment financed under a capital lease agreement, net	$ 746	$ 816

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 $324,000 and $336,000 for the years ended December 31, 2018 and 2017, respectively.

E. Accounts Payable and Accrued Expenses

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

	December 31,	
	2018	**2017**
Accrued interest	$ 1,921	$ 2,222
Accrued banking fees	700	700
Accrued severance	193	—
Accrued payroll	731	1,118
Accounts payable	3,715	2,177
Other accrued expenses	1,082	1,658
Total accounts payable and accrued expenses	$ 8,342	$ 7,875

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 Note”). 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 Note into shares of the Company’s common stock at an initial conversion price of $5.85 per share (the "Deerfield Note Conversion Feature").

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 N). 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. The outstanding principal amount due on the fourth anniversary of the Deerfield Facility Agreement and the related accrued but unpaid interest as of such date was converted in common stock of the Company in accordance with the provisions of the Deerfield Convertible Note, as amended. Refer to the section entitled *"Facility Agreement Waiver and Fifth Amendment to Senior Secured Convertible Note"* below.

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.

First Amendment to Facility Agreement, Senior Secured Convertible Note and Warrant

In connection with the IPO, on March 6, 2015, the Company entered into a First Amendment (the “First Amendment) to the Deerfield Facility Agreement, the Deerfield Convertible Note and Deerfield Warrant, by and between the Company and Deerfield. The First Amendment, among other things, clarified that all references to the conversion of shares of Series D Preferred into the Company’s common stock in the Deerfield Facility Agreement, the Deerfield Convertible Note and Deerfield Warrant shall include any reclassification of the outstanding shares of Series D Preferred into shares of the Company’s common stock.

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 Note 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 Note and Deerfield Warrant, respectively, in the event that the Company effects a firm commitment underwritten public offering of its securities.

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.

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 (the "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 Note and Deerfield Warrant with Deerfield. The Third Amendment, among other things, eliminated the Company's ability to require Deerfield to convert the Deerfield Convertible Note 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.

Refer to the section entitled Exchange Agreement below for a further discussion of an exchange of a certain portion of the 2021 Notes for shares of the Company's Series A Convertible Preferred Stock, par value $0.0001 per share (the "Series A Preferred Stock").

Fourth Amendment to Senior Secured Convertible Note and 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.

Facility Agreement Waiver and Fifth Amendment to Senior Secured Convertible Note

On June 11, 2018, the Company entered into the Facility Agreement Waiver and Fifth Amendment (the "Fifth Amendment") to the Deerfield Convertible Note with Deerfield. The Fifth Amendment, among other things, provided that (i) $3,333,333 of the principal amount, plus $168,288 of accrued interest, of the Deerfield Convertible Note was converted into 598,568 shares of the Company's common stock, with such principal conversion amount being applied against and in full satisfaction of the amortization payment due June 2, 2018; (ii) Deerfield waived specified rights under the Deerfield Facility Agreement with regards to such principal and interest amount; and (iii) specified provisions of the Deerfield Convertible Note were amended as they relate to the delivery of shares of the Company's common stock in connection with any conversion of the Deerfield Convertible Note.

Exchange Agreement

On October 5, 2018, the Company entered into an Exchange Agreement (the "Exchange Agreement") with Deerfield and Deerfield Special Situations Fund, L.P. (the "Holders"). Under the Exchange Agreement, the Holders exchanged an aggregate of $9,577,000 principal amount of the 2021 Notes for an aggregate of 9,577 shares of Series A Preferred Stock. The Company also agreed to pay the Holders an amount of $95,105 in cash, which represented the amount of accrued and unpaid interest on the exchanged notes. The Exchange Agreement contains customary representations, warranties and covenants made by the Company and the Holders. The Exchange Agreement required the Company to reimburse the Holders for up to $25,000 of expenses relating to the exchange.

As a condition to closing of the Exchange Agreement, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock (the "Certificate of Designation") with the Secretary of State of the State Delaware, setting forth the preferences, rights and limitations of the Series A Preferred Stock.

Each share of Series A Preferred Stock has an aggregate stated value of $1,000 and is convertible into shares of common stock at a price equal to $3.00 per share (subject to adjustment to reflect stock splits and similar events). Immediately following the exchange, there were an aggregate of 3,192,334 shares of common stock issuable upon conversion of the Series A Preferred Stock (without giving effect to the limitation on conversion described below). The Series A Preferred Stock is convertible at any time at the option of the Holders, provided that the Holders are prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such Holders (together with certain affiliates and "group" members) would beneficially own more than 4.985% of the total number of shares of the Company's common stock then issued and outstanding. The Series A Preferred Stock is not redeemable. In the event of the Company's liquidation, dissolution or winding up, the Holders will receive an amount equal to $0.0001 per share of Series A Preferred Stock, plus any declared but unpaid dividends, and thereafter will share ratably in any distribution of the Company's assets with holders of common stock on an as-converted basis. With respect to rights upon liquidation, the Series A Preferred Stock ranks senior to the common stock and junior to existing and future indebtedness. Except as otherwise required by law (or with respect to approval of certain actions involving the Company's organizational documents that materially and adversely affect the holders of Series A Preferred Stock), the Series A Preferred Stock does not have voting rights. The Series A Preferred Stock is not subject to any price-based anti-dilution protections and does not provide for any accruing dividends, but provides that holders of Series A Preferred Stock will participate in any dividends on the common stock on an as-converted basis (without giving effect to the limitation on conversion described above). The Certificate of Designation also provides for partial liquidated damages in the event that the Company fails to timely convert shares of Series A Preferred Stock into common stock in accordance with the Certificate of Designation.

First Supplemental Indenture, Sixth Amendment to Deerfield Convertible Note and Fifth Amendment to Deerfield Warrant

On November 20, 2018, the Company entered into a First Supplemental Indenture (the "Supplemental Indenture") with the Trustee, to the Indenture, relating to the 2021 Notes. Pursuant to the Supplemental Indenture, the Indenture was amended to allow each Holder (as defined in the Indenture) or any beneficial holder of any 2021 Notes to, at its option, elect a limit on beneficial ownership as to such Holder or beneficial owner (but not as to any other Holder or beneficial owner) that is less than or equal to the 9.985% Cap (as defined in the Indenture) or any other limit previously elected and then applicable to such Holder or beneficial owner upon written notice delivered to the Company at least three (3) business days prior to the date of effectiveness of such beneficial ownership limit (or such shorter period as may be agreed upon by the Company), specifying the percentage of shares of the Company's common stock outstanding for the beneficial ownership limit that shall apply to such Holder or beneficial owner.

Also on November 20, 2018, in connection with entering into the Supplemental Indenture, the Company entered into an amendment (the "Sixth Amendment") with Deerfield to the Deerfield Convertible Note and Deerfield Warrant. The Sixth Amendment, among other things, lowers the beneficial ownership limit under both the Deerfield Convertible Note and Deerfield Warrant to 4.985% of the Company's outstanding common stock. The Sixth Amendment also includes a notice from Deerfield that it has elected to lower the beneficial ownership limit under the 2021 Notes, as to Deerfield and its affiliates, to 4.985%.

Seventh Amendment to Deerfield Convertible Note and Sixth Amendment to Deerfield Warrant

On February 28, 2019, in connection with entering into the Purchase Agreement, the Company entered into an amendment (the "Seventh Amendment"), with Deerfield to the Deerfield Convertible Note and Deerfield Warrant. The Seventh Amendment, among other things, clarified that the anti-dilution protections contained in the Deerfield Convertible Note and Deerfield Warrant would not apply to sales made under the Purchase Agreement or Second ATM Agreement. The Seventh Amendment also includes a waiver from Deerfield regarding any rights it may have under the Company's amended and restated investor rights agreement in connection with the Registration Rights Agreement.

Except as modified by the First Amendment, Second Amendment, Third Amendment, Fourth Amendment, Fifth Amendment, Sixth Amendment and Seventh Amendment, all terms and conditions of the Deerfield Facility Agreement, Deerfield Warrant and Deerfield Convertible Note remained in full force and effect.

Convertible Notes

Future minimum principal payments under convertible notes as of December 31, 2018, were as follows (in thousands):

Year Ending December 31,	**Convertible Notes**
2019	3,333
2020	3,334
2021	76,673
Total minimum principal payments	83,340
Less: debt issuance costs and discount	(1,902)
Convertible notes, net	$ 81,438

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, 2018 and 2017, 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, 2018 and 2017, 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 letters of credit outstanding which are supported by the line of credit. 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 4.35%, as of December 31, 2018.

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, 2018 and 2017, no accruals have been made related to commitments and contingencies.

Lease Agreements

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.

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 2019 and includes a renewal option that could extend the lease for successive one-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 2019.

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, 2018 and 2017, the interest rates for assets under remaining capital leases range from 7.19% to 9.57%.

Rent expense for non-cancelable operating leases was $0.7 million and $0.6 million for the years ended December 31, 2018 and 2017, respectively.

Future minimum lease payments under capital leases and non-cancelable operating leases as of December 31, 2018, were as follows (in thousands):

Year Ending December 31,	Capital Leases	Operating Leases
2019	$ 254	$ 714
2020	251	499
2021	163	449
2022	11	461
2023	—	472
Thereafter	—	903
Total minimum lease payments	679	$ 3,498
Less: amounts representing interest	(69)	
Total minimum capital lease principal payments	$ 610	

H. Supply Arrangement

As of December 31, 2018 and 2017, 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 benzhydrocodone 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 benzhydrocodone. The Company's FDA-approved drug, APADAZ, contains benzhydrocodone. Expense of $3.6 million was recorded under this agreement for the year ended December 31, 2018. No expense was recorded under this agreement for the year ended December 31, 2017. The Company must purchase all of its U.S. benzhydrocodone needs from JMI and JMI cannot supply benzhydrocodone to other companies. The term of the Supply Agreement extends as long as the Company holds a valid and enforceable patent for benzhydrocodone or until the tenth anniversary of a commercial launch of a FDA-approved drug incorporating benzhydrocodone, 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 benzhydrocodone. No reliable estimate of the future payments can be made at this time.

I. Preferred Stock and Warrants

Authorized, Issued, and Outstanding Preferred Stock

As of December 31, 2018, the Company had 10,000,000 shares of authorized preferred stock, of which 9,578 shares were designated as Series A Preferred Stock, 9,577 shares of which were issued in the fiscal year ended December 31, 2018 and 3,337 shares of which were outstanding at year-end. As of December 31, 2017, the Company had 10,000,000 shares of authorized and undesignated preferred stock.

On October 5, 2018, the Company entered into the Exchange Agreement. Under the Exchange Agreement the Company issued to the Holders 9,577 shares of Series A Preferred Stock. Each share of Series A Preferred Stock has an aggregate stated value of $1,000 and is convertible into shares of common stock at a price equal to $3.00 per share (subject to adjustment to reflect stock splits and similar events). Immediately following the exchange, there were an aggregate of 3,192,334 shares of common stock issuable upon conversion of the Series A Preferred Stock (without giving effect to the limitation on conversion described below). The Series A Preferred Stock is convertible at any time at the option of the Holders, provided that the Holders are prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such Holders (together with certain affiliates and "group" members) would beneficially own more than 4.985% of the total number of shares of the Company's common stock then issued and outstanding. The Series A Preferred Stock is not redeemable. In the event of the Company's liquidation, dissolution or winding up, the Holders will receive an amount equal to $0.0001 per share of Series A Preferred Stock, plus any declared but unpaid dividends, and thereafter will share ratably in any distribution of the Company's assets with holders of common stock on an as-converted basis. With respect to rights upon liquidation, the Series A Preferred Stock ranks senior to the common stock and junior to existing and future indebtedness. Except as otherwise required by law (or with respect to approval of certain actions involving the Company's organizational documents that materially and adversely affect the holders of Series A Preferred Stock), the Series A Preferred Stock does not have voting rights. The Series A Preferred Stock is not subject to any price-based anti-dilution protections and does not provide for any accruing dividends, but provides that the holders of Series A Preferred Stock will participate in any dividends on the common stock on an as-converted basis (without giving effect to the limitation on conversion described above). The Certificate of Designation also provides for partial liquidated damages in the event that the Company fails to timely convert shares of Series A Preferred Stock into common stock in accordance with the Certificate of Designation. As of February 28, 2019, 6,240 shares of Series A Preferred Stock have been converted into 2,080,000 shares of common stock.

As of February 28, 2019, the Company has 3,337 shares of Series A Preferred Stock outstanding, which are convertible into 1,112,334 shares of common stock. Refer to Note F for a further discussion over the Exchange Agreement.

Warrants

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 Note 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

As of December 31, 2018 and 2017, the Company had authorized shares of common stock of 250,000,000 shares. Of the authorized shares, 26,455,352 and 14,657,430 shares of common stock were issued and outstanding as of December 31, 2018 and 2017, respectively.

As of December 31, 2018 and 2017, the Company had reserved authorized shares of common stock for future issuance as follows:

	December 31,	
	2018	2017
Conversion of Deerfield Convertible Note	1,167,607	1,751,410
Conversion of 2021 Notes	4,481,182	5,040,914
Outstanding awards under equity incentive plans	3,704,755	2,853,924
Outstanding common stock warrants	2,527,763	2,027,763
Conversion of Series A Convertible Preferred Stock	1,112,334	—
Possible future issuances under equity incentive plans	648,272	944,700
Total common shares reserved for future issuance	13,641,913	12,618,711

Common Stock Activity

The following table summarizes common stock activity for the years ended December 31, 2018 and 2017:

	Shares of Common Stock
Balance as of January 1, 2017	14,646,982
Common stock warrants exercised	698
Common stock options exercised	9,750
Balance as of December 31, 2017	14,657,430
Common stock sold under First ATM Agreement	762,338
Common stock issued as a result of Deerfield Convertible Note principal and interest conversion	598,568
Common stock options exercised	23,682
Common stock sold under underwritten public offering	8,333,334
Common stock issued as a result of Series A Convertible Preferred Stock conversion	2,080,000
Balance as of December 31, 2018	26,455,352

On September 4, 2018, the Company terminated the First ATM Agreement with Cowen. Prior to termination of the First ATM Agreement, the Company sold an aggregate of 762,338 shares of common stock under the First ATM Agreement resulting in gross proceeds to the Company of $4.9 million. As of February 28, 2019, the Company has not sold any shares of common stock under the Second ATM Agreement. Refer to Note A for a further discussion of the First and Second ATM Agreements.

On October 5, 2018, the Company entered into an underwriting agreement with RBCCM pursuant to which the Company issued and sold 8,333,334 shares of common stock of the Company in an underwritten public offering pursuant to the Company's registration statement on Form S-3. Refer to Note A for a further discussion of the underwritten public offering.

Also on October 5, 2018, the Company entered into the Exchange Agreement pursuant to which the Company issued to the Holders 9,577 shares of Series A Preferred Stock. As of February 28, 2019, 6,240 shares of Series A Preferred Stock have been converted into 2,080,000 shares of common stock. Refer to Note F for a further discussion of the Exchange Agreement.

Warrants

The Company calculates the fair value of common stock warrants (other than the KVK Warrant, as defined below) using a Monte Carlo simulation. There were warrants exercised for an aggregate of 698 shares of common stock during the year ended December 31, 2017. No warrants were exercised during the year ended December 31, 2018. 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.

In connection with a Collaboration and License Agreement (the "License Agreement") with KVK Tech, Inc. ("KVK"), on October 25, 2018, the Company issued to KVK a warrant to purchase up to 500,000 shares of common stock of the Company at an exercise price of $2.30 per share, which reflects the closing price of the Company's common stock on the Nasdaq Global Market on October 25, 2018 (the "KVK Warrant"). The KVK Warrant is initially not exercisable for any shares of common stock. Upon the achievement of each of four specified milestones under the KVK Warrant, the KVK Warrant will become exercisable for an additional 125,000 shares for each of the four specified milestones, up to an aggregate of 500,000 shares of the Company's common stock. The exercise price and the number and type of shares underlying the KVK Warrant are subject to adjustment in the event of specified events, including a reclassification of the Company's common stock, a subdivision or combination of the Company's common stock, or in the event of specified dividend payments. The KVK Warrant is exercisable until October 24, 2023. Upon exercise, the aggregate exercise price may be paid, at KVK's election, in cash or on a net issuance basis, based upon the fair market value of the Company's common stock at the time of exercise.

The Company determined that, since KVK qualifies as a customer under ASC 606, the KVK Warrant should be recorded as a contract asset and recognized as contra-revenue as the Company recognizes revenue from the License Agreement. In addition, the Company determined that the KVK Warrant qualifies as a derivative under ASC 815 and should be recorded as a liability and stated at fair value each reporting period. The Company calculates the fair value of KVK Warrant using a probability-weighted Black-Scholes option pricing model. Changes in fair value resulting from changes in the inputs to the Black Scholes model are accounted for as changes in the fair value of the derivative under ASC 815 and are recorded as fair value adjustment related to derivative and warrant liability in the statement of operations. Changes in the number of shares that are expected to be issued are treated as changes in variable consideration under ASC 606 and are recorded as a reduction in contract asset in the balance sheet.

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 4,018,480 as of December 31, 2018. 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, 2019, the common stock reserved for issuance under the 2014 Plan automatically increased by 1,058,214 shares.

During the years ended December 31, 2018 and 2017, stock options to acquire 23,682 and 9,750 shares of common stock were exercised for approximately $68,000 and $7,000 with an intrinsic value of approximately $69,000 and $32,000, 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,	
	2018	2017
Research and development	$ 1,608	$ 1,304
General and administrative	3,651	3,258
Severance expense	1,236	—
Total stock-based compensation expense	$ 6,495	$ 4,562

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 for options granted prior to the second anniversary of the IPO 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. For options granted after the second anniversary of the IPO, expected volatility is based on the Company's historical volatility 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, 2018 and 2017, fair value was $4.05 and $2.77 per share, respectively. The assumptions used to estimate fair value are as follows:

	December 31,	
	2018	2017
Risk-free interest rate	2.43% - 2.91%	1.88% - 2.26%
Expected term (in years)	5.50 - 6.79	5.12 - 7.00
Expected volatility	83.10% - 85.05%	85.35% - 95.08%
Expected dividend yield	0%	0%

The activity under the Incentive Stock Plan and the 2014 Plan for the year ended December 31, 2018, 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, 2018	2,853,924	$ 10.50	7.90	$ 471,539
Granted	898,000	$ 5.54		
Exercised	(23,682)	$ 3.15		
Canceled or forfeited	(20,821)	$ 10.63		
Expired	(2,666)	$ 3.00		
Outstanding balance as of December 31, 2018	3,704,755	$ 9.35	7.48	$ —
Exercisable as of December 31, 2018	1,837,582	$ 11.56	6.67	$ —
Vested and expected to vest as of December 31, 2018	3,656,474	$ 9.40	7.47	$ —

Information regarding currently outstanding and exercisable options as of December 31, 2018, 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	1,024,995	7.89	390,244	7.59
$5.01 to $10.00	1,256,427	7.85	437,527	5.50
$10.01 to $15.00	471,833	6.94	285,249	6.85
$15.01 to $20.00	603,700	6.89	463,712	6.88
$20.01 to $22.12	347,800	6.68	260,850	6.68
	3,704,755	7.48	1,837,582	6.67

The total fair value of stock options vested during the years ended December 31, 2018 and 2017, was $5.9 million and $4.1 million, respectively.

Unvested stock options as of December 31, 2018 and 2017, were as follows:

	Number of Unvested Shares December 31,	
Exercise Price	2018	2017
$2.75 to $5.00	634,751	979,000
$5.01 to $10.00	818,900	21,301
$10.01 to $15.00	186,584	282,542
$15.01 to $20.00	139,988	352,789
$20.01 to $22.12	86,950	173,900
Total number of unvested shares	1,867,173	1,809,532

As of December 31, 2018, there was $6.0 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 1.84 years.

There was no stock-based compensation expense related to performance-based awards recognized during the years ended December 31, 2018 or 2017.

L. Fair Value of Financial Instruments

The carrying amounts of certain financial instruments, including cash and cash equivalents, restricted cash and accounts payable and accrued expenses, approximate their respective fair values due to the short-term nature of such instruments.

The fair value of the Deerfield Convertible Note was $6.2 million and $11.0 million, respectively, as of December 31, 2018 and 2017. The fair value of the 2021 Notes was $51.2 million and $51.9 million, respectively, as of December 31, 2018 and 2017. Both the Deerfield Convertible Note 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 Note and 2021 Notes as of December 31, 2018 and 2017.

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, 2018 and 2017 (in thousands):

	Balance as of December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Deerfield Warrant liability	$ 1,557	$ —	$ —	$ 1,557
Embedded Warrant Put Option	154	—	—	154
Fundamental change and make-whole interest provisions embedded in 2021 Notes	—	—	—	—
Deerfield Note Conversion Feature	134	—	—	134
KVK Warrant liability	273	—	273	—
Total liabilities	$ 2,118	$ —	$ 273	$ 1,845
Trading securities:				
Certificates of deposit	246	246	—	—
U.S. Treasury securities	3,014	3,014	—	—
Total assets	$ 3,260	$ 3,260	$ —	$ —

	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
Deerfield Note Conversion Feature	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	$ —

The Company's Deerfield Warrant liability, embedded Warrant Put Option, the fundamental change and the make-whole interest provisions embedded in the 2021 Notes and the Deerfield Note Conversion Feature, as well as the trading securities are measured at fair value on a recurring basis. As of December 31, 2018 and 2017, the Deerfield Warrant liability, embedded Warrant Put Option the fundamental change and make-whole interest provisions embedded in the 2021 Notes and the Deerfield Note Conversion Feature 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. The Company used a Monte Carlo simulation to value the Deerfield Warrant liability, embedded Warrant Put Option, the fundamental change and make-whole interest provisions embedded in the 2021 Notes and the Deerfield Note Conversion Feature as of December 31, 2018 and 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 Deerfield Warrant liability, embedded Warrant Put Option, the fundamental change and make-whole interest provisions embedded in the 2021 Notes and the Deerfield Note Conversion Feature are reflected in the statements of operations for the years ended December 31, 2018 and 2017 as a fair value adjustment related to derivative and warrant liability.

The Company's KVK Warrant liability is measured at fair value on a recurring basis. As of December 31, 2018, the KVK Warrant liability is reported on the balance sheets in derivative and warrant liability. The Company estimates the fair value of KVK Warrant using a probability-weighted Black-Scholes option-pricing model, which requires the use of subjective assumptions, including the expected term of the warrant, the expected stock price volatility, expected dividend yield and the risk-free interest rate for the expected term of the warrant. The expected term represents the period of time the warrant is expected to be outstanding. For the warrant, the Company used an expected term equal to the contractual term of the warrant. Expected volatility is based on the Company's historical volatility since IPO. 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. Changes in the fair value of the KVK Warrant liability are reflected in the statements of operations for the years ended December 31, 2018 as a fair value adjustment related to derivative and warrant liability. The KVK Warrant liability had no value as of December 31, 2017 since it was issued in October 2018.

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):

	2018	2017
Balance as of beginning of period	$ 7,709	$ 4,618
Gain on extinguishment of debt	(2)	—
Adjustment to fair value	(5,862)	3,091
Balance as of end of period	$ 1,845	$ 7,709

M. Income Taxes

The Company's financial statements include a total state tax benefit related to research and development credits of $126,000 and $43,000 on a loss before income taxes of $56.6 million and $43.4 million for the years ended December 31, 2018 and 2017, 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,	
	2018	**2017**
Federal statutory rate	21.00%	34.00%
Effect of:		
Change in valuation allowance	(30.44)	13.38
Return to provision and deferred true-up	0.38	2.18
Change in rate	0.03	(49.06)
State tax benefit (net of federal)	4.35	2.71
Warrant liability	2.02	(2.42)
State research and development credit	0.22	0.10
Federal research and development credit	3.30	1.50
Amortization	—	(1.22)
Stock-based compensation	(0.63)	(1.03)
Other	(0.01)	(0.04)
Federal income tax benefit effective rate	0.22%	0.10%

The components of deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2018	**2017**
Deferred tax assets relating to:		
Net operating loss carryforwards	$ 51,269	$ 37,028
Research and development tax carryforward	5,657	3,788
Other deferred tax assets	3,437	2,409
Total gross deferred tax assets	60,363	43,225
Deferred tax liabilities relating to:		
Property and equipment	161	260
Other deferred tax liabilities	10	—
Total gross deferred tax liabilities	171	260
Deferred tax assets less liabilities	60,192	42,965
Valuation allowance	(60,192)	(42,965)
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.

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, 2018 (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	15,897	894	2034
2015	23,496	598	2035
2016	41,580	745	2036
2017	34,776	652	2037
2018	56,105	1,869	Indefinite
	$ 194,251	$ 5,657	

The Company also has certain state net operating loss carryforwards totaling $136.0 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,	
	2018	**2017**
Net loss - basic and diluted	$ (56,466)	$ (43,386)
Weighted average number of shares of common stock - basic and diluted	17,930,023	14,652,898
Net loss per share - basic and diluted	$ (3.15)	$ (2.96)

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,	
	2018	**2017**
Deerfield Convertible Note	1,167,607	1,751,410
2021 Notes	4,481,182	5,040,914
Awards under equity incentive plans	3,704,755	2,853,924
Warrants to purchase common stock	2,527,763	2,027,763
Series A Convertible Preferred Stock	1,112,334	—
Total securities excluded from the calculation of weighted average number of shares of common stock outstanding	12,993,641	11,674,011

O. Severance Expense

On August 31, 2018, Daniel L. Cohen resigned from his position as the executive vice president, government and public relations of the Company, effective immediately. In connection with his resignation, Mr. Cohen and the Company entered into a separation and release agreement which included among other items, severance benefits. The severance benefits consisted of personnel and other related charges of approximately $0.4 million and stock compensation expense of approximately $1.2 million related to the acceleration of vesting on unvested shares subject to certain stock options and the extension of the exercise period for certain stock options. These severance benefits are presented as severance expense in the statements of operations for the fiscal year ended December 31, 2018. As of December 31, 2018, the Company had accrued severance expense recorded within accounts payable and accrued expenses in the amount of $0.2 million.

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 $212,000 and $207,000 for the years ended December 31, 2018 and 2017, 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 2018 or 2017.

EXHIBITS

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).
3.1.1	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock of KemPharm, Inc. (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on October 5, 2018).
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).
4.3.1	First Supplemental Indenture, dated November 20, 2018, between the Company and U.S. Bank National Association, as trustee (as incorporated herein by reference to the Company's Current Report on Form 8-K as filed with the SEC on November 20, 2018).
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).
4.5*	Registration Rights Agreement dated February 28, 2019 by and between the Company and Lincoln Park Capital Fund, LLC.
5.1*	Opinion of Cooley LLP.
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 between 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).
10.3.3	Facility Agreement Waiver and Fifth Amendment to Senior Secured Convertible Note by and between Registrant and Deerfield Private Design Fund III, L.P., dated as of June 11, 2018 (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on June 11, 2018).
10.3.4	Amendment to Convertible Note and Warrant Agreement, dated November 20, 2018, between the Company and Deerfield Private Design Fund III, L.P. (as incorporated herein by reference to the Company's Current Report on Form 8-K filed with the SEC on November 20, 2018).
10.3.5*	Seventh Amendment to Senior Secured Convertible Note and Sixth Amendment to Warrant, dated February 28, 2019, between the Company and Deerfield Private Design Fund III, L.P.
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 warrant holders (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#*	Amended Non-Employee Director Compensation Policy
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	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).
10.23	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).
10.24	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).
10.25	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).
10.26	Separation Agreement and General Release by and between the Registrant and Daniel L. Cohen, dated as of September 5, 2018 (incorporated herein by reference to the Registrant's Quarterly Report on Form 10-Q as filed with the SEC on November 9, 2018).
10.27	Common Stock Sales Agreement, dated September 4, 2018, by and between KemPharm, Inc. and RBC Capital Markets, LLC (incorporated herein by reference to the Registrant's Current Report on Form 8-K as filed with the SEC on September 4, 2018).
10.28*^	Collaboration and License Agreement by and between the Company and KVK Tech, Inc. dated as of October 25, 2018.
10.29*^	Warrant to Purchase Shares of Common Stock issued to KVK Tech, Inc. dated October 25, 2018.
10.30*	Purchase Agreement dated February 28, 2019 by and between the Company and Lincoln Park Capital Fund, LLC.
23.1*	Consent of RSM US LLP, Independent Registered Public Accounting Firm.
23.2*	Consent of Cooley LLP (included in Exhibit 5.1).
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.
^	Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request 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 1, 2019

By: /s/ Travis C. Mickle
Travis C. Mickle, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 1, 2019

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 Travis C. Mickle, Ph.D.	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	March 1, 2019
/s/ R. LaDuane Clifton R. LaDuane Clifton, CPA	Chief Financial Officer, Secretary and Treasurer (Principal Financial Officer)	March 1, 2019
/s/ Timothy J. Sangiovanni Timothy J. Sangiovanni, CPA	Vice President, Corporate Controller (Principal Accounting Officer)	March 1, 2019
/s/ Danny L. Thompson Danny L. Thompson	Director	March 1, 2019
/s/ Matthew R. Plooster Matthew R. Plooster	Director	March 1, 2019
/s/ Richard W. Pascoe Richard W. Pascoe	Director	March 1, 2019
/s/ Joseph B. Saluri Joseph B. Saluri	Director	March 1, 2019
/s/ David S. Tierney David S. Tierney	Director	March 1, 2019

Exhibit 4.5

REGISTRATION RIGHTS AGREEMENT

THIS REGISTRATION RIGHTS AGREEMENT (this "Agreement"), dated as of February 28, 2019, is entered into by and between **KEMPHARM, INC.**, a Delaware corporation (the "Company"), and **LINCOLN PARK CAPITAL FUND, LLC**, an Illinois limited liability company (together with its permitted assigns, the "Investor"). Capitalized terms used herein and not otherwise defined herein shall have the respective meanings set forth in the Purchase Agreement by and between the parties hereto, dated as of the date hereof (as amended, restated, supplemented or otherwise modified from time to time, the "Purchase Agreement").

WHEREAS:

A. Upon the terms and subject to the conditions of the Purchase Agreement, (i) the Company has agreed to issue to the Investor, and the Investor has agreed to purchase, up to Fifteen Million Dollars ($15,000,000) of the Company's Common Stock, par value $0.0001 per share (the "Common Stock"), pursuant to Section 2 of the Purchase Agreement (such shares, the "Purchase Shares"), and (ii) the Company has agreed to issue to the Investor such number of shares of Common Stock as is required pursuant to Section 5(e) of the Purchase Agreement (the "Commitment Shares"); and

B. To induce the Investor to enter into the Purchase Agreement, the Company has agreed to provide certain registration rights under the Securities Act of 1933, as amended, and the rules and regulations thereunder, or any similar successor statute (collectively, the "Securities Act"), and applicable state securities laws.

NOW, THEREFORE, in consideration of the promises and the mutual covenants contained herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Company and the Investor hereby agree as follows:

1. Definitions.

For purposes of this Agreement, the following terms shall have the following meanings:

(a) "Register," "Registered," and "Registration" refer to a registration effected by preparing and filing one or more registration statements of the Company in compliance with the Securities Act and providing for offering securities on a continuous basis, and the declaration or ordering of effectiveness of such registration statement(s) by the SEC.

(b) "Registrable Securities" means the Purchase Shares that may from time to time be issued or issuable to the Investor upon purchases of the Available Amount under the Purchase Agreement (without regard to any limitation or restriction on purchases) (including the Initial Purchase Shares), the Commitment Shares issued or issuable to the Investor, and any Common Stock issued or issuable with respect to the Purchase Shares, the Commitment Shares or the Purchase Agreement as a result of any stock split, stock dividend, recapitalization, exchange or similar event, without regard to any limitation on purchases under the Purchase Agreement.

(c) "Registration Statement" means the Shelf Registration Statement and any other registration statement of the Company, as amended when it became effective, including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus subsequently filed with the SEC.

(d) "Shelf Registration Statement" means the Company's existing registration statement on Form S-3 (File No. 333-213926).

2. Registration.

(a) Mandatory Registration. The Company agrees that it shall, within the time required under Rule 424(b) under the Securities Act, file with the SEC the Initial Prospectus Supplement pursuant to Rule 424(b) under the Securities Act specifically relating to the transactions contemplated by, and describing the material terms and conditions of, the Transaction Documents, containing information previously omitted at the time of effectiveness of the Registration Statement in reliance on Rule 430B under the Securities Act, and disclosing all information relating to the transactions contemplated hereby required to be disclosed in the Registration Statement and the Prospectus as of the date of the Initial Prospectus Supplement, including, without limitation, information required to be disclosed in the section captioned "Plan of Distribution" in the Prospectus. The Investor acknowledges that it will be identified in the Initial Prospectus Supplement as an underwriter within the meaning of Section 2(a)(11) of the Securities Act. The Company shall permit the Investor to review and comment upon the Initial Prospectus Supplement at least two (2) Business Days prior to its filing with the SEC, the Company shall give due consideration to all such comments, and the Company shall not file the Initial Prospectus Supplement with the SEC in a form to which the Investor reasonably objects. The Investor shall use its reasonable best efforts to provide any comments upon the Initial Prospectus Supplement within one (1) Business Day from the date the Investor receives a substantially complete draft thereof from the Company. The Investor shall furnish to the Company such information regarding itself, the Securities held by it and the intended method of distribution thereof, including any arrangement between the Investor and any other Person relating to the sale or distribution of the Securities, as shall be reasonably requested by the Company in connection with the preparation and filing of the Initial Prospectus Supplement, and shall otherwise cooperate with the Company as reasonably requested by the Company in connection with the preparation and filing of the Initial Prospectus Supplement with the SEC.

(b) Effectiveness. The Company shall use its reasonable best efforts to keep the Registration Statement effective under the Securities Act (including through any necessary renewals), and to keep the Registration Statement and the Prospectus current and available (including through any necessary renewals) for issuances and sales of all possible Registrable Securities by the Company to the Investor, and for the resale of all of the Registrable Securities by the Investor, at all times during the Registration Period. Without limiting the generality of the foregoing, during the Registration Period, the Company shall (a) take all action necessary to cause the Common Stock to continue to be Registered as a class of securities under Section 12(b) of the Exchange Act and shall not take any action or file any document (whether or not permitted by the Exchange Act) to terminate or suspend such registration and (b) file or furnish on or before their respective due dates all reports and other documents required to be filed or furnished by the Company pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act, and shall not take any action or file any document (whether or not permitted by the Exchange Act) to terminate or suspend its reporting and filing obligations under the Exchange Act. The Registration Statement (including any amendments or supplements thereto and prospectuses contained therein) shall not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in light of the circumstances under which they were made, not misleading.

(c) Prospectus Amendments or Supplements. Except as provided in this Agreement and other than periodic and current reports required to be filed pursuant to the Exchange Act, the Company shall not file with the SEC any amendment to the Registration Statement or any supplement to the Base Prospectus in each case that refers to the Investor, the Transaction Documents or the transactions contemplated thereby (including, without limitation, any Prospectus Supplement filed in connection with the transactions contemplated by the Transaction Documents), in each case with respect to which (a) the Investor shall not previously have been advised and afforded the opportunity to review and comment thereon at least two (2) Business Days prior to filing with the SEC, as the case may be, (b) the Company shall not have given due consideration to any comments thereon received from the Investor or its counsel, or (c) the Investor shall reasonably object, unless the Company reasonably has determined that it is necessary to amend the Registration Statement or make any supplement to the Prospectus to comply with the Securities Act or any other applicable law or regulation, in which case the Company shall promptly (but in no event later than 24 hours) so inform the Investor. In addition, for so long as, in the reasonable opinion of counsel for the Investor, the Prospectus is required to be delivered in connection with any acquisition or sale of Securities by the Investor, the Company shall not file any Prospectus Supplement with respect to the Securities without furnishing to the Investor as many copies of such Prospectus Supplement, together with the Prospectus, as the Investor may reasonably request.

(d) Sufficient Number of Shares Registered. In the event the number of shares available under the Shelf Registration Statement is insufficient to cover the Registrable Securities, the Company shall, to the extent necessary and permissible, amend the Shelf Registration Statement or file a new registration statement (together with any prospectuses or prospectus supplements thereunder, a "New Registration Statement"), so as to cover all of such Registrable Securities as soon as reasonably practicable, but in any event not later than ten (10) Business Days after the necessity therefor arises, subject to any limits that may be imposed by the SEC pursuant to Rule 415 promulgated under the Securities Act. The Company shall permit the Investor to review and comment upon any such New Registration Statement at least two (2) Business Days prior to its filing with the SEC, the Company shall give due consideration to all such comments, and the Company shall not file any such New Registration Statement with the SEC in a form to which the Investor reasonably objects. The Company shall use its reasonable best efforts to have such amendment and/or New Registration Statement become effective as soon as reasonably practicable following the filing thereof.

(e) Offering. If the SEC seeks to characterize any offering pursuant to a Registration Statement filed pursuant to this Agreement as constituting an offering of securities that does not permit such Registration Statement to become effective and be used by the Investor under Rule 415 promulgated under the Securities Act at then-prevailing market prices (and not fixed prices), or if after the filing of the Initial Prospectus Supplement with the SEC pursuant to Section 2(a), the Company is otherwise required by the Staff or the SEC to reduce the number of Registrable Securities included in such initial Registration Statement, then the Company shall reduce the number of Registrable Securities to be included in such initial Registration Statement (after consultation with the Investor and its legal counsel as to the specific Registrable Securities to be removed therefrom) until such time as the SEC shall so permit such Registration Statement to become effective and be used as aforesaid. In the event of any reduction in Registrable Securities pursuant to this paragraph, the Company shall file one or more New Registration Statements in accordance with Section 2(d) until such time as all Registrable Securities have been included in Registration Statements that have been declared effective and the prospectuses contained therein is available for use by the Investor. Notwithstanding any provision herein or in the Purchase Agreement to the contrary, the Company's obligations to register Registrable Securities (and any related conditions to the Investor's obligations) shall be qualified as necessary to comport with any requirement of the SEC as addressed in this Section 2(e).

3. Related Obligations.

With respect to the Registration Statement and whenever any Registrable Securities are to be Registered pursuant to Section 2, including on the Shelf Registration Statement or on any New Registration Statement, the Company shall use its reasonable best efforts to effect the registration of the Registrable Securities in accordance with the intended method of disposition thereof and, pursuant thereto, the Company shall have the following obligations:

(a) Notifications. The Company will notify the Investor promptly of the time when any subsequent amendment to the Shelf Registration Statement or any New Registration Statement, other than documents incorporated by reference, has been filed with the SEC and/or has become effective or where a receipt has been issued therefor or any subsequent supplement to a Prospectus has been filed and of any request by the SEC for any amendment or supplement to the Registration Statement, any New Registration Statement or any Prospectus or for additional information.

(b) Amendments. The Company will prepare and file with the SEC, promptly upon the Investor's request, any amendments or supplements to the Shelf Registration Statement, any New Registration Statement or any Prospectus, as applicable, that, in the Investor's reasonable opinion, may be necessary or advisable in connection with any acquisition or sale of Registrable Securities by the Investor (provided, however, that the failure of the Investor to make such request shall not relieve the Company of any obligation or liability hereunder).

(c) Form S-3. The Company will cause each amendment or supplement to the Prospectus, other than documents incorporated by reference, to be filed with the SEC as required pursuant to the rules of Form S-3.

(d) Copies Available. The Company will furnish to the Investor and its counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all documents incorporated by reference therein), any Prospectus Supplement, any New Registration Statement and all amendments and supplements to the Registration Statement, the Prospectus or any New Registration Statement that are filed with the SEC during the Registration Period (including all documents filed with or furnished to the SEC during such period that are deemed to be incorporated by reference therein), in each case as soon as reasonably practicable and in such quantities as the Investor may from time to time reasonably request and, at the Investor's request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Registrable Securities may be made; provided, however, that the Company shall not be required to furnish any document (other than the Prospectus) to the Investor to the extent such document is available on EDGAR.

(e) Qualification. The Company shall take all such action, if any, as is reasonably necessary in order to obtain an exemption for or to qualify (i) the issuance of the Commitment Shares and the sale of the Purchase Shares to the Investor under this Agreement and (ii) any subsequent resale of all Commitment Shares and all Purchase Shares by the Investor, in each case, under applicable securities or "Blue Sky" laws of the states of the United States in such states as is reasonably requested by the Investor during the Registration Period, and shall provide evidence of any such action so taken to the Investor. The Company shall promptly notify the Investor who holds Registrable Securities of the receipt by the Company of any notification with respect to the suspension of the registration or qualification of any of the Registrable Securities for sale under the securities or "blue sky" laws of any jurisdiction in the United States or its receipt of actual notice of the initiation or threat of any proceeding for such purpose.

(f) Notification of Stop Orders. The Company shall advise the Investor promptly (but in no event later than 24 hours) and shall confirm such advice in writing, in each case: (i) of the Company's receipt of notice of any request by the SEC or any other federal or state governmental authority for amendment of or a supplement to the Registration Statement or any Prospectus or for any additional information; (ii) of the Company's receipt of notice of the issuance by the SEC or any other federal or state governmental authority of any stop order suspending the effectiveness of the Registration Statement or prohibiting or suspending the use of the Prospectus or Prospectus Supplement, or any New Registration Statement, or of the Company's receipt of any notification of the suspension of qualification of the Registrable Securities for offering or sale in any jurisdiction or the initiation or contemplated initiation of any proceeding for such purpose; and (iii) of the Company becoming aware of the happening of any event, which makes any statement of a material fact made in the Registration Statement or any Prospectus untrue or which requires the making of any additions to or changes to the statements then made in the Registration Statement or any Prospectus in order to state a material fact required by the Securities Act to be stated therein or necessary in order to make the statements then made therein (in the case of any Prospectus, in light of the circumstances under which they were made) not misleading, or of the necessity to amend the Registration Statement or any Prospectus to comply with the Securities Act or any other law. The Company shall not be required to disclose to the Investor the substance or specific reasons of any of the events set forth in clauses (i) through (iii) of the immediately preceding sentence, but rather, shall only be required to disclose that the event has occurred. If at any time the SEC, or any other federal or state governmental authority shall issue any stop order suspending the effectiveness of the Registration Statement or prohibiting or suspending the use of the Prospectus or Prospectus Supplement, the Company shall use its reasonable best efforts to obtain the withdrawal of such order at the earliest practicable time. The Company shall furnish to the Investor, without charge upon request, a copy of any correspondence from the SEC or the staff of the SEC, or any other federal or state governmental authority to the Company or its representatives relating to the Shelf Registration Statement, any New Registration Statement or any Prospectus, or Prospectus Supplement as the case may be. The Company shall not deliver to the Investor any Regular Purchase Notice, Accelerated Purchase Notice or Additional Accelerated Purchase Notice, and the Investor shall not be obligated to purchase any shares of Common Stock under this Agreement, during the continuation or pendency of any of the foregoing events. If at any time the SEC shall issue any stop order suspending the effectiveness of the Registration Statement or prohibiting or suspending the use of the Prospectus or any Prospectus Supplement, the Company shall use its reasonable best efforts to obtain the withdrawal of such order at the earliest practicable time. The Company shall furnish to the Investor, without charge upon request, a copy of any correspondence from the SEC or the staff of the SEC to the Company or its representatives relating to the Registration Statement or the Prospectus, as the case may be.

(g) Listing on the Principal Market. The Company shall promptly secure the listing, or conditional listing as applicable, of all of the Purchase Shares and Commitment Shares to be issued to the Investor hereunder on the Principal Market (subject to standard listing conditions, if any, for transactions of this nature, official notice of issuance and the Exchange Cap) and upon each other national securities exchange or automated quotation system, if any, upon which the Common Stock are then listed, and shall maintain, so long as any Common Stock shall be so listed, such listing of all such Registrable Securities from time to time issuable hereunder. The Company shall use reasonable best efforts to maintain the listing of the Common Stock on the Principal Market and shall comply in all respects with the Company's reporting, filing and other obligations under the bylaws or rules and regulations of the Principal Market. Neither the Company nor any of its Subsidiaries shall take any action that would reasonably be expected to result in the delisting or suspension of the Common Stock on the Principal Market. The Company shall promptly, and in no event later than the following Business Day, provide to the Investor copies of any notices it receives from any Person regarding the continued eligibility of the Common Stock for listing on the Principal Market. The Company shall pay all fees and expenses in connection with satisfying its obligations under this Section 3(h).

(h) Delivery of Shares. The Company shall cooperate with the Investor to facilitate the timely preparation and delivery of DWAC Shares (not bearing any restrictive legend) representing the Registrable Securities to be offered pursuant to the Shelf Registration Statement or any New Registration Statement and enable such DWAC Shares to be in such denominations or amounts as the Investor may reasonably request and registered in such names as the Investor may request.

(i) Transfer Agent. The Company shall at all times maintain the services of the Transfer Agent with respect to its Common Stock.

(j) Approvals. The Company shall use its reasonable best efforts to cause the Registrable Securities covered by any Registration Statement to be Registered with or approved by such other governmental agencies or authorities in the United States as may be necessary to consummate the disposition of such Registrable Securities.

(k) Confirmation of Effectiveness. If reasonably requested in writing by the Investor at any time, the Company shall deliver to the Investor a written confirmation from the Company of whether or not the effectiveness of such Registration Statement has lapsed at any time for any reason (including, without limitation, the issuance of a stop order) and whether or not the Registration Statement is currently effective and available to the Company for sale of all of the Registrable Securities.

(l) Further Assurances. The Company agrees to take all other reasonable actions as necessary and reasonably requested in writing by the Investor to expedite and facilitate disposition by the Investor of Registrable Securities pursuant to any Registration Statement.

(m) Suspension of Sales. The Investor agrees that, upon receipt of any notice from the Company of the existence of any suspension or stop order as set forth in Section 3(f) or 3(g), the Investor will immediately discontinue disposition of Registrable Securities pursuant to any Registration Statement covering such Registrable Securities until the Investor's receipt of the copies of a notice regarding the resolution or withdrawal of the suspension or stop order as contemplated by Section 3(f) or 3(g). Notwithstanding anything to the contrary, the Company shall cause its transfer agent to promptly deliver DWAC Shares of Common Stock without any restrictive legend in accordance with the terms of the Purchase Agreement in connection with any sale of Registrable Securities with respect to which an Investor has entered into a contract for sale prior to the Investor's receipt of a notice from the Company of the happening of any event of the kind described in Section 3(f) or 3(g) and for which the Investor has not yet settled.

4. Obligations of the Investor.

(a) Investor Information. The Investor has furnished to the Company in Exhibit A hereto such information regarding itself, the Registrable Securities held by it, the Registrable Securities held by it and the intended method of disposition thereof, including any arrangement between the Investor and any other Person relating to the sale or distribution of the Securities, as required to effect the registration of such Registrable Securities and shall execute such documents in connection with such registration as the Company may reasonably request. The Company shall notify the Investor in writing of any other information the Company reasonably requires from the Investor in connection with any Registration Statement hereunder. The Investor will as promptly as practicable notify the Company of any material change in the information set forth in Exhibit A, other than changes in its ownership of Common Stock.

(b) Investor Cooperation. The Investor agrees to cooperate with the Company as reasonably requested by the Company in connection with the preparation and filing of any amendments and supplements to any Registration Statement or New Registration Statement hereunder.

5. Expenses of Registration.

All reasonable expenses of the Company, other than sales or brokerage commissions and fees and disbursements of counsel for the Investor, incurred in connection with registrations, filings or qualifications pursuant to Sections 2 and 3, including, without limitation, all registration, listing and qualifications fees, printers and accounting fees, and fees and disbursements of counsel for the Company, shall be paid by the Company.

6. Indemnification.

(a) To the fullest extent permitted by law, the Company will, and hereby does, indemnify, hold harmless and defend the Investor, each Person, if any, who controls the Investor, the members, the directors, officers, partners, employees, managers, agents, representatives of the Investor and each Person, if any, who controls the Investor within the meaning of the Securities Act or the Exchange Act (each, an "Indemnified Person"), against any losses, claims, damages, liabilities, judgments, fines, penalties, charges, costs, reasonable attorneys' fees, amounts paid in settlement (with the consent of the Company, such consent not to be unreasonably withheld) or reasonable expenses, (collectively, "Claims") reasonably incurred in investigating, preparing or defending any action, claim, suit, inquiry, proceeding, investigation or appeal taken from the foregoing by or before any court or governmental, administrative or other regulatory agency or body or the SEC, whether pending or threatened, whether or not an indemnified party is or may be a party thereto ("Indemnified Damages"), to which any of them may become subject insofar as such Claims (or actions or proceedings, whether commenced or threatened, in respect thereof) arise out of or are based upon: (i) any untrue statement or alleged untrue statement of a material fact in the Shelf Registration Statement, any New Registration Statement or any post-effective amendment thereto or in any filing made in connection with the qualification of the offering under the securities or other "blue sky" laws of any jurisdiction in which Registrable Securities are offered ("Blue Sky Filing"), or the omission or alleged omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading, (ii) any untrue statement or alleged untrue statement of a material fact contained in the final Prospectus or the omission or alleged omission to state therein any material fact necessary to make the statements made therein, in light of the circumstances under which the statements therein were made, not misleading, (iii) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any other law, including, without limitation, any state securities law, or any rule or regulation thereunder relating to the offer or sale of the Registrable Securities pursuant to the Shelf Registration Statement or any New Registration Statement or (iv) any material violation by the Company of this Agreement (the matters in the foregoing clauses (i) through (iv) being, collectively, "Violations"). The Company shall reimburse each Indemnified Person promptly as such expenses are incurred and are due and payable, for any reasonable legal fees or other reasonable expenses incurred by them in connection with investigating or defending any such Claim. Notwithstanding anything to the contrary contained herein, the indemnification agreement contained in this Section 6(a): (A) shall not apply to a Claim by an Indemnified Person arising out of or based upon a Violation which occurs in reliance upon and in conformity with information furnished in writing to the Company by the Investor or such Indemnified Person expressly for use in connection with the preparation of the Registration Statement, any New Registration Statement, the Prospectus or any such amendment thereof or supplement thereto, if such in each case if the foregoing was timely made available by the Company; (B) with respect to any superseded prospectus, shall not inure to the benefit of any such Person from whom the Person asserting any such Claim purchased the Registrable Securities that are the subject thereof (or to the benefit of any other Indemnified Person) if the untrue statement or omission of material fact contained in the superseded prospectus was corrected in the revised prospectus, as then amended or supplemented, if such revised prospectus was timely made available by the Company pursuant to Section 3(c) or Section 3(e), and the Indemnified Person was promptly advised in writing not to use the incorrect prospectus prior to the use giving rise to a violation; (C) shall not be available to the extent such Claim is based on a failure of the Investor to deliver, or to cause to be delivered, the prospectus made available by the Company, if such prospectus was theretofore made available by the Company pursuant to Section 3(c) or Section 3(e); and (D) shall not apply to amounts paid in settlement of any Claim if such settlement is effected without the prior written consent of the Company, which consent shall not be unreasonably withheld. Such indemnity shall remain in full force and effect regardless of any investigation made by or on behalf of the Indemnified Person and shall survive the transfer of the Registrable Securities by the Investor pursuant to Section 8.

(b) In connection with the Shelf Registration Statement any New Registration Statement or Prospectus, the Investor agrees to indemnify, hold harmless and defend, to the same extent and in the same manner as is set forth in Section 6(a), the Company, each of its directors, each of its officers who signed the Shelf Registration Statement or signs any New Registration Statement, each Person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act (collectively and together with an Indemnified Person, an "Indemnified Party"), against any Claim or Indemnified Damages to which any of them may become subject, under the Securities Act, the Exchange Act or otherwise, insofar as such Claim or Indemnified Damages arise out of or are based upon any Violation, in each case to the extent, and only to the extent, that such Violation occurs in reliance upon and in conformity with written information about the Investor set forth on Exhibit A attached hereto or updated from time to time in writing by the Investor and furnished to the Company by the Investor expressly for inclusion in the Shelf Registration Statement or Prospectus or any New Registration Statement or from the failure of the Investor to deliver or to cause to be delivered the prospectus made available by the Company, if such prospectus was timely made available by the Company pursuant to Section 3(c) or Section 3(e); and, subject to Section 6(d), the Investor will reimburse any legal or other expenses reasonably incurred by them in connection with investigating or defending any such Claim; provided, however, that the indemnity agreement contained in this Section 6(b) and the agreement with respect to contribution contained in Section 7 shall not apply to amounts paid in settlement of any Claim if such settlement is effected without the prior written consent of the Investor, which consent shall not be unreasonably withheld; provided, further, however, that the Investor shall be liable under this Section 6(b) for only that amount of a Claim or Indemnified Damages as does not exceed the net proceeds to the Investor as a result of the sale of Registrable Securities pursuant to such Registration Statement. Such indemnity shall remain in full force and effect regardless of any investigation made by or on behalf of such Indemnified Party and shall survive the transfer of the Registrable Securities by the Investor pursuant to Section 8.

(c) Promptly after receipt by an Indemnified Person or Indemnified Party under this Section 6 of notice of the commencement of any action or proceeding (including any governmental action or proceeding) involving a Claim, such Indemnified Person or Indemnified Party shall, if a Claim in respect thereof is to be made against any indemnifying party under this Section 6, deliver to the indemnifying party a written notice of the commencement thereof, and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume control of the defense thereof with counsel mutually satisfactory to the indemnifying party and the Indemnified Person or the Indemnified Party, as the case may be; provided, however, that an Indemnified Person or Indemnified Party shall have the right to retain its own counsel with the fees and expenses to be paid by the indemnifying party, if, in the reasonable opinion of counsel retained by the indemnifying party, the representation by such counsel of the Indemnified Person or Indemnified Party and the indemnifying party would be inappropriate due to actual or potential differing interests between such Indemnified Person or Indemnified Party and any other party represented by such counsel in such proceeding. The Indemnified Party or Indemnified Person shall cooperate with the indemnifying party in connection with any negotiation or defense of any such action or claim by the indemnifying party and shall furnish to the indemnifying party all information reasonably available to the Indemnified Party or Indemnified Person which relates to such action or claim. The indemnifying party shall keep the Indemnified Party or Indemnified Person fully apprised as to the status of the defense or any settlement negotiations with respect thereto. No indemnifying party shall be liable for any settlement of any action, claim or proceeding effected without its written consent, provided, however, that the indemnifying party shall not unreasonably withhold, delay or condition its consent. No indemnifying party shall, without the consent of the Indemnified Party or Indemnified Person, consent to entry of any judgment or enter into any settlement or other compromise which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party or Indemnified Person of a release from all liability in respect to such claim or litigation. Following indemnification as provided for hereunder, the indemnifying party shall be subrogated to all rights of the Indemnified Party or Indemnified Person with respect to all third parties, firms or corporations relating to the matter for which indemnification has been made. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action shall not relieve such indemnifying party of any liability to the Indemnified Person or Indemnified Party under this Section 6, except to the extent that the indemnifying party is prejudiced in its ability to defend such action.

d. The indemnification required by this Section 6 shall be made by periodic payments of the amount thereof during the course of the investigation or defense, as and when bills are received or Indemnified Damages are incurred. Any Person receiving a payment pursuant to this Section 6 which person is later determined to not be entitled to such payment shall return such payment to the person making it.

e. The indemnity agreements contained herein shall be in addition to (i) any cause of action or similar right of the Indemnified Party or Indemnified Person against the indemnifying party or others, and (ii) any liabilities the indemnifying party may be subject to pursuant to the law.

7. Contribution.

To the extent any indemnification by an indemnifying party is prohibited or limited by law, the indemnifying party agrees to make the maximum contribution with respect to any amounts for which it would otherwise be liable under Section 6 to the fullest extent permitted by law; provided, however, that: (i) no seller of Registrable Securities guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any seller of Registrable Securities who was not guilty of fraudulent misrepresentation; and (ii) contribution by any seller of Registrable Securities shall be limited in amount to the net amount of proceeds received by such seller from the sale of such Registrable Securities.

8. Assignment of Registration Rights.

The Company shall not assign this Agreement or any rights or obligations hereunder without the prior written consent of the Investor; provided, however, that any transaction, whether by merger, reorganization, restructuring, consolidation, financing or otherwise, whereby the Company remains the surviving entity immediately after such transaction shall not be deemed an assignment. The Investor may not assign its rights under this Agreement without the prior written consent of the Company, other than to an affiliate of the Investor controlled by Jonathan Cope or Josh Scheinfeld, in which case the assignee must agree in writing to be bound by the terms and conditions of this Agreement.

9. Amendment of Registration Rights.

No provision of this Agreement may be amended or waived by the parties from and after the date that is one Business Day immediately preceding the initial filing of the Initial Prospectus Supplement with the SEC. Subject to the immediately preceding sentence, no provision of this Agreement may be (i) amended other than by a written instrument signed by both parties hereto or (ii) waived other than in a written instrument signed by the party against whom enforcement of such waiver is sought. Failure of any party to exercise any right or remedy under this Agreement or otherwise, or delay by a party in exercising such right or remedy, shall not operate as a waiver thereof.

10. Miscellaneous.

(a) Notices. Any notices, consents or other communications required or permitted to be given under the terms of this Agreement must be in writing and will be deemed to have been delivered: (i) upon receipt, when delivered personally; (ii) upon receipt, when sent by facsimile (provided confirmation of transmission is mechanically or electronically generated and kept on file by the sending party); (iii) upon receipt, when sent by electronic message (provided the recipient responds to the message and confirmation of both electronic messages are kept on file by the sending party); or (iv) one (1) Business Day after timely deposit with a nationally recognized overnight delivery service, in each case properly addressed to the party to receive the same. The addresses and facsimile numbers for such communications shall be:

If to the Company:

KemPharm, Inc.
1180 Celebration Boulevard
Suite 103
Celebration, FL 34747
Telephone: (321) 939-3416
E-mail: lclifton@kempharm.com
Attention: R. LaDuane Clifton

With a copy (which shall not constitute notice) to:

Cooley LLP
1299 Pennsylvania Avenue, NW, Suite 700
Washington, DC 2004
E-mail: bsiler@cooley.com \
Attention: Brent Siler

If to the Investor:

Lincoln Park Capital Fund, LLC
440 North Wells, Suite 410
Chicago, IL 60654
Telephone: 312.822.9300
Facsimile: 312.822.9301
E-mail: jscheinfeld@lpcfunds.com/jcope@lpcfunds.com
Attention: Josh Scheinfeld/Jonathan Cope

With a copy (which shall not constitute notice) to:

K&L Gates, LLP
200 South Biscayne Boulevard
Suite 3900
Miami, Florida 33131
Telephone: 305.539.3300
Facsimile: 305.358.7095
E-mail: clayton.parker@klgates.com/matthew.ogurick@klgates.com
Attention: Clayton E. Parker, Esq./Matthew Ogurick, Esq.

or at such other address, e-mail address and/or facsimile number and/or to the attention of such other person as the recipient party has specified by written notice given to each other party at least one (1) Business Day prior to the effectiveness of such change. Written confirmation of receipt (A) given by the recipient of such notice, consent or other communication, (B) mechanically or electronically generated by the sender's facsimile machine containing the time, date, and recipient facsimile number, (C) electronically generated by the sender's electronic mail containing the time, date and recipient email address or (D) provided by a nationally recognized overnight delivery service, shall be rebuttable evidence of receipt in accordance with clause (i), (ii), (iii) or (iv) above, respectively. Any party to this Agreement may give any notice or other communication hereunder using any other means (including messenger service, ordinary mail or electronic mail), but no such notice or other communication shall be deemed to have been duly given unless it actually is received by the party for whom it is intended.

(b) No Waiver No failure or delay in the exercise of any power, right or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise of any such power, right or privilege preclude other or further exercise thereof or of any other right, power or privilege.

(c) Governing Law. All questions concerning the construction, validity, enforcement and interpretation of this Agreement and other Transaction Documents shall be governed by the internal laws of the State of New York, without giving effect to any choice of law or conflict of law provision or rule (whether of the State of New York or any other jurisdictions) that would cause the application of the laws of any jurisdictions other than the State of New York. Each party hereby irrevocably submits to the exclusive jurisdiction of and venue in the U.S. District Court for the Southern District of New York or, if that court does not have subject matter jurisdiction, in any state court located in the City and County of New York for the adjudication of any dispute hereunder or in connection herewith or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof to such party at the address for such notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law. If any provision of this Agreement shall be invalid or unenforceable in any jurisdiction, such invalidity or unenforceability shall not affect the validity or enforceability of the remainder of this Agreement in that jurisdiction or the validity or enforceability of any provision of this Agreement in any other jurisdiction. **EACH PARTY HEREBY IRREVOCABLY WAIVES ANY RIGHT IT MAY HAVE, AND AGREES NOT TO REQUEST, A JURY TRIAL FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HEREWITH OR ARISING OUT OF THIS AGREEMENT OR ANY TRANSACTION CONTEMPLATED HEREBY.**

(d) Integration. This Agreement**,** the Purchase Agreement and the other Transaction Documents constitute the entire understanding among the parties hereto with respect to the subject matter hereof and thereof. There are no restrictions, promises, warranties or undertakings, other than those set forth or referred to herein and therein. This Agreement**,** the Purchase Agreement and the other Transaction Documents supersede all other prior oral or written agreements between the Investor, the Company, their affiliates and persons acting on their behalf with respect to the subject matter hereof and thereof.

(e) No Third Party Benefits. Subject to the requirements of Section 8, this Agreement shall inure to the benefit of and be binding upon the permitted successors and assigns of each of the parties hereto.

(f) Headings. The headings in this Agreement are for convenience of reference and shall not form part of, or affect the interpretation of, this Agreement.

(g) Counterparts. This Agreement may be executed in two or more identical counterparts, all of which shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to the other party; provided that a facsimile or pdf (or other electronic reproduction of a) signature shall be considered due execution and shall be binding upon the signatory thereto with the same force and effect as if the signature were an original, not a facsimile or pdf (or other electronic reproduction of a) signature.

(h) Each party shall do and perform, or cause to be done and performed, all such further acts and things, and shall execute and deliver all such other agreements, certificates, instruments and documents as the other party may reasonably request in order to carry out the intent and accomplish the purposes of this Agreement and the consummation of the transactions contemplated hereby.

(i) The language used in this Agreement will be deemed to be the language chosen by the parties to express their mutual intent and no rules of strict construction will be applied against any party.

(j) This Agreement is intended for the benefit of the parties hereto and their respective permitted successors and assigns, and is not for the benefit of, nor may any provision hereof be enforced by, any other Person.

(k) Termination. The obligations of the Company contained in Sections 2, 3, 5 and 8 of this Agreement shall terminate in their entirety upon the earlier of (i) the date on which the Investor shall have sold all the Securities and no Available Amount remains under the Purchase Agreement and (ii) 180 days following the earlier of (A) the Maturity Date and (B) the date of termination of the Purchase Agreement; provided that as long as any Securities remain unsold by the Investor, the Company must make available "current public information" pursuant to Rule 144 promulgated under the Securities Act until the Investor may sell the Securities thereunder without any restrictions (including any restrictions under Rule 144(c) or Rule 144(i)).

*** * * * * ***

IN WITNESS WHEREOF, the parties have caused this Registration Rights Agreement to be duly executed as of day and year first above written.

THE COMPANY:

KEMPHARM, INC.

By: /s/ R. LaDuane Clifton
Name: R. LaDuane Clifton
Title: Chief Financial Officer

INVESTOR:

LINCOLN PARK CAPITAL FUND, LLC
BY: LINCOLN PARK CAPITAL, LLC
BY: ALEX NOAH INVESTORS, INC.

By: /s/ Jonathan Cope
Name: Jonathan Cope
Title: President

EXHIBIT A

Information About The Investor Furnished To The Company By The Investor
Expressly For Use In Connection With The Registration Statement and Prospectus

Information With Respect to Lincoln Park Capital

Immediately prior to the date of the Purchase Agreement, Lincoln Park Capital Fund, LLC, beneficially owned 300,000 shares of Common Stock. Josh Scheinfeld and Jonathan Cope, the Managing Members of Lincoln Park Capital, LLC, the manager of Lincoln Park Capital Fund, LLC, are deemed to be beneficial owners of all of the Common Stock owned by Lincoln Park Capital Fund, LLC. Messrs. Cope and Scheinfeld have shared voting and investment power over the shares being offered under the prospectus supplement filed with the SEC in connection with the transactions contemplated under the Purchase Agreement. Lincoln Park Capital, LLC is not a licensed broker dealer or an affiliate of a licensed broker dealer.

Exhibit 5.1

Cooley

Matthew P. Dubofsky
+1 720 566 4244
mdubofsky@cooley.com

March 1, 2019

KemPharm, Inc.
1180 Celebration Boulevard, Suite 103
Celebration, Florida 34747

Ladies and Gentlemen:

You have requested our opinion, as counsel to KemPharm, Inc., a Delaware corporation (the "***Company***"), with respect to certain matters in connection with the issuance and sale by the Company of 120,200 shares (the "***Commitment Shares***") of the Company's common stock, par value $0.0001 per share ("***Common Stock***"), and additional shares of Common Stock having aggregate sales proceeds of up to $15,000,000 (together with the Commitment Shares, the "***Shares***"), pursuant to a Registration Statement on Form S-3 (No. 333-213926) (the "***Registration Statement***"), filed with the Securities and Exchange Commission (the "***Commission***") under the Securities Act of 1933, as amended (the "***Act***"), the prospectus included within the Registration Statement (the "***Base Prospectus***"), and the prospectus supplement dated March 1, 2019, filed with the Commission pursuant to Rule 424(b) of the Rules and Regulations of the Act (together with the Base Prospectus, the "***Prospectus***."). The Shares are to be sold by the Company in accordance with a Purchase Agreement, dated February 28, 2019, between the Company and Lincoln Park Capital Fund, LLC (the "***Agreement***"), as described in the Prospectus.

In connection with this opinion, we have examined and relied upon the Registration Statement and the Prospectus, the Agreement, the Company's Amended and Restated Certificate of Incorporation, as amended, its Amended and Restated Bylaws, and the originals or copies certified to our satisfaction of such records, documents, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below. In rendering this opinion, we have assumed the genuineness and authenticity of all signatures on original documents; the genuineness and authenticity of all documents submitted to us as originals; the conformity to originals of all documents submitted to us as copies; and the accuracy, completeness and authenticity of certificates of public officials.

We have assumed (i) that each sale of Shares will be duly authorized by the Board of Directors of the Company, a duly authorized committee thereof or a person or body pursuant to an authorization granted in accordance with Section 152 of the General Corporation Law of the State of Delaware (the "***DGCL***"), (ii) that no more than 15,120,200 Shares will be sold under the Agreement and (iii) that the price at which the Shares are sold will equal or exceed the par value of the Shares. We express no opinion to the extent that future issuances of securities of the Company and/or anti-dilution adjustments to outstanding securities of the Company cause the number of shares of the Company's common stock outstanding or issuable upon conversion or exercise of outstanding securities of the Company to exceed the number of Shares then issuable under the Agreement.

Our opinion herein is expressed solely with respect to the General Corporation Law of the State of Delaware. Our opinion is based on these laws as in effect on the date hereof. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when sold and issued against payment therefor in accordance with the Agreement, the Registration Statement and the Prospectus, will be validly issued, fully paid and non-assessable.

We consent to the reference to our firm under the caption "Legal Matters" in the Prospectus and to the filing of this opinion as an exhibit to the Company's Annual Report on Form 10-K to be filed with the Commission for incorporation by reference into the Registration Statement.

Very truly yours,

Cooley LLP

By: /s/ Matthew P. Dubofsky
Matthew P. Duboksky

Exhibit 10.3.5

SEVENTH AMENDMENT TO
SENIOR SECURED CONVERTIBLE NOTE AND SIXTH AMENDMENT TO WARRANT

THIS SEVENTH AMENDMENT TO SENIOR SECURED CONVERTIBLE NOTE AND SIXTH AMENDMENT WARRANT (this "Amendment"), effective as of February 28, 2019, amends certain terms of (i) that certain Senior Secured Convertible Note in the original principal amount of $10,000,000 issued by KemPharm, Inc., a Delaware corporation (the "Company"), to Deerfield Private Design Fund III, L.P. (the "Holder") on June 2, 2014 (as the same may be amended, restated, modified or otherwise supplemented from time to time, the "Note"), and (ii) that certain warrant number W-74, issued by the Company to the Holder on June 2, 2014, relating to the right of the Holder to purchase from the Company 1,923,077 fully paid and nonassessable shares of common stock of the Company (as the same may be amended, restated, supplemented or otherwise modified from time to time, the "Warrant").

WHEREAS, the Company and the Holder desire to revise certain terms of the Note and Warrant as provided herein.

In consideration of the promises and mutual covenants contained herein and in the Note and Warrant, the undersigned hereby agree as follows:

1. Section 2(f)(i)(A) of the Note is hereby amended by adding the following paragraph immediately after the third paragraph of such section:

"Notwithstanding anything to the contrary contained herein, this Section 2(f)(i)(A) shall not apply to any issuance or sale of Common Stock, Convertible Securities or Options by the Company if such issuance or sale is made pursuant to the terms of (x) that certain Purchase Agreement, dated February 28, 2019 , by and between the Company and Lincoln Park Capital Fund, LLC, or (y) that certain Common Stock Sales Agreement, dated as of September 4, 2018, by and between the Company and RBC Capital Markets, LLC."

2. Section 5(f)(i) of the Warrant is hereby amended by adding the following paragraph immediately after the third paragraph of such section:

"Notwithstanding anything to the contrary contained herein, this Section 5(f)(i) shall not apply to any issuance or sale of Common Stock, Convertible Securities or Options by the Company if such issuance or sale is made pursuant to the terms of (x) that certain Purchase Agreement, dated February 28, 2019 , by and between the Company and Lincoln Park Capital Fund, LLC, or (y) that certain Common Stock Sales Agreement, dated as of September 4, 2018, by and between the Company and RBC Capital Markets, LLC."

3. Any warrants issuable in the future pursuant to Section 2.10 of that certain Facility Agreement, dated as of June 2, 2014, by and between the Company and the Holder, as amended, shall reflect the amendments set forth in paragraph 2 above.

4. Effect on the Note and Warrant. Except as amended herein, the Note and Warrant shall continue in full force and effect as originally executed and delivered, as previously amended prior to the date hereof. Any reference in the Note and the Warrant to "this Warrant," "this "Note" "hereunder," hereof," "herein," or words of like import referring to such agreement shall refer to the Warrant or Note, as the case may be, as amended by this Amendment.

5. Registration Rights Consent. The Holder hereby (i) consents to the Company's entry into (x) that certain Registration Rights Agreement, dated on or around the date hereof, by and between the Company and Lincoln Park Capital Fund, LLC ("LPCF"); and (y) that certain Purchase Agreement, dated on or around the date hereof, by and between the Company and LPCF, pursuant to which, in each case, the Company has agreed to provide LPCF with certain registration rights specified therein (the "Registration Rights"), and (ii) waives any and all rights the Holder may have with regard to the Registration Rights and the Company's compliance therewith, including without limitation under Section 2.10 of that certain Amended and Restated Investors' Rights Agreement, dated as of February 19, 2015, by and among the Company, the Holder and other parties thereto.

6. Governing Law. This Amendment shall be governed by and construed and enforced in accordance with the internal laws of the State of New York, without regard to the principles of conflicts of law thereof.

7. Counterparts. This Amendment may be executed on separate counterparts that may be transmitted via an email .pdf file or facsimile, each of which, when so executed and delivered, shall be deemed an original and all of which counterparts, taken together, shall constitute one and the same Amendment.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Company and Holder have caused this Amendment to be duly executed and delivered as of the date first above written.

KEMPHARM, INC.

By: /s/ R. LaDuane Clifton
Name: R. LaDuane Clifton
Title: Chief Financial Officer

IN WITNESS WHEREOF, the Company and Holder have caused this Amendment to be duly executed and delivered as of the date first above written.

HOLDER:

DEERFIELD PRIVATE DESIGN FUND III, L.P.

By: Deerfield Mgmt III, L.P., General Partner
By: J. E. Flynn Capital III LLC, General Partner

By: /s/ David Clark
Name: David Clark
Title: Authorized Signatory

Exhibit 10.14

KemPharm, Inc.
Third 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 30,000 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.

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

COLLABORATION AND LICENSE AGREEMENT

BY AND BETWEEN

KVK TECH, INC.

AND

KEMPHARM, INC.

DATED AS OF OCTOBER 25, 2018

COLLABORATION AND LICENSE AGREEMENT

This **Collaboration and License Agreement** (the "**Agreement**") is entered into as of October 25, 2018 (the "**Effective Date**") by and between **KemPharm, Inc.**, a Delaware corporation, with its principal place of business at 2500 Crosspark Road, Suite E126, Coralville, IA 52241 ("**KemPharm**") and **KVK Tech, Inc.**, a Delaware corporation having a place of business at 110 Terry Drive, Newtown, PA, 18940 ("**KVK**"). KemPharm and KVK are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, KEMPHARM HAS DEVELOPED THE PRODUCT, AS DEFINED BELOW, FOR THE SHORT-TERM MANAGEMENT OF ACUTE PAIN, AND HAS OBTAINED REGULATORY APPROVAL OF THE PRODUCT IN THE U.S. FOR SUCH INDICATION, AS DEFINED BELOW; AND

WHEREAS, KVK DESIRES TO OBTAIN FROM KEMPHARM AN EXCLUSIVE LICENSE TO CONDUCT REGULATORY ACTIVITIES WITH RESPECT TO, MANUFACTURE AND COMMERCIALIZE, THE LICENSED PRODUCTS IN THE U.S., AND KEMPHARM IS WILLING TO GRANT SUCH LICENSE TO KVK, ALL UNDER THE TERMS AND CONDITIONS HEREOF, WITH CAPITALIZED TERMS AS DEFINED BELOW.

NOW, THEREFORE, IN CONSIDERATION OF THE FOREGOING PREMISES AND THE MUTUAL PROMISES, COVENANTS AND CONDITIONS CONTAINED IN THIS AGREEMENT, THE PARTIES AGREE AS FOLLOWS:

Article 1
Definitions

1.1 "**Act**" shall mean, as applicable, the United States Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§301 et seq., and/or the Public Health Service Act, 42 U.S.C. §§262 et seq., as such may be amended from time to time.

1.2 "**Affiliate**" means, with respect to a particular Party, a Person that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock of such entity, or by contract or otherwise. For clarity, once a Person ceases to be an Affiliate of a Party, then, without any further action, such Person shall cease to have any rights, including license and sublicense rights, under this Agreement by reason of being an Affiliate of such Party.

1.3 "**Authorized Generic"** means any version of Apadaz® specifically authorized by KVK for marketing and distribution as a generic in the Collaboration Territory.

1.4 "**Business Day**" means a day other than Saturday, Sunday or any day that banks in New York, New York are required or permitted to be closed.

1.5 "**Change of Control**" means with respect to either Party: (a) the sale of all or substantially all of such Party's assets or business relating to this Agreement; (b) a merger, reorganization or consolidation involving such Party in which the voting securities of such Party outstanding immediately prior thereto cease to represent at least fifty percent (50%) of the combined voting power of the surviving entity immediately after such merger, reorganization or consolidation; or (c) a person or entity, or group of persons or entities, acting in concert acquire more than fifty percent (50%) of the voting equity securities or management control of such Party.

1.6 "**Collaboration Territory**" means the U.S., including its territories and possessions.

1.7 "**CMC Information**" means Information related to the chemistry, manufacturing and controls of the Licensed Products, as specified by the FDA and other applicable Regulatory Authorities.

1.8 "**Commercialization**," with a correlative meaning for "**Commercialize**" and "**Commercializing**," means all activities undertaken before and after obtaining Regulatory Approvals relating specifically to the pre-launch, launch, promotion, detailing, medical education and medical liaison activities, marketing, pricing, reimbursement, sale, and distribution of Licensed Products, including strategic marketing, sales force detailing, advertising, market Licensed Product support, all customer support, Licensed Product distribution and invoicing and sales activities.

1.9 "**Commercialization/Regulatory Expenses**" means the actual, out-of-pocket costs and expenses, in U.S. Dollars, as defined by KVK's consistent application of U.S. GAAP, incurred by or on behalf of KVK in (a) the Commercialization of Licensed Products in the Field in the Collaboration Territory, including any payments made by KVK to Third Parties in connection with obtaining or maintaining intellectual property rights that are necessary or useful for the Commercialization of Licensed Products under this Agreement ("**Third Party Commercial IP Costs**") (it being understood that, in the event that any other Third Party is receiving the benefit of such Third Party intellectual property from the applicable Third Party licensor, then the Parties, through the JSC, as defined in Section 3.2(a), shall mutually agree upon an appropriate allocation of such Third Party Commercial IP Costs as between, on the one hand, KVK and KemPharm, and on the other hand, such Third Party licensee, prior to KVK entering into an agreement with such Third Party) and (b) the maintenance of Regulatory Approvals for Licensed Products.

1.10 "**Commercially Reasonable Efforts**" means, with respect to either Party's obligations under this Agreement, the carrying out of such obligations with a level of efforts and resources consistent with the commercially reasonable practices of a similarly situated company in the pharmaceutical industry for the active and diligent commercialization of a similarly situated branded pharmaceutical product as the Licensed Product at a similar stage of commercialization, taking into account efficacy, safety, patent and regulatory exclusivity, anticipated or approved labeling, present and future market potential, competitive market conditions, the profitability of the product in light of pricing and reimbursement issues, and all other relevant factors, but not taking into account any payment owed to KemPharm under this Agreement or any other pharmaceutical product that KVK is then researching, developing or commercializing, alone or with one or more collaborators.

1.11 [*].

1.12 "**Confidential Information**" of a Party means any and all Information, separately or in combination, of such Party that is disclosed to the other Party under this Agreement, whether in oral, written, graphic, or electronic form. In addition, all Information disclosed by a Party pursuant to the confidentiality agreement between the Parties dated November 28, 2017 (the "**Confidentiality Agreement**") shall be deemed to be Confidential Information of such Party disclosed hereunder; *provided, however,* that any use or disclosure of any such Information that is authorized under Article 12 shall not be restricted by, or be deemed a violation of, the Confidentiality Agreement.

1.13 "**Control**" means, with respect to any material, Information, or intellectual property right, that a Party (a) owns or (b) has a license, other than a license granted to such Party under this Agreement, to such material, Information, or intellectual property right and, in each case, has the ability to grant to the other Party access, a license, or a sublicense, as applicable, to the foregoing on the terms and conditions set forth in this Agreement without violating the terms of any existing agreement or other arrangement with any Third Party or being obligated to pay any royalties or other consideration therefor.

1.14 "**Data**" means all data generated by or on behalf of a Party or its Affiliate or their respective sublicensees pursuant to activities conducted under this Agreement. For clarity, Data does not include (a) any patentable inventions or (b) any formulations of benzhydrocodone or (c) any patentable inventions or any formulations of benzhydrocodone with any other pharmaceutical ingredient(s) other than acetaminophen.

1.15 "**Development**," with a correlative meaning for "**Develop**" and "**Developing**," means all activities relating to preclinical and clinical trials, toxicology testing, statistical analysis and publication and presentation of study results with respect to Licensed Products (collectively, "**Development Activities**") and (b) the reporting, preparation and submission of applications (including any CMC Information) for obtaining, registering and/or maintaining Regulatory Approval of Licensed Products (collectively, "**Regulatory Activities**").

1.16 "**FDA**" means the U.S. Food and Drug Administration or any successor entity.

1.17 "**Field**" means the therapeutic treatment of any and all human diseases and conditions that are included in the KemPharm Indications for the Licensed Product(s) and as are specifically indicated and included as per the Label.

1.18 "**First Commercial Sale**" means the first sale of a Licensed Product in the Collaboration Territory to a Third Party after Regulatory Approval has been obtained in the Collaboration Territory.

1.19 "**Fiscal Year**" means KVK's fiscal year that starts from January 1st and ends on December 31st.

1.20 "**GCP**" or "**Good Clinical Practices**" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines entitled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," including related regulatory requirements imposed by the FDA, as they may be updated from time to time.

1.21 "**GLP**" or "**Good Laboratory Practices**" means the then-current good laboratory practice standards promulgated or endorsed by the FDA as defined in 21 C.F.R. Part 58, as they may be updated from time to time.

1.22 "**Governmental Authority**" means any multi-national, national, federal, state, local, municipal, provincial or other governmental authority of any nature (including any governmental division, prefecture, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

1.23 "**Government Official**" means (a) any official or employee of any Governmental Authority, or any department, agency, or instrumentality thereof (including without limitation commercial entities owned or controlled, directly or indirectly, by a Governmental Authority), (b) any political party or official thereof, or any candidate for political office, in the Collaboration Territory or any other country, or (c) any official or employee of any public international organization.

1.24 "**IND**" means an Investigational New Drug application filed with the FDA, or an equivalent filing outside of the U.S.

1.25 "**Indication**" means a separately defined, well-categorized class of human disease or condition for which a separate NDA (including any extensions or supplements) may be, or has been, filed with the FDA. For clarity, if an NDA is approved for a Licensed Product in a particular Indication and patient population, a Label expansion for such Licensed Product to include such Indication in a different patient population shall not be considered a separate Indication.

1.26 "**Information**" means any data, results, technology, business or financial information or information of any type whatsoever, in any tangible or intangible form, including know-how, copyrights, trade secrets, practices, techniques, methods, processes, inventions, developments, specifications, formulae, software, algorithms, marketing reports, expertise, technology, test data (including pharmacological, biological, chemical, biochemical, clinical test data and data resulting from non-clinical studies), CMC Information, stability data and other study data and procedures.

1.27 "**Inventions**" means any inventions and/or discoveries, including Information, processes, methods, assays, designs, protocols, and formulas, and improvements or modifications thereof, patentable or otherwise, that is generated, developed, conceived or reduced to practice by or on behalf of a Party or its Affiliate or their respective sublicensees pursuant to activities conducted under this Agreement and that are directly related to the Licensed Product (combination product of benzhydrocodone and acetaminophen, e.g. Apadaz® , in each case including all rights, title and interest in and to the intellectual property rights therein and thereto; *provided, however,* that Inventions shall exclude Data.

1.28 "**KemPharm Indications**" means (a) any separately defined, well-categorized class of human disease or condition for which KemPharm has filed either a separate IND to an appropriate Regulatory Authority or a separate application to an appropriate Regulatory Authority for approval to market Licensed Products in the Collaboration Territory, or for which KemPharm is otherwise developing or commercializing Licensed Products in the Collaboration Territory (whether before or after the Effective Date) (which, for clarity, includes the short-term management of acute pain) or (b) the Label

1.29 "**KemPharm Product Mark**" means KemPharm's (or its Affiliates) trademark Apadaz®, or the alternative trademark selected by KemPharm for the Licensed Products in the Collaboration Territory pursuant to Section 9.6(a)(i), and related trade dress.

1.30 "**KVK Inventions**" means any Inventions generated by or on behalf of KVK, its Affiliates and their respective sublicensees, including their employees, agents and contractors.

1.31 "**KVK Patents**" means any Patents that claim KVK Inventions.

1.32 "Label" means any and all Indications as approved by an appropriate Regulatory Authority (e.g. FDA) for which the Licensed Product may be marketed, sold and used in the Collaboration Territory. For purposes of clarity, as of the Execution Date of this Agreement, the Label for the Licensed Product is attached to this Agreement as **Exhibit C**.

1.33 "**Laws**" means all laws, statutes, rules, regulations, ordinances and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.

1.34 "**Licensed IP**" means the Licensed Know-How and Licensed Patents.

1.35 "**Licensed Know-How**" means all Information (including Data and Regulatory Materials) that (a) (i) is Controlled by KemPharm or its Affiliates as of the Effective Date or (ii) becomes Controlled by KemPharm or its Affiliates during the Term, and (b) is necessary for the conduct of Regulatory Activities with respect to, Commercialization of, or the manufacture of, Licensed Products in the Field in the Collaboration Territory.

1.36 "**Licensed Patents**" means (a) with respect to Patents Controlled by KemPharm or any of its Affiliates as of the Effective Date, the Patents set forth in **Exhibit A**; and (b) with respect to any Patents that become Controlled by KemPharm or its Affiliates during the Term, such Patents that (i) are necessary for the conduct of Regulatory Activities with respect to, Commercialization of, or the manufacture of Licensed Products in the Field in the Collaboration Territory.

1.37 "Limited Licensed Priority Patents" means (a) with respect to Patents Controlled by KemPharm or any of its Affiliates as of the Effective Date, the Patents set forth in **Exhibit A-1** which are those Patents from any of the Patents set forth in **Exhibit A** as noted in Section 1.35 herein. For sake of clarity, issued claims within said Limited Licensed Priority Patents directly related to, or encompassing, products, combinations, compounds etc. other than the combination product of benzhydrocodone with acetaminophen are not included in the scope of the Limited License.

1.38 "**Licensed Product**" shall mean (a) the Product (e.g. Apadaz®), including any Authorized Generic version thereof, or (b) any other salt or polymorphic form of the Product being developed or commercialized by KemPharm in the Collaboration Territory. For clarity, Licensed Products shall exclude any product that (i) contains benzhydrocodone, benzhydrocodone pro-drug or benzyhydrocodone product candidate as the sole active ingredient, or (ii) contains benzhydrocodone in combination with any pharmaceutical ingredient(s) other than acetaminophen

1.39 "**Manufacturing Expenses**" means the fully burdened manufacturing cost in U.S. Dollars, as defined by applicable Party's consistent application of U.S. GAAP, of producing or obtaining supply of Licensed Products, which cost shall include, labor and material costs, quality assurance and control expenses, including required stability monitoring, and allocable facilities costs; provided, however, that if the applicable Party uses a contract manufacturer to perform any manufacturing activities with respect to the supply of Licensed Product under this Agreement, "Manufacturing Expenses" for such activities will be the sum of: (a) the price such Party pays such contract manufacturer for such activities, (b) such Party's fully burdened cost of supporting the contract manufacturer's performance of manufacturing activities with respect to Licensed Products and (c) any payments made by such Party to Third Parties in connection with obtaining or maintaining intellectual property rights that are necessary or useful for the manufacture of Licensed Products under this Agreement (irrespective of whether such agreements with Third Parties were entered into prior to the Effective Date or during the Term).

1.40 "**NDA**" means a New Drug Application filed with the FDA required for marketing approval for a Licensed Product in the U.S., but excluding pricing approvals.

1.41 "**Net Profits**" means, with respect to a given Rolling Year, the amount of Net Sales received by KVK, its Affiliates and their respective sublicensees in the Field in the Collaboration Territory for sales of Licensed Products, minus: (a) [*] incurred in such Rolling Year for Licensed Products and (b) [*] incurred in such Rolling Year for Licensed Products. If the amount received by KVK for Net Sales of Licensed Products in a given Rolling Year is less than the sum of the [*] and [*] in such Rolling Year, then the amount of such deficit shall be deemed a "**Net Loss**".

1.42 "**Net Sales**" means the gross amounts billed or invoiced by KVK, its Affiliates and their respective sublicensees for sales of Licensed Products to unaffiliated Third Parties, less the following deductions to the extent reasonable and customary, provided to unaffiliated entities and actually allowed and taken with respect to such sales:

(a) [*]

(b) [*]

(c) [*]

(d) [*] and

(e) [*].

Notwithstanding the foregoing, amounts received, billed or invoiced by KVK, its Affiliates, or their respective sublicensees for the sale of Licensed Product among KVK, its Affiliates or their respective sublicensees shall not be included in the computation of Net Sales hereunder unless the purchasing entity is the end-user. For purposes of determining Net Sales, the Licensed Product shall be deemed to be sold when billed or invoiced. Net Sales shall be accounted for in accordance with standard KVK practices for operation by KVK, its Affiliates or their respective sublicensees, as practiced in the Collaboration Territory, but in any event in accordance with U.S. GAAP, consistently applied in the Collaboration Territory. For clarity, a particular item may only be deducted once in the calculation of Net Sales.

With respect to any transfer of any Licensed Product in the Collaboration Territory for any substantive consideration other than monetary consideration on arm's length terms, for the purposes of calculating the Net Sales under this Agreement, such Licensed Product shall be deemed to be sold exclusively for money at the average Net Sales price charged to Third Parties for cash sales in the Collaboration Territory during the applicable reporting period, or if there were only de minimis cash sales in the Collaboration Territory, at the fair market value as determined by comparable markets.

KVK, its Affiliates, and their respective sublicensees shall sell the Licensed Product as a standalone product and will not sell the Licensed Product as a part of a bundle with other products or offer packaged arrangements to customers that include the Licensed Product, except with KemPharm's prior written consent.

1.43 "**Patents**" means (a) pending patent applications, issued patents, utility models and designs; (b) all patents issuing from patent applications of any of the foregoing; (c) reissues, substitutions, confirmations, registrations, validations, re-examinations, additions, continuations, continued prosecution applications, continuations-in-part, or divisions of or to any of the foregoing; and (d) extensions, renewals or restorations of any of the foregoing by existing or future extension, renewal or restoration mechanisms, including supplementary protection certificate or the equivalent thereof.

1.44 "Patent Term Adjustment" means the calculation of an adjustment to any United States Patent term pursuant to the Rules of the United States Patent Office and U. S. patent law.

1.45 "Patent Term Extension" means extension of U.S. patent term under 35 U.S.C. § 156 and related statutes to compensate for product commercialization delays due to regulatory review of the Licensed Product.

1.46 "**Person**" means an individual, corporation, partnership, limited liability company, limited partnership, trust, business trust, association, joint stock company, joint venture, pool, syndicate, "group" as defined in Section 13(d)(3) of the Securities Exchange Act of 1934, as amended, sole proprietorship, unincorporated organization, Governmental Authority or any other form of entity not specifically listed herein.

1.47 "**Product**" means specifically KemPharm's benzhydrocodone/acetaminophen combination product for the short-term management of acute pain, which is branded in the U.S. as Apadaz® and sold in tablet form.

1.48 "**Proper Conduct Practices**" means, KVK and each of its Representatives not, directly or indirectly, (a) making, offering, authorizing, providing or paying anything of value in any form, whether in money, property, services or otherwise to any Government Official, or other Person charged with similar public or quasi-public duties, or to any customer, supplier, or any other Person, or to any employee thereof, or failing to disclose fully any such payments in violation of the laws of any relevant jurisdiction to (i) obtain favorable treatment in obtaining or retaining business for it or any of its Affiliates, (ii) pay for favorable treatment for business secured, (iii) obtain special concessions or for special concessions already obtained, for or in respect of it or any of its Affiliates, in each case which would have been in violation of any applicable Law, (iv) influence an act or decision of the recipient (including a decision not to act) in connection with the Person's or its Affiliate's business, (v) induce the recipient to use his or her influence to affect any government act or decision in connection with the Person's or its Affiliate's business or (vi) induce the recipient to violate his or her duty of loyalty to his or her organization, or as a reward for having done so; (b) engaging in any transactions, establishing or maintaining any fund or assets in which it or any of its Affiliates shall have proprietary rights that have not been recorded in the books and records of it or any of its Affiliates; (c) making any unlawful payment to any agent, employee, officer or director of any Person with which it or any of its Affiliates does business for the purpose of influencing such agent, employee, officer or director to do business with it or any of its Affiliates; (d) making any payment in the nature of bribery, fraud, or any other unlawful payment under the applicable Laws of any jurisdiction where it or any of its Affiliates conducts business or is registered; or, (e) if such Person or any of its Representatives is a Government Official, improperly using his or her position as a Government Official to influence the award of business or regulatory approvals to or for the benefit of such Person, its Representatives or any of their business operations, or failing to recuse himself or herself from any participation as a Government Official in decisions relating to such Person, its Representatives or any of their business operations.

1.49 "**Regulatory Approval**" means all approvals necessary for the commercial sale of a Licensed Product in the Field in a given country or regulatory jurisdiction.

1.50 "**Regulatory Authority**" means, in a particular country or jurisdiction, any applicable Governmental Authority involved in granting Regulatory Approval in such country or jurisdiction.

1.51 "**Regulatory Materials**" means regulatory applications, submissions, notifications, communications, correspondence, registrations, Regulatory Approvals and/or other filings made to, received from or otherwise conducted with a Regulatory Authority in order to develop, manufacture, market, sell or otherwise commercialize Licensed Products in a particular country or jurisdiction.

1.52 "**Representatives**" means, as to any Person, such Person's Affiliates and its and their successors, controlling Persons, directors, officers and employees.

1.53 "**Retained Territory**" means the world except for the Collaboration Territory.

1.54 "**Rolling Year**" means, with respect to a given quarter, the period of four (4) consecutive quarters immediately prior to such quarter.

1.55 "**Territory**" means worldwide.

1.56 "**Third Party**" means any entity other than KemPharm or KVK or an Affiliate of either of them.

1.57 "**Third Party Supply Agreement**" means, collectively (a) the Material Supply Agreement, dated November 2, 2009, by and between KemPharm, Inc. and Johnson Matthey Inc., as amended by the First Amendment to the Material Supply Agreement, dated December 9, 2016; (b) the Letter Agreement, dated February 19, 2018, by and between KemPharm, Inc. and Johnson Matthey Inc., in each case, as amended; and (c) the Quality Agreement dated May 2, 2018, by and between KemPharm, Inc. and Johnson Matthey Inc.

1.58 "**Transaction Agreements**" means, collectively, (a) this Agreement and (b) any other agreement executed between the Parties in connection with any of the foregoing.

1.59 "**U.S. Dollar**" means a U.S. dollar, and "**US$**" shall be interpreted accordingly.

1.60 "**U.S.**" means the United States of America, including all possessions and territories thereof.

1.61 "**U.S. GAAP**" means the generally accepted accounting principles as applied to the U.S., including other comprehensive basis of accounting ("**OCBOA**") as consistently applied by KVK.

1.62 Additional Definitions: The following table identifies the location of definitions set forth in various Sections of the Agreement:

Defined Terms	Section
Agreement	Preamble
Alliance Manager	3.1
Claims	11.1
Commercialization Budget	6.2(a)
Commercialization Plan	6.2(a)
Confidentiality Agreement	1.11
Development Activities	1.14
Effective Date	Preamble
Enforcing Party	9.3(c)
Executive Officers	14.1
ICC Rules	14.2(a)
Indemnified Party	11.3
Indemnifying Party	11.3
Infringement	9.3(a)
Infringement Actions	9.4
Joint Steering Committee or JSC	3.2(a)
KemPharm	Preamble
KemPharm Indemnitees	11.2
KemPharm Partner	2.2
KVK	Preamble
KVK Housemarks	9.6(b)
KVK Indemnitees	11.1
KVK Sublicense Agreement	2.1(c)
Losses	11.1
NDA	1.38
Net Loss	1.39
Net Profit Report	8.4(b)
Net Profit Share	8.4(a)
Profit Sharing Percentage	8.4(a)
Party	Preamble
Pharmacovigilance Agreement	5.9
POMV Fee	8.1
Proof of Market Viability	6.9
Proof of Market Viability Termination	6.9
Regulatory Activities	1.14
Remedial Action	5.10
Subcommittee	3.2(b)
Tax Withholding	8.9(c)
Term	13.1
Third Party Commercial IP Costs	61.9
VAT	8.9(d)

Article 2
License

2.1 License to KVK.

(a) License Grant. Subject to the terms and conditions of this Agreement, KemPharm hereby grants KVK an exclusive, even as to KemPharm except as provided in Section 2.1(b) below, license, with the right to sublicense solely as provided in Section 2.1(c), under the Licensed IP, to conduct Regulatory Activities, distribute, market, promote, sell, have sold, offer for sale, import and otherwise Commercialize or manufacture, Licensed Products in the Field in the Collaboration Territory. For clarity, the foregoing license does not include a right for KVK to (i) Develop, except to conduct Regulatory Activities, or (ii) change the content of the Label or package of any Licensed Product, except to provide applicable labeling or packaging material for Licensed Products to KemPharm in accordance with Section 6.8. For further sake of clarity, the License Grant of this section does include the right for KVK, pursuant to the terms of the instant Agreement, to (1) Commercialize, including, but not limited to, as permitted or obligated to perform under Article 6 or the Commercialization Plan, (2) manufacture the Licensed Product, and (3) conduct other permitted activities, utilize any rights or perform any obligations under this Agreement or a Transaction Agreement.

(i) Furthermore, Subject to the terms and conditions of this Agreement, KemPharm grants KVK a limited non-exclusive license, with no right to sublicense without the prior express written consent of KemPharm, under the Limited License Priority Patents, for only Patent Enforcement and Third-Party Patent Infringement Actions as per Article 9 herein.

(b) KemPharm Retained Rights. Notwithstanding the exclusive rights granted to KVK in Section 2.1(a), KemPharm and its Affiliates retain the following: (i) the right to practice the Licensed IP within the scope of the license granted to KVK under Section 2.1(a) only in order to perform, or have performed by a Third Party contractor, KemPharm's obligations under this Agreement or a Transaction Agreement; (ii) the right to use and conduct Development Activities with respect to Licensed Products anywhere in the world, including the Collaboration Territory not otherwise in violation of this Agreement or a Transaction Agreement; (iii) the right to manufacture or have manufactured Licensed Products in the Retained Territory for sale and use in the Retained Territory or for sale to KVK not otherwise in violation of this Agreement or a Transaction Agreement; and (iv) the right to practice and license the Licensed IP outside the scope of the license granted to KVK in Section 2.1(a). and (v) the right to manufacture, subject to the Third Party Supply Agreement, practice and license and otherwise commercialize the Limited License Priority Patents in full.

(c) Sublicense Rights. KVK shall have the right to grant sublicenses of the license granted in Section 2.1(a) only with KemPharm's express prior written consent, not to be unreasonably denied or unreasonably conditioned. Following receipt of KemPharm's consent, KVK shall, within [*] days after granting any sublicense under Section 2.1(a), notify KemPharm of the grant of such sublicense and provide KemPharm with a true and complete copy of the sublicense agreement (each, a "**KVK Sublicense Agreement**"). Unless agreed to in writing by KemPharm, each KVK Sublicense Agreement shall be consistent with the terms and conditions of this Agreement, and KVK shall be solely responsible for all of its sublicensees' activities and any and all failures by its sublicensees to comply with the terms of this Agreement. Without limiting the foregoing, each KVK Sublicense Agreement shall include the following additional terms and conditions:

(i) the sublicensee shall be bound by non-use and non-disclosure obligations no less stringent than those set forth in this Agreement;

(ii) the sublicensee shall not have any right to grant further sublicenses to the Licensed IP or to engage subcontractors to perform its obligations to KVK, without the consent of KVK and KemPharm;

(iii) the sublicensee shall not have any right to prosecute or maintain or enforce any Licensed Patents;

(iv) the sublicensee shall assign to KVK all Data and Inventions generated by such sublicensee;

(v) the sublicensee shall not have the right to submit, own or control any Regulatory Materials for Licensed Products; and

(vi) if this Agreement terminates, KemPharm shall, at its sole option and discretion, have the right to either (a) assume KVK's rights and obligations under the KVK Sublicense Agreement or (b) terminate the KVK Sublicense Agreement in its entirety without penalty or other obligation to the sublicensee.

2.2 KemPharm Partner. KemPharm has the right, in its sole discretion, to enter into one or more agreements with Third Parties and grant such Third Parties the right to exercise any of KemPharm's retained rights under Section 2.1(b), including to conduct Development Activities or to manufacture Licensed Products in the Collaboration Territory, or to Develop, manufacture or Commercialize Licensed Products in the Retained Territory (each such Third Party, a "**KemPharm Partner**"), and KemPharm shall have the right, but not the obligation, to exercise any and/or all of its rights and/or fulfill any and/or all of its obligations under this Agreement through KemPharm Partner(s), including granting KemPharm Partner(s) the right to participate in any Committee meetings as one or more of KemPharm's representatives. KemPharm Partner(s) shall be bound by the obligations of this Agreement to the extent applicable to any rights of KVK herein and KemPharm shall be held solely responsible for any breaches of this Agreement by KemPharm Partner(s). KVK shall cooperate fully with KemPharm Partner(s) to the extent that KVK has the obligation under this Agreement to cooperate with KemPharm. KemPharm shall have the right to disclose to KemPharm Partner(s) all information regarding Licensed Products, including all Regulatory Materials, disclosed by KVK to KemPharm under this Agreement, for use by KemPharm Partner(s) in their conduct of Development Activities or manufacturing of Licensed Products in the Collaboration Territory, or their Development, manufacture or Commercialization of Licensed Products in the Retained Territory, *provided*, *however*, that all such information disclosed to KemPharm Partner(s) by KemPharm shall be deemed the Confidential Information of KVK and KemPharm and KemPharm Partner(s) that receive any such information shall be obligated to abide by restrictions on disclosure and use substantially similar to the provisions set forth in Section 12.1.

2.3 Negative Covenant. KVK covenants that it will not, and further that it will not permit any of its Affiliates or sublicensees to, use or practice (i) any Licensed IP outside the scope of the license granted to it under Section 2.1(a) and (ii) any Limited Licensed Priority Patents outside the scope of the limited license granted to it under Section 2.1(a)(i). KemPharm covenants that it will not and will not permit any of its Affiliates or KemPharm Partner(s) to, use or practice any Licensed IP except as explicitly permitted under Section 2.1(b).

2.4 No Implied Licenses. Except as explicitly set forth in this Agreement, neither Party shall be deemed by estoppel or implication to have granted the other Party any license or other right to any intellectual property of such Party.

2.5 Exclusivity.

(a) During the Term of this Agreement with respect to any country in the Territory, [*] shall not, directly or indirectly, either by itself or through its Affiliates or any arrangement, or series of arrangements, with a Third Party, [*]; provided that, [*].

(b) During the Term of this Agreement. [*] shall not, directly or indirectly, either by itself or through its Affiliates or any arrangement, or series of arrangements, with a Third Party, [*].

Article 3
Governance

3.1 Alliance Managers. Within [*] days after the Effective Date, each Party shall appoint and notify the other Party of the identity of a representative having the appropriate qualifications, including a general understanding of pharmaceutical development and commercialization issues, to act as its alliance manager under this Agreement (the "**Alliance Manager**"). The Alliance Managers shall serve as the primary contact points between the Parties for the purpose of providing each Party with information on the progress and results of KVK's conduct of Regulatory Activities with respect to, and Commercialization of, Licensed Products. The Alliance Managers shall also be primarily responsible for facilitating the flow of information and otherwise promoting communication, coordination and collaboration between the Parties with respect to Licensed Products. Each Party may replace its Alliance Manager at any time upon written notice to the other Party.

3.2 Joint Committees.

(a) JSC Formation and Role. Within [*] days after the Effective Date, the Parties shall establish a joint steering committee (the "**Joint Steering Committee**" or "**JSC**") for the overall coordination and oversight of the Parties' activities under this Agreement. The role of the JSC shall be:

(i) to review, discuss, coordinate, and approve the overall strategy for the conduct of Regulatory Activities with respect to, and Commercialization of, Licensed Products in the Collaboration Territory;

(ii) to review, discuss and coordinate the conduct of any Development Activities by KemPharm;

(iii) to discuss and coordinate manufacturing matters with respect to Licensed Products, including discussing and coordinating the commercial supply needs of KVK and sharing related supply forecasts, to ensure compliance with the requirements of the Third Party Supply Agreement;

(iv) to review, discuss and approve the Commercialization Plan and any proposed amendments or revisions to such plan, and review and discuss the Commercialization of Licensed Products in the Collaboration Territory;

(v) to coordinate the Commercialization of Licensed Products in the Collaboration Territory and Retained Territory to ensure consistent global marketing of Licensed Products;

(vi) to oversee the activities of the Subcommittees and attempt to resolve issues presented to it by and disputes within the Subcommittees; and

(vii) to perform such other functions as appropriate to further the purposes of this Agreement, as expressly set forth in this Agreement or as determined by the Parties in writing.

(b) Subcommittee(s). From time to time, the JSC may establish joint subcommittees to oversee particular projects or activities, such as Licensed Product supply and manufacturing, conduct of Regulatory Activities and Commercialization, as it deems necessary or advisable (each, a "**Subcommittee**", and together with the JSC, the "**Committees**").

(c) Members. Each Committee shall be comprised of an equal number of representatives from each Party. Each Party's representatives shall be officer or employee of such Party or its Affiliate having sufficient seniority within the applicable Party to make decisions arising within the scope of the applicable Committee's responsibilities. Each Party shall initially appoint [*] representatives to the JSC. Each Committee may change its size from time to time by mutual consent of its representatives, and each Party may replace its representatives at any time upon written notice to the other Party. Each Party shall appoint one (1) of its representatives on each Committee to act as the co-chairperson of such Committee. The role of the co-chairpersons shall be to convene and preside at the Committee meetings and to ensure the circulation of meeting agendas at least [*] days in advance of Committee meetings and the preparation of meeting minutes in accordance with Section 3.2(d), but the co-chairpersons shall have no additional powers or rights beyond those held by other Committee representatives.

(d) Meetings. The JSC shall meet at least twice per calendar year during the Term, unless the Parties mutually agree in writing to a different frequency for such meetings. Either Party may also call a special meeting of any Committee, by videoconference or teleconference, by at least [*] Business Days prior written notice to the other Party in the event such Party reasonably believes that a significant matter must be addressed prior to the next regularly scheduled meeting, and such Party shall provide the applicable Committee no later than [*] Business Days prior to the special meeting with materials reasonably adequate to enable an informed decision. Each Committee may meet in person, by videoconference or by teleconference, *provided, however,* that, unless the Parties otherwise mutually agree, at least one such JSC meeting per calendar year shall be in person, alternating between the headquarters of KemPharm and KVK. All Committee meetings shall be conducted in English and all communications under this Agreement shall be in English. The co-chairpersons shall be responsible for preparing reasonably detailed written minutes of the Committee meetings that reflect, without limitation, all material decisions made at such meetings. The co-chairpersons shall send draft meeting minutes to each representative of the applicable Committee for review and approval within [*] Business Days after the Committee meeting. Such minutes shall be deemed approved unless one or more Committee representatives object to the accuracy of such minutes within [*] Business Days of receipt.

3.3 Decision Making. Each Committee shall strive to seek consensus in its actions and decision-making process and all decisions by the Committees shall be made by consensus, with each Party having collectively one (1) vote in all decisions. If after reasonable discussion and good faith consideration of each Party's view on a particular matter before any Subcommittee, the representatives of the Parties cannot reach an agreement as to such matter within [*] Business Days after such matter was brought to such Subcommittee for resolution, such disagreement shall be referred to the JSC for resolution. If after reasonable discussion and good faith consideration of each Party's view on a particular matter before the JSC, the representatives of the Parties cannot reach an agreement as to such matter within [*] Business Days after such matter was brought to the JSC for resolution or after such matter has been referred to the JSC, such disagreement shall be referred to the Executive Officers for resolution. If the Executive Officers cannot resolve such matter within [*] days after such matter has been referred to them, then: (i) KemPharm's Executive Officer shall have the final decision-making authority with respect to matters related [*]; and (ii) KVK's Executive Officer shall have the final decision making authority with respect to [*], *provided, however,* that KemPharm's Executive Officer shall have the right to [*], any such determination by KemPharm's Executive Officer shall be in writing and provided to KVK:

(a) [*]; and

(b) [*].

For sake of clarity, KemPharm retains all authority and all decision-making authority with respect to matters related to [*], other than the [*] herein.

3.4 Limitation of Committee Authority. Each Committee shall only have the powers expressly assigned to it in this Article 3 and elsewhere in this Agreement and shall not have the authority to: (a) modify or amend the terms and conditions of this Agreement; (b) waive or determine either Party's compliance with the terms and conditions of under this Agreement; or (c) decide any issue in a manner that would conflict with the express terms and conditions of this Agreement. In no event shall KemPharm's Executive Officer pursuant to Section 3.3(i) or KVK's Executive Officer pursuant to Section 3.3(ii) make any decision contrary to this Agreement without the written consent of the other Party.

3.5 Discontinuation of Committees. The activities to be performed by each Committee shall solely relate to governance under this Agreement and are not intended to be or involve the delivery of services. Each Committee shall continue to exist until the Parties mutually agreeing to disband such Committee. Once the Parties mutually agree, such Committee shall have no further obligations under this Agreement and, thereafter, each Party shall designate a contact person for the exchange of information relevant to such Committee under this Agreement and decisions of such Committee shall be decisions as between the Parties, subject to the other terms and conditions of this Agreement.

Article 4
DEVELOPMENT

4.1 Overview. Except with respect to the conduct of Regulatory Activities, as further described in Article 5, KemPharm will be solely responsible for the Development of Licensed Products in the Field in the Territory, at [*]. KVK shall not conduct any Development Activities, other than to conduct Regulatory Activities, with respect to Licensed Products at any time during the Term, including in the Field in the Collaboration Territory.

4.2 Transfer of Licensed Know-How. Promptly after the Effective Date, KemPharm shall provide KVK with complete and accurate copies of the Licensed Know-How that is reasonably necessary to maintain Regulatory Approval of, Commercialize of and manufacture of Licensed Products in the Field in the Collaboration Territory in existence as of the Effective Date; provided that, to the extent KVK requires additional Licensed Know-How during the Term in connection with the conduct of Regulatory Activities or Commercialization activities, KemPharm shall reasonably cooperate with KVK in providing KVK with copies of such Licensed Know-How promptly (but in no event later than [*] after receipt of KVK's request. The Parties shall establish a process for ensuring that such Licensed Know-How, including CMC Information, is treated as the Confidential Information of KemPharm.

Article 5
Regulatory Matters

5.1 Regulatory Responsibilities. Subject to the terms and conditions of this Agreement, KVK will be responsible, at its sole cost and expense, for the conduct of all Regulatory Activities required to obtain and maintain Regulatory Approval of Licensed Products in the Field in the Collaboration Territory, including the preparation of all Regulatory Materials and all communications and interactions with Regulatory Authorities in the Collaboration Territory with respect to Licensed Products. Promptly after the Effective Date, in connection with the transfer of Licensed Know-How under Section 4.2, KemPharm shall transfer ownership of the NDA for the Product to KVK in accordance with 21 C.F.R. 314.72. For clarity, notwithstanding anything to the contrary in this Agreement, as of the Effective Date, KemPharm has obtained Regulatory Approval of the Product in the Collaboration Territory; as such, solely with respect to the Product, and for clarity, excluding other Licensed Products that are not the Product, the definition of "Regulatory Activities" shall be limited to the reporting, preparation and submission of applications for maintaining (i.e., not obtaining or registering) Regulatory Approval of Licensed Products in accordance with the applicable sections of 21 C.F.R. 314, as well as all post-marketing requirements and all post-approval activities, such as participation in required REMS programs, PREA deferred pediatric studies and annual PDUFA program fees; any other sections of this Agreement that reference the conduct of Regulatory Activities, even without using such defined term, shall be deemed amended accordingly.

5.2 Pricing. KVK shall be solely responsible for negotiating with applicable Governmental Authorities regarding the price and reimbursement status of Licensed Products in the Field in the Collaboration Territory. KVK shall keep KemPharm timely informed on the status of any applications for pricing approvals in the Collaboration Territory, including any discussion and correspondence with any Regulatory Authority with respect thereto. KVK shall, subject to KVK's reasonable discretion, implement KemPharm's reasonable comments with respect to such applications, discussions or correspondences. In the event of a dispute between KVK and KemPharm with respect to the inclusion of such a comment, KVK shall prevail. KVK shall promptly notify KemPharm of pricing approvals obtained for the Licensed Products in the Collaboration Territory.

5.3 Regulatory Information Sharing. KVK shall (i) provide KemPharm with the original documents, in the electronic format in which it has been prepared by KVK, of any supplemental NDA x related to the Regulatory Activities for the Licensed Products, for KemPharm's review and comment, in connection with obtaining or maintaining any NDA approval for Licensed Products in the Field in the Collaboration Territory, prior to the submission of such documents to the Regulatory Authority in the Collaboration Territory; (ii) provide KemPharm with the original documents, in the electronic format in which it has been prepared by KVK, of any annual report or other regulatory submission within a reasonable time after each has been submitted to FDA; and (iii) shall keep KemPharm informed of any material verbal or written communication or question relating to Licensed Products received by KVK from the Regulatory Authority in the Collaboration Territory. Except as required by applicable Law, KVK, its Affiliates and sublicensees shall not submit any Regulatory Materials to, or communicate with, any Regulatory Authority in the Retained Territory regarding any Licensed Products. If such submission or communication is required by applicable Law, KVK shall promptly notify KemPharm in writing of such requirement and the content of such submission or communication.

5.4 Meetings with Regulatory Authorities. KVK shall lead all interactions with Regulatory Authorities in the Collaboration Territory with respect to Licensed Products. KVK shall keep KemPharm reasonably informed of regulatory developments related to Licensed Products in the Field in the Collaboration Territory. At each regularly scheduled JSC meeting, KVK shall provide KemPharm with a list and schedule of any in-person meeting or teleconference with the applicable Regulatory Authorities, or related advisory committees, in the Collaboration Territory planned for the next calendar quarter that relates to any Licensed Product in the Field. In addition, KVK shall notify KemPharm as soon as reasonably possible, but in no event later than [*], after KVK becomes aware of any additional such meetings or teleconferences that become scheduled for such calendar quarter. KemPharm shall provide all reasonable assistance requested by KVK to prepare for any such meeting or teleconference. To the extent permitted by applicable Laws, KemPharm shall have the right to participate, whether directly or through a representative, in all such meetings and teleconferences, at [*].

5.5 Regulatory Costs. Unless otherwise provided in this Agreement, KVK shall be responsible for the costs and expenses incurred in connection with the preparation and filing of any and all Regulatory Materials and the maintenance of any and all Regulatory Approvals, including supplemental NDA approvals, if any, participation in any required REMS programs, annual PDUFA program fees and any required PREA deferred pediatric studies for Licensed Products in the Field in the Collaboration Territory.

5.6 Right of Reference to Regulatory Materials. Each Party hereby grants to the other Party the right of reference to all Regulatory Materials pertaining to Licensed Products submitted by or on behalf of such Party. The receiving Party may use such right of reference solely for the purpose of seeking, obtaining and maintaining Regulatory Approval of Licensed Products in its respective territory.

5.7 No Harmful Actions. If KemPharm believes that KVK is taking or intends to take any action with respect to any Licensed Product that could reasonably be expected to have a material adverse impact upon the development, manufacture, commercialization or regulatory status of any Licensed Product in the Retained Territory, KemPharm may bring the matter to the attention of the JSC and the Parties shall discuss in good faith to promptly resolve such concern.

5.8 Notification of Threatened Action. Each Party shall immediately notify the other Party of any information it receives regarding any threatened or pending action, inspection or communication by or from any Third Party, including without limitation a Regulatory Authority, which may affect the development, manufacture, commercialization or regulatory status of any Licensed Product. Upon receipt of such information, the Parties shall consult with each other in an effort to arrive at a mutually acceptable procedure for taking appropriate action.

5.9 Adverse Event Reporting and Safety Data Exchange. No later than [*] days before the anticipated launch date of any Licensed Product in the Collaboration Territory, the Parties shall enter into a written pharmacovigilance agreement (the "**Pharmacovigilance Agreement**") for the Commercialization of the Licensed Product. These responsibilities shall include mutually acceptable guidelines and procedures for the receipt, investigation, recordation, communication, and exchange, as between the Parties, of adverse event reports, pregnancy reports, and any other information concerning the safety of the Licensed Product. Such guidelines and procedures shall be in accordance with, and enable the Parties to fulfill, local and national regulatory reporting obligations under applicable Laws. Furthermore, such agreed procedure shall be consistent with relevant ICH guidelines, except where said guidelines may conflict with existing local regulatory reporting safety reporting requirement, in which case local reporting requirement shall prevail. The Pharmacovigilance Agreement shall provide for an adverse event database for the Licensed Products in the Collaboration Territory to be maintained by KVK at KVK's expense, and also a global safety database for the Licensed Products to be maintained by KemPharm at KemPharm's expense. As between the Parties, KVK shall be responsible for preparing and filing with Regulatory Authorities in the Collaboration Territory all adverse event reports and responses to safety issues and requests of Regulatory Authorities relating to Licensed Products in the Collaboration Territory. As between the Parties, KVK shall also be responsible for reporting quality complaints, adverse events and safety data related to Licensed Products to KemPharm for inclusion in the global safety

database. Each Party hereby agrees to comply with its respective obligations under such Pharmacovigilance Agreement and to cause its Affiliates and permitted sublicensees to comply with such obligations.

5.10 Remedial Actions. Each Party will notify the other Party immediately, and promptly confirm such notice in writing, if it obtains information indicating that any Licensed Product may be subject to any recall, corrective action or other regulatory action taken by virtue of applicable Laws (a "**Remedial Action**"). The Parties will assist each other in gathering and evaluating such information as is necessary to determine the necessity of conducting a Remedial Action. KVK shall, and shall ensure that its Affiliates and sublicensees will, maintain adequate records to permit the Parties to trace the distribution, sale and use, to the extent possible, of the Licensed Product in the Collaboration Territory. KVK shall have sole discretion with respect to any matters relating to any Remedial Action in the Collaboration Territory, including the decision to commence such Remedial Action and the control over such Remedial Action in its territory, at its cost and expense; *provided, however,* that if KemPharm determines that any Remedial Action with respect to any Licensed Product in the Collaboration Territory should be commenced or is required by applicable Laws or Regulatory Authority, KemPharm shall discuss such Remedial Action with KVK and KVK shall carry out such Remedial Action upon KemPharm's request. Each Party shall provide the other Party, at the other Party's expense, with such assistance in connection with a Remedial Action as may be reasonably requested by such other Party.

Article 6
Commercialization

6.1 Overview. Subject to the terms and conditions of this Agreement, including the diligence obligations set forth below, KVK will be primarily responsible for and have primary operational control over all aspects of the Commercialization of Licensed Products in the Field in the Collaboration Territory, including: (a) negotiating with applicable Governmental Authorities regarding the price and reimbursement status of Licensed Products, subject to Section 5.2; (b) marketing, advertising and promotion; (c) booking sales and distribution and performance of related services; (d) handling all aspects of order processing, invoicing and collection, inventory and receivables; (e) providing customer support, including handling medical queries, and performing other related functions; and (f) conforming its practices and procedures to applicable Laws relating to the marketing, detailing and promotion of Licensed Products in the Field in the Collaboration Territory; provided that, the Parties shall jointly develop and execute a Commercialization Plan, as defined below, for the Licensed Products in the Field in the Collaboration Territory, pursuant to Section 6.2, including the Commercialization Budget (as defined below) described therein, and (y) KemPharm shall exercise operational control over certain aspects of Commercialization, as specified in the Commercialization Plan. KVK shall fund all of the costs and expenses incurred by or on behalf of KVK in connection with such Commercialization activities, and such costs and expenses shall constitute "Commercialization/Regulatory Expenses".

6.2 Commercialization Plan.

(a) General. KVK shall Commercialize Licensed Products in the Field in the Collaboration Territory pursuant to a commercialization plan (the "**Commercialization Plan**"). The Commercialization Plan shall include (i) a detailed description of all key strategic decisions (including messaging, branding, marketing, advertising, sales force positioning, number of representatives and details, pricing strategy, etc.), implementation tactics and pre-launch and post-launch activities; (ii) a reasonably detailed description and timeline of KVK's, its Affiliates' and their respective sublicensees' Commercialization activities for Licensed Products in the Collaboration Territory for the next Fiscal Year, including medical marketing activities, sales forecasts and projections, pricing, reimbursement, market research, sales training, distribution channels, customer service and sales force matters related to the launch and sale of Licensed Products in the Collaboration Territory, (iii) a mutually agreed-upon Commercialization budget ("**Commercialization Budget**"), it being understood that any proposed increase in the Commercialization Budget by either Party that is reasonably likely to result in the Commercialization Budget being [*] greater than the previously approved Commercialization Budget shall require mutual agreement of the Parties; and (iv) a strategic plan for Commercialization of Licensed Products in the Collaboration Territory for the following [*]. KemPharm shall provide ongoing support with respect to the Commercialization of Licensed Products in the Field in the Collaboration Territory, as specified in the Commercialization Plan.

(b) Initial Plan and Amendments. The initial Commercialization Plan is attached hereto as **Exhibit B**. Within a reasonable time, but no later than [*] months, prior to the anticipated Regulatory Approval of the technology transfer to KVK of each Licensed Product in the Collaboration Territory, the Parties shall jointly, through the JSC, prepare updates and amendments, as appropriate, to the initial Commercialization Plan, and shall present such plan to the JSC for its review and approval. Thereafter, from time to time during the Term, but at least on an annual basis, the Parties shall jointly, through the JSC, prepare further updates and amendments, as appropriate, to the then-current Commercialization Plan, and shall submit all updates and amendments to the Commercialization Plan to the JSC for review and approval. Once approved by the JSC, the Commercialization Plan shall become effective and supersede the previous Commercialization Plan as of the date of such approval. The Commercialization Plan shall specify the specific obligations of each Party with respect to the Commercialization of Licensed Products in the Field in the Collaboration Territory.

6.3 Pricing. Subject to any determination by applicable Regulatory Authorities, KVK shall have the sole right to determine the pricing of the Licensed Products in the Collaboration Territory, *provided*, *however*, that KVK shall price Licensed Products in a manner that is intended to maximize the profit of the Licensed Products and shall not price the Licensed Products in a manner intended to induce the sale of any other products. KemPharm shall not have any right to direct, control, or approve KVK's pricing of the Licensed Products in the Collaboration Territory.

6.4 Commercial Diligence.

(a) KVK shall use Commercially Reasonable Efforts to Commercialize the Licensed Products in the Field in the Collaboration Territory.

6.5 Commercialization Reports. KVK shall keep KemPharm reasonably informed of KVK's, its Affiliates' and their respective sublicensees' Commercialization activities with respect to the Licensed Products in the Field in the Collaboration Territory. Without limiting the foregoing, at each regularly scheduled JSC meeting, KVK shall provide KemPharm with a written report summarizing the significant Commercialization activities performed with respect to the Licensed Products since the last JSC meeting and comparing such activities with the Commercialization Plan for such time period. Such reports shall be at a level of detail reasonably requested by KemPharm and sufficient to enable KemPharm to determine KVK's compliance with its diligence obligations under Section 6.4. At such JSC meeting, the Parties shall discuss the status, progress and results of KVK's Commercialization activities. KVK shall promptly respond to KemPharm's reasonable questions or requests for additional information relating to such Commercialization activities. In addition, within [*] days after the end of each Fiscal Year, KVK shall provide KemPharm with a detailed written annual report regarding the progress under the Commercialization Plan and results thereof.

6.6 Cross-Territorial Restrictions. KVK hereby covenants and agrees that it shall not, and shall ensure that its Affiliates and sublicensees will not, either directly or indirectly, promote, market, distribute, import, sell or have sold the Licensed Products, including via internet or mail order, into countries in the Retained Territory. As to such countries in the Retained Territory (which are exclusively reserved for KemPharm), KVK shall not, and shall ensure that its Affiliates and their respective sublicensees will not: (a) establish or maintain any branch, warehouse or distribution facility for Licensed Products in such countries, (b) engage in any advertising or promotional activities relating to Licensed Products that are directed primarily to customers or other purchaser or users of Licensed Products located in such countries, (c) solicit orders for Licensed Products from any prospective purchaser located in such countries, or (d) sell or distribute Licensed Products to any person in the Collaboration Territory who intends to sell or has in the past sold Licensed Products in such countries. If KVK receives any order for any Licensed Product from a prospective purchaser located in a country in the Retained Territory, KVK shall promptly refer that order to KemPharm and KVK shall not accept any such orders. KVK shall not deliver or tender, or cause to be delivered or tendered, Licensed Products into a country in the Retained Territory. KVK shall not, and shall ensure, that its Affiliates and their respective sublicensees will not, restrict or impede in any manner KemPharm's exercise of its retained exclusive rights in the Retained Territory.

6.7 Label and Field Restrictions. KVK hereby covenants that it shall not, nor shall it permit any Affiliate or sublicensee to, directly or indirectly, market, promote, detail, sell or offer for sale Licensed Products in the Collaboration Territory for any use outside (1) the Label or (2) the Field. KemPharm acknowledges and understands that KVK cannot control the ultimate use of Licensed Products it sells and that the purpose of the foregoing covenant is to prevent KVK and its Affiliates and sublicensees from facilitating or encouraging uses outside (1) the Label and/or (2) the Field.

6.8 Labeling. KVK shall provide KemPharm with proposed content for labeling and packaging (including with respect to any product inserts) of Licensed Products in the Field in the Collaboration Territory, for KemPharm's review and approval prior to use. Except with respect to KVK's use of any KVK Housemark, as defined below, for the Licensed Product, KVK shall not materially deviate from KemPharm's approved label for the Product in the design or content of the label for any Licensed Product unless required to by Law or approved by KemPharm in writing. KemPharm shall review KVK's proposed labeling and packaging content and shall provide comments to KVK within [*] days of delivery of such materials to KemPharm, which comments KVK shall incorporate into the final labeling and packaging content provided to KemPharm.

6.9 Payors and PBMs. Subject to the direction and authorization of the JSC, and as set forth in the Commercialization Plan, KemPharm shall have the responsibility for outreach to pharmacy benefit managers and other payors to negotiate for utilization of the Licensed Products in place of traditional hydrocodone/acetaminophen combination products for their members where appropriate.

6.10 Proof of Market Viability Termination. In the event that the Parties' joint efforts to Commercialize Licensed Products in the Field in the Collaboration Territory pursuant to this Article 6 does not result by the [*] of the effective date of this Agreement in KVK entering into agreements with Third Party payors and/or pharmacy benefit managers whereby, based on such Third Parties' usage of hydrocodone and/or acetaminophen (for clarity, in all strengths, and irrespective of whether branded or generic) in the immediately preceding [*], KVK would be reasonably likely sell or have sold at least [*] units of tablets of Licensed Product within a given [*] period (the achievement of such result, the "**Proof of Market Viability**"), then either Party may, in its sole discretion, elect to terminate this Agreement in its entirety (the "**Proof of Market Viability Termination**").

Article 7
API

7.1 Manufacture and Supply. As of the Effective Date, KemPharm has entered into a Third Party Supply Agreement, including a Third Party Supply Quality Agreement as per Section 1.56, pursuant to which Johnson Matthey is manufacturing and supplying KemPharm API (benzhydrocodone hydrochloride) to KemPharm.

(a) KemPharm shall seek [*], pursuant to the terms of the Third Party Supply Agreement, from the Third Party Supplier (Johnson Matthey) to [*] subject to the provisions of Section 7.1(c) below.

(b) KVK shall subsequently execute [*]. As part of this transfer assignment agreement, to be attached hereto as **Exhibit D**, KVK will [*] and shall [*] pursuant to Section 7.2 for purposes of manufacturing and commercializing the Licensed Product. KVK agrees that, [*], it shall [*], such that KemPharm's supply obligations herein do not result in KemPharm's breach of its Third Party Supply Agreement.

(c) Notwithstanding the above Section 7.1(a)-(b), KemPharm shall retain the rights to purchase API (benzhydrocodone hydrochloride), alone or in combination with other pharmaceutical ingredients, except for acetaminophen, for any and all products, other than the Licensed Product(s), from the Third Party Supplier pursuant to either the Third Party Supply Agreement or another agreement with Johnson Matthey with substantially the same terms.

7.2 KVK shall exclusively purchase, subject to Section 7.1(c) above, the KemPharm API through KemPharm by way of the Third Party Supply Agreement, and KemPharm will use Commercially Reasonable Efforts to have manufactured and supplied directly to KVK through the Third Party Supply Agreement, all of KVK's and its Affiliates' and sublicensee's requirements of KemPharm API and other raw materials for Commercialization use and manufacture in the Field in the Collaboration Territory under this Agreement. Johnson Matthey shall supply the KemPharm API and other raw materials, and KVK shall be responsible for the transportation, import and storage of the KemPharm API and/or raw materials at KVK's own cost and expense. All KemPharm API shall be delivered by Johnson Matthey to KVK in accordance with the terms of the Third Party Supply Agreement. The price for KemPharm API and other raw materials supplied by Johnson Matthey through KemPharm to KVK Pursuant to the Third Party Supply Agreement for Commercial use in the Field in the Collaboration Territory shall equal [*] (the "**Supply Price**").

7.3 Notwithstanding the foregoing, nothing contained in this Section 7 shall require that [*]. Any requirement for KemPharm to make any extra payments of any kind to Johnson Matthey, [*], shall be paid by [*]. Regarding the [*], [*] shall be responsible to pay an amount equal to Johnson Matthey's cost, while [*] shall pay all other sums due to Johnson Matthey under [*].

7.4 Distribution. KVK will be solely responsible for the distribution of Licensed Products in the Field in the Collaboration Territory.

7.5 Brand Security and Anti-Counterfeiting. The Parties will establish contacts for communication regarding brand security issues and will each reasonably cooperate with the other with respect thereto. Practices around these incidents will comply with KemPharm's then-current standards, where they define product security features, warehouse/cargo protection requirements, and response and communication process for such incidents. KemPharm shall inform KVK of any changes to KemPharm's standards with sufficient time for KVK to change any practices, if necessary.

Article 8
Compensation

8.1 POMV Fee. Within ten (10) Business Days after achievement of the Proof of Market Viability, KVK shall pay to KemPharm a one-time, upfront payment of two million U.S. Dollars (US$2,000,000), free of any Tax Withholding pursuant to Section 8.9, (the "**POMV Fee**"). The POMV Fee shall be fully creditable against the future amount of any Net Profit Share payments owed to KemPharm pursuant to Section 8.4.

8.2 Commercialization/Regulatory Expenses. Prior to achievement of Proof of Market Viability pursuant to Article 6, KemPharm shall fund [*] Commercialization/Regulatory Expenses incurred in connection with the Commercialization or maintenance of Regulatory Approvals of Licensed Products in the Field in the Collaboration Territory, in accordance with Articles 5 and 6. Subsequent to achievement of Proof of Market Viability pursuant to Article 6, KVK shall either directly fund, or reimburse KemPharm for, any expenses incurred in connection with the Commercialization/Regulatory Expenses of Licensed Products in the Field in the Collaboration Territory, such reimbursements to be paid within [*] days after receipt of the applicable invoice from KemPharm. For the avoidance of doubt, [*], as applicable.

8.3 Manufacturing Expenses. [*], as applicable.

8.4 Net Profit Share.

(a) Following the First Commercial Sale of any Licensed Product in the Field in the Collaboration Territory, KVK shall pay to KemPharm an initial percentage of the Net Profits (if any), in accordance with the table below ("**Net Profit Sharing Percentage**"; such profit share, the "**Net Profit Share**").

Aggregate amount of Net Sales of Licensed Products sold in previous Rolling Year	**Net Profit Share**
Less than or equal to [*]	70% to KVK / 30% to KemPharm
Greater than [*] but less than or equal to [*]	[*]% to KVK / [*]% to KemPharm
Greater than [*]	50% to KVK / 50% to KemPharm

For clarity, once a certain Net Profit Sharing Percentage is reached with respect to a given Rolling Year, irrespective of the amount of future Net Sales in subsequent calendar quarters, the Net Profit Sharing Percentage shall not reset to a lower Net Profit Sharing Percentage for subsequent Rolling Years. An hypothetical example computation of Net Profit Share is attached hereto as Exhibit E.

(b) Net Profit Share Payments; Reports. Within [*] days after the end of each Calendar Quarter following the First Commercial Sale of a Licensed Product in the Field in the Collaboration Territory, KVK shall submit to KemPharm a report setting forth, with respect to the previous Rolling Year: (a) the amount of gross sales and Net Sales of Licensed Products in the Field in the Collaboration Territory in such Rolling Year, (b) an itemized calculation showing the deductions from gross sales (by major category as set forth in the definition of Net Sales) to determine Net Sales, (c) the amount of Manufacturing Expenses paid by KVK to KemPharm for Licensed Products purchased by KVK during such Rolling Year and (d) the amount of Commercialization/Regulatory Expenses incurred by KVK, which shall include amounts paid to KemPharm pursuant to Section 8.2, with respect to Licensed Products in the Field in the Collaboration Territory during such Rolling Year and (e) a calculation of the Net Profits or Net Losses, as applicable, for such Licensed Products (the "**Net Profit Report**").

(c) Payment of Net Profit Sharing Percentage. KVK shall pay all Net Profit Share payments owed to KemPharm pursuant to this Section 8.4, if any, at the time of submission of the Net Profit Report. In any quarter in which there is a Net Loss, KVK shall be bear the full amount of such loss; provided that, KVK shall be entitled to [*]. Notwithstanding this Section 8.4, KVK shall not [*].

8.5 Sales Milestone Payments. KVK shall promptly notify KemPharm upon the achievement of the sales milestone events set forth below with respect to Net Sales of Licensed Products in the Field in the Collaboration Territory in a given Rolling Year. KVK shall pay to KemPharm the corresponding one-time, non-refundable and non-creditable sales milestone payments set forth below within [*] days after the achievement of such milestone event. For clarity, the sales milestone payments herein are free of any Tax Withholding pursuant to Section 8.9.

Sales Milestone Event	**Milestone Payment**
Net Sales in a Rolling Year equal or exceed [*]	[*]
Net Sales in a Rolling Year equal or exceed [*]	[*]
Net Sales in a Rolling Year equal or exceed [*]	[*]
Net Sales in a Rolling Year equal or exceed [*]	[*]
Net Sales in a Rolling Year equal or exceed [*]	[*]

8.6 Payment Method; Foreign Exchange. All payments owed by KVK under this Agreement shall be made by wire transfer in immediately available funds to a bank and account designated in writing by KemPharm. For clarity, all payments by KVK to KemPharm pursuant to Sections 8.1, 8.3, 8.4 and 8.5 shall be in U.S. Dollars. If applicable, the rate of exchange to be used in computing the amount of currency equivalent in U.S. Dollars of any amounts payable in U.S. Dollars by KVK to KemPharm under this Agreement shall be calculated in accordance with U.S. GAAP. KemPharm shall invoice KVK for all amounts payable under Sections 8.2 and 8.3 in U.S. Dollars.

8.7 Interest on Late Payments. If KemPharm does not receive payment of any sum due to it on or before the due date, [*] interest shall thereafter accrue on the sum due to KemPharm until the date of payment at the [*] rate of [*] over the then-current prime rate reported in The Wall Street Journal or the maximum rate allowable by applicable Laws, whichever is lower.

8.8 Records; Audits.

(a) KVK shall and shall ensure that its Affiliates and its and their respective sublicensees, maintain complete and accurate records in sufficient detail to permit KemPharm to confirm the accuracy of the calculation of Net Loss and/or Net Profit Share payments and the achievement of the sales milestone events, and KVK shall provide reconciliations of gross sales to net sales and cost of goods sold, detailing any adjustments made by KVK as a result of its application of OCBOA. All payments and other amounts under this Agreement shall be accounted for in accordance with U.S. GAAP. Upon

reasonable prior notice, such records shall be available for examination during regular business hours for a period of [*] years from the end of the Fiscal Year to which they pertain, and not more often than once each Fiscal Year, by an independent certified public accountant selected by KemPharm and reasonably acceptable to KVK, for the sole purpose of verifying the accuracy of the financial reports furnished by KVK pursuant to this Agreement and any payments with respect thereto. Any such auditor shall not disclose KVK's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by KVK or the amount of payments due under this Agreement. Any amounts shown to be owed but unpaid shall be paid within [*] days from the accountant's report, plus interest, as set forth in Section 8.7, from the original due date. [*] shall bear the full cost of such audit unless such audit discloses an [*] of more than [*] of the amount due for the audited period, in which case [*] shall bear the full cost of such audit.

(b) KemPharm shall, and shall ensure that its Affiliates and KemPharm Partners, maintain complete and accurate records in sufficient detail to permit KVK to confirm the accuracy of the calculation of the Commercialization/Regulatory Expenses and the Manufacturing Expenses. All such expenses shall be accounted for in accordance with U.S. GAAP. Upon reasonable prior notice, such records shall be available for examination during regular business hours for a period of [*] years from the end of the Fiscal Year to which they pertain, and not more often than once each Fiscal Year, by an independent certified public accountant selected by KVK and reasonably acceptable to KemPharm, for the sole purpose of verifying the accuracy of the amount of expenses furnished by KemPharm pursuant to this Agreement and any payments with respect thereto. Any such auditor shall not disclose KemPharm's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the amount of expenses furnished by KVK or the amount of payments due under this Agreement. Any overage assessed to KVK shall be refunded, if applicable, within [*] days from the accountant's report, plus interest, in equal amounts as set forth in Section 8.7, from the original date such overage was applied. [*] shall bear the full cost of such audit unless such audit discloses an [*] of more than [*] of the for the audited period, in which case [*] shall bear the full cost of such audit

8.9 Taxes.

(a) Taxes on Income. Except as otherwise provided in this Section 8.9, each Party shall be solely responsible for the payment of all taxes imposed on its share of income arising directly or indirectly from the efforts of the Parties under this Agreement.

(b) Tax Cooperation. The Parties agree to cooperate with one another and use reasonable efforts to reduce or eliminate tax withholding or similar obligations in respect of the upfront fee, Net Profit Share payments, sales milestone payments or other payments made by KVK to KemPharm under this Agreement. To the extent KVK is required to deduct and withhold taxes from any payment to KemPharm, KVK shall pay the amounts of such taxes to the proper Governmental Authority in a timely manner and promptly transmit to KemPharm an official tax certificate or other evidence of such withholding sufficient to enable KemPharm to demonstrate such payment of taxes to any applicable Government Authority. KemPharm shall provide KVK any tax forms that may be reasonably necessary in order for KVK not to withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty. Each Party shall provide the other with reasonable assistance to enable the recovery, as permitted by applicable Laws, of withholding taxes or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party bearing such withholding tax.

(c) Withholding Taxes. If KVK is required by applicable Laws to make any tax deduction, tax withholding or similar payment from any amount paid or payable by KVK to KemPharm (a "**Tax Withholding**") under this Agreement, then KVK will pay KemPharm the actual stated amount set forth under this Agreement in full and shall also pay any such Tax Withholding, including any additional Tax Withholding required with respect to KVK's additional payments under this Section 8.9, directly to the proper Governmental Authority. For clarity, KemPharm shall receive, without any deduction or offset with respect to taxes and free of any Tax Withholding, a net amount equal to, after payment of any Tax Withholding, the amount to which KemPharm was otherwise entitled under this Agreement and would have received had no Tax Withholding been required by Laws to be made.

(d) VAT. All payments due to KemPharm from KVK pursuant to this Agreement shall be paid exclusive of, and without reduction for, any value-added tax ("**VAT**") (which, if applicable, shall be payable by KVK upon receipt of a valid VAT invoice). If KemPharm determines that it is required to report any such tax, KVK shall promptly provide KemPharm with applicable receipts and other documentation necessary or appropriate for such report. For clarity, this Section 8.9(d) is not intended to limit KVK's right to deduct VAT in determining Net Sales.

Article 9
Intellectual Property Matters

9.1 Ownership of Data and Inventions.

(a) Data. KemPharm shall solely own all Data generated by KemPharm. The Data Controlled by KemPharm and related solely and specifically to the Licensed Products are included in the Licensed Know-How and licensed to KVK under Section 2.1(a). KVK shall solely own all Data generated by KVK in the conduct of Regulatory Activities that is solely and specifically related to Licensed Products in the Field in the Collaboration Territory. KVK hereby grants KemPharm an irrevocable, perpetual, royalty-free, fully paid-up, exclusive license with the right to grant sublicenses to use such Data generated and owned by KVK in the Retained Territory for all purposes, and a non-exclusive license in the Collaboration Territory upon expiration or termination of the Agreement, other than termination of the Agreement by KVK pursuant to Sections 13.4 or 13.5.

(b) Inventions. Inventorship of any Inventions will be determined in accordance with the standards of inventorship and conception under U.S. patent laws. For clarity, all Inventions directly related to the Licensed Product(s) (i.e. combination product of benzhydrocodone and acetaminophen) made by KemPharm are included in the Licensed IP and licensed to KVK under Section 2.1(a). KVK shall promptly disclose in writing to KemPharm all KVK Inventions. KVK hereby grants KemPharm an irrevocable, perpetual, royalty-free, fully paid-up, non-exclusive license with the right to grant sublicenses in such KVK Inventions directly related to the Licensed Products and invented during the Term in the Retained Territory, and in the Collaboration Territory upon expiration or termination of the Agreement. KVK shall have the sole right to file for patent protection for such KVK Inventions. However, KVK shall have no duty to file for patent protection for such KVK Inventions and shall prosecute such KVK Inventions in its sole discretion, subject to KemPharm having an opportunity to comment on any prosecution of KVK inventions which may affect the Licensed IP. If KVK elects not to file or continue prosecution of the KVK Inventions, and if KemPharm desires at its option to file or pursue prosecution of the KVK Inventions, KVK may, at its option, assign said KVK Inventions to KemPharm and KemPharm shall have the right to prosecute the assigned KVK Invention(s). KemPharm shall provide KVK with all reasonable assistance and cooperation in the patent prosecution efforts by KVK provided in this Section 9.1.

i. For sake of clarity, all inventions made by KemPharm, including but not limited to any benzhydrocodone, benzhydrocodone compounds, inventions, pro-drugs or combination of thereof with one or more additional pharmaceutical ingredients, other than Apadaz®, are not included in the Licensed IP and are not licensed to KVK.

(c) KVK's Affiliates, Sublicensees and Subcontractors. KVK shall ensure that each of its Affiliates, sublicensees and subcontractors under this Agreement has a contractual obligation to disclose to KVK all Data and Inventions generated, invented, discovered, developed, made or otherwise created by them or their employees, agents or independent contractors, and to provide sufficient rights with respect thereto, so that KVK can comply with its obligations under Section 9.1(a).

9.2 Patent Prosecution.

(a) Prosecution by KemPharm. As between the Parties, KemPharm shall have the sole right to prepare, file, prosecute and maintain or abandon the Licensed Patents during the term of this Agreement. KemPharm will use Commercially Reasonable Efforts to prepare, file, prosecute, defend and maintain all Licensed Patents; provided, however, that KemPharm does not represent or warrant that any patent will issue or be granted based on patent applications contained in the Licensed Patents. KemPharm shall provide KVK reasonable opportunity to review and comment on such prosecution efforts regarding the Licensed Patents as follows: KemPharm shall promptly provide KVK with copies of all material communications from any patent authority and any translations in KemPharm possession in the Collaboration Territory regarding the Licensed Patents, and shall provide KVK, for its review and comment, with drafts of any material filings or responses to be made to such patent authorities in a reasonable amount of time in advance of submitting such filings or responses. KemPharm shall consider in good faith comments thereto provided by KVK in connection with the prosecution of the Licensed Patents. For the purpose of this Article 9, "prosecution" shall include any post-grant proceeding in the Collaboration Territory, including opposition proceedings.

(b) Retained Territory. For clarity, KVK does not have any rights pursuant to this Agreement with respect to any Licensed Patents in the Retained Territory and, as between the Parties, KemPharm shall have the sole right in its sole discretion to prepare, file, prosecute and maintain the Licensed Patents in the Retained Territory.

(c) Collaboration. KVK shall provide KemPharm with all reasonable assistance and cooperation in the patent prosecution efforts by KemPharm provided in this Section 9.2, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution, including but not limited to the filing of Terminal Disclaimers.

9.3 Patent Enforcement.

(a) Notification. If either Party becomes aware of any existing or threatened infringement of any Licensed Patent ("**Infringement**"), it shall promptly notify the other Party in writing to that effect and the Parties will consult with each other regarding any actions to be taken with respect to such Infringement.

(b) Enforcement Rights. Each Party shall share with the other Party all Information available to it regarding such alleged Infringement, pursuant to a mutually agreeable "common interest agreement" executed by the Parties under which the Parties agree to their shared, mutual interest in the outcome of any suit to enforce the Licensed Patents against such Infringement. KemPharm shall have the first right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such Infringement, at [*]. If KemPharm elects to commence a suit to enforce the applicable Licensed Patents against such Infringement, then KVK shall have the right but not the obligation, to join such enforcement action upon notice to KemPharm, and in this case, the Parties shall [*] of the enforcement action. If KemPharm notifies KVK that it does not intend to commence a suit to enforce the applicable Licensed Patents against such Infringement or to take other action to secure the abatement of such Infringement, then, to the extent that such Infringement is resulting from a Third Party's use or sale of a product that (i) competes with a Licensed Product in the Field and in the Collaboration Territory and (ii) consists of a combination of benzhydrocodone and acetaminophen, KVK shall have the right, subject to the foregoing, but not the obligation, to commence such a suit or take such action. In such case, [*] related to such actions. KVK shall not have the right to commence such an action without KemPharm's consent if KemPharm believes in good faith that the commencement of any such suit or action by KVK would reasonably be likely to have a negative impact on any similar action that KemPharm is pursuing against such person or entity. In such case, KemPharm shall take reasonably appropriate actions in order to enable KVK to commence a suit or take the actions set forth in the preceding sentence. Neither Party shall settle any such suit or action in any manner that would negatively impact the Licensed Patents or that would limit or restrict the ability of KVK to sell the Licensed Products in the Collaboration Territory without the prior written consent of the other Party.

(c) Collaboration. Each Party shall provide to the Party bringing a claim, suit or action under Section 9.3(b) (the "**Enforcing Party**") with reasonable assistance in such enforcement, at such Enforcing Party's request and the Party's expense, including joining such action as a party plaintiff if required by applicable Laws to pursue such action. If KVK is required to join such action as a party plaintiff, KemPharm shall reimburse KVK's reasonable costs and attorney's fees. The Enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts and shall reasonably consider the other Party's comments on any such efforts. The non-enforcing Party shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense, except as otherwise provided herein, but such Party shall at all times cooperate fully with the Enforcing Party.

(d) Expenses and Recoveries. Subject to the terms of this Section 9.3(d), [*] shall be [*] it incurs as a result of such enforcement action, except that the Parties shall [*] of the enforcement action when [*] If the Enforcing Party recovers monetary damages in such claim, suit or action brought under Section 9.3(b), such recovery shall be allocated first to the reimbursement of any documented expenses incurred by the Parties in such enforcement action, and any remaining amounts shall be shared by the Parties as follows:

(i) [*];

(ii) [*];

(iii) [*];

(iv) [*];

(v) [*].

(e) Other Infringements. KemPharm shall have the sole right to enforce Licensed Patents in the Retained Territory, KemPharm shall be entitled to retain all recoveries resulting from all such enforcements, and KVK shall not be obligated to participate or assist in such enforcements.

9.4 Third Party Infringement Claims. If the manufacture, sale or use of the Licensed Products in the Field in the Collaboration Territory pursuant to this Agreement results in a claim, suit or proceeding alleging patent infringement against KemPharm or KVK, or their respective Affiliates, licensees or sublicensees (collectively, "**Infringement Actions**"), such Party shall promptly notify the other Party hereto in writing. KemPharm shall direct and control the defense of such Infringement Action, [*] with counsel of its choice; *provided, however,* that if KVK has not been named as a defendant, KVK may participate in the defense and/or settlement thereof, [*] with counsel of its choice. If KVK has been named as a defendant, KemPharm shall, whether through its own counsel or separate counsel in the event of a conflict, defend KVK [*], with regard solely to said Third Party Infringement Claims. In any event, KemPharm agrees to keep KVK reasonably informed of all material developments in connection with any such Infringement Action for which KemPharm exercises its right to direct and control the defense and shall provide any additional information about the Infringement Action that KVK reasonably requests. Each Party shall share with the other Party all Information available to it regarding such Infringement Actions, pursuant to a mutually agreeable "common defense agreement" executed by the Parties under which the Parties agree to their shared, mutual interest in the outcome of any such Infringement Actions. KemPharm agrees not to settle such Infringement Action, or make any admissions or assert any position in such Infringement Action, in a manner that would materially adversely affect the rights or interests of KVK, without the prior written consent of KVK, which shall not be unreasonably withheld or delayed. If a license from a Third Party is reasonably required in order for KVK to Commercialize the Licensed Products or otherwise perform its obligations under this agreement, the Parties shall mutually agree on such license and negotiate in good faith as to the allocation of such license. The JSC shall review the Third-Party licensed IP expenses at least annually. Notwithstanding the foregoing, under no circumstances shall KVK be responsible or pay for any licensing fees related to use or sale (i) prior to the Effective Date, (ii) after the Term of this Agreement, (iii) outside of the Field, or (iv) outside of the Collaboration Territory.

9.5 Patent Term Extensions. KemPharm will cooperate with KVK, [*] in seeking and obtaining patent term extensions, including any pediatric exclusivity extensions as may be available, patent term adjustments or supplemental protection certificates or their equivalents in the Collaboration Territory with respect to any Licensed Patents or Licensed Products. If elections with respect to obtaining such patent term extensions are to be made, KemPharm shall have the sole right to make such elections.

9.6 Trademarks.

(a) KemPharm Product Mark.

(i) KVK shall Commercialize Licensed Products in the Collaboration Territory under the applicable KemPharm Product Mark selected by KemPharm. KVK shall, and shall ensure that its Affiliates and sublicensees will, (1) use the KemPharm Product Mark solely in connection with the Commercialization and manufacture of Licensed Products in the Field in the Collaboration Territory, (2) comply with the requirements of KemPharm as to the form, manner, scale and context of the use of the KemPharm Product Mark, the use of the statements to accompany the KemPharm Product Mark, and the presentation or performance of the Licensed Products, and (3) adhere to any branding strategy policies, including, without limitation, logo design, product labeling, messaging points, and visual branding elements, implemented by KemPharm for the use of the KemPharm Product Mark. KVK shall display the proper form of trademark notice associated with the KemPharm Product Mark in accordance with instructions received from KemPharm.

(ii) Upon KemPharm's request, to the extent permitted by applicable Laws, KVK shall include KemPharm's name and corporate logo on Licensed Product label, packaging, promotional/marketing materials to indicate that the Licensed Product is in-licensed from KemPharm, and shall display KemPharm's name and corporate logo with equal prominence and comparable size, resolution, print quality, and location, as instructed by KemPharm from time to time, as KVK's name and corporate logo is displayed.

(iii) KVK shall provide KemPharm with samples of proposed content for Licensed Product labeling and packaging in accordance with Section 6.8, together with any promotional/marketing materials that include the KemPharm Product Marks, for review and approval prior to use. If concerns arise based upon reviews of samples provided, KemPharm shall have a right to audit all uses of the KemPharm Product Mark.

(iv) KVK shall use the KemPharm Product Mark upon or in relation to the Licensed Products only in such manner where the distinctiveness, reputation, and validity of the KemPharm Product Mark shall not be impaired. Without prejudice to the generality of the foregoing, KVK shall ensure in particular that the KemPharm Product Mark is correctly spelled, and that any text, graphics, or designs adjacent to the KemPharm Product Mark do not put the KemPharm Product Mark or KemPharm in a negative or derogatory light. KVK shall not, and shall ensure, that its Affiliates and sublicensees will not, engage in any action that will interfere with or diminish KemPharm's rights or goodwill in the KemPharm Product Mark, including related names and logos.

(v) KemPharm shall register and maintain in the Collaboration Territory, at KemPharm's cost and expense, the applicable KemPharm Product Mark that KemPharm wishes to use in connection with the Commercialization of the Licensed Products in the Collaboration Territory.

(vi) KemPharm shall own all rights to the KemPharm Product Mark throughout the world. KVK acknowledges that all use of the KemPharm Product Mark and all rights and goodwill attached to or arising out of such use, shall accrue to the benefit of KemPharm. KVK shall at any time,

whether during or after the Term, execute any documents that shall reasonably be required by KemPharm to confirm KemPharm's ownership of the KemPharm Product Mark.

(b) KVK Housemarks. In addition to the KemPharm Product Mark, KVK shall have the right to brand the Licensed Products in the Field in the Collaboration Territory with those trademarks of KVK that are associated with KVK's name or identity ("**KVK Housemarks**"); *provided, however*, that KVK shall not, and shall ensure that its Affiliates and sublicensees will not, make any use of trademarks that are confusingly similar to any trademarks or house marks of KemPharm or its Affiliates, including the corporate name of KemPharm or any of its Affiliates, without KemPharm's prior written consent. KVK shall own all rights in the KVK Housemarks, and all goodwill in the KVK Housemarks shall accrue to KVK. KVK and its Affiliates and sublicensees shall not use any trademarks, other than the KemPharm Product Marks and the KVK Housemarks, in connection with the Commercialization of Licensed Products in the Field in the Collaboration Territory, without the prior written consent of KemPharm.

Article 10
Representations And Warranties; covenants

10.1 Mutual Representations and Warranties. Each Party hereby represents and warrants to the other Party as follows:

(a) Corporate Existence. As of the Effective Date, it is a company or corporation duly organized, validly existing, and in good standing under the Laws of the jurisdiction in which it is incorporated.

(b) Corporate Power, Authority and Binding Agreement. As of the Effective Date, (i) it has the corporate power and authority and the legal right to enter into this Agreement and perform its obligations hereunder; (ii) it has taken all necessary corporate action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder; and (iii) this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium and similar Laws affecting creditors' rights and remedies generally.

(c) No Debarment. Neither such Party nor any of its Affiliates is debarred or disqualified under the Act or comparable applicable Laws outside the U.S.

10.2 Additional Representations and Warranties of KemPharm. KemPharm represents and warrants to KVK as follows, as of the Effective Date:

(a) Title; Encumbrances. It has sufficient legal and/or beneficial title, ownership or license, free and clear from any mortgages, pledges, liens, security interests, conditional and installment sale agreement, encumbrances, charges or claim of any kind, of the Licensed IP to grant the licenses to KVK as purported to be granted pursuant to this Agreement;

(b) Notice of Infringement or Misappropriation. It has not received any notice, written or otherwise, from any Third Party asserting or alleging that the Commercialization of the Licensed Products in the Collaboration Territory would infringe or misappropriate the intellectual property rights of such Third Party;

(c) No Proceeding. There is no pending, and to KemPharm's knowledge, no threatened, adverse action, suit or proceeding in the Collaboration Territory against KemPharm involving Licensed IP or the Licensed Products; and

(d) No Conflicts. KemPharm has not entered, and shall not enter, into any agreement with any Third Party that is in conflict with the rights granted to KVK under this Agreement with respect to the Licensed Product, and has not taken and shall not take any action that would in any way prevent it from granting the rights granted to KVK under this Agreement, or that would otherwise materially conflict with or adversely affect KVK's rights under this Agreement.

(e) No Other Licenses. KemPharm has not granted and will not grant any licenses or other contingent or non-contingent right, title, or interest under or relating to Licensed IP that conflicts with the exclusivity granted to KVK herein, and is not nor will be under any obligation, that does or will conflict with or otherwise affect this Agreement with respect to such exclusivity.

(f) Prior Art; Litigation. No prior art or other information exists, as of the date of the execution of this Agreement, that would adversely affect the validity, enforceability, term, or scope of any Licensed IP (**Exhibit A**) and there is no settled, pending, or to its knowledge threatened litigation or reissue application, re-examination, post-grant, inter partes, or covered business method patent review, interference, derivation, opposition, claim of invalidity, or other claim or proceeding, including in the form of any offer to obtain a license, with respect to the Licensed IP.

(g) Non-Infringement. The Licensed Products do not infringe any Third Party's intellectual property.

10.3 Additional Representations and Warranties of KVK. KVK represents and warrants to KemPharm as follows, as of the Effective Date:

(a) KVK has not entered, and shall not enter, into any agreement with any Third Party that is in conflict with the rights granted to KemPharm under this Agreement with respect to the Licensed Product, and has not taken and shall not take any action that would in any way prevent it from granting the rights granted to KemPharm under this Agreement, or that would otherwise materially conflict with or adversely affect KemPharm's rights under this Agreement;

(b) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, any and all agreements, including, but not limited to confidentiality agreements, sale agreements, purchase agreements, license agreements, commercialization agreements, development agreements, or other agreements between KVK and any Third Party does not relate to, affect, involve, or impact any Intellectual Property rights of KVK for the manufacture and commercialization of the Licensed Product pursuant to this Agreement.

(c) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, any and all settlement agreements of past litigation, including, but not limited to actual or threatened litigation, do not adversely affect, in any material manner or regard, KVK's ability to manufacture, market, sell or otherwise commercialize the Licensed Product(s) herein pursuant to this Agreement.

(d) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, that there is no action, suit, claim, investigation or proceeding pending or, to the reasonable knowledge of KVK, threatened against it which questions the validity of this Agreement or the transactions contemplated hereby, or any action taken or to be taken pursuant hereto or thereto. There are no outstanding orders, judgments, injunctions, awards or decrees of any court, arbitrator or Governmental Entity or agency against KVK that adversely affect, in any material manner or regard, KVK's ability to manufacture, market, sell or otherwise commercialize the Licensed Product(s) herein pursuant to this Agreement.

(e) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, KVK does not Control any Patent that is necessary to make, use, import, offer for sale or sell Licensed Products in the Field.

(f) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, that its material representations of financial viability, stability, and general corporate financial health to KemPharm fairly represent the financial condition of the KVK at the dates of said materials representations and further represents and warrants that such material representations of financial viability, stability, and general corporate health are supported by information and documents prepared in accordance with U.S. GAAP consistently applied and consistent with the books and records of KVK.

(g) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, as evidenced as of the dates of the KVK's financial statements kept solely by the Company and not disclosed to KemPharm, KVK had no liabilities, either accrued or contingent, of a nature required to be reflected in the financial statements in accordance with U.S. GAAP, and whether due or to become due, which individually or in the aggregate are reasonably likely to have a material adverse effect on KVK or its ability to perform its duties and obligations under this Agreement.

(h) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, there are no foreign party, foreign actor, domestic party, domestic actor, or any other third party known to KVK, or alternatively in contractual relationship with KVK, which will materially impact the operation and performance of this Agreement by KVK.

(i) KVK represents and warrants to KemPharm that, to KVK's knowledge as of the Effective Date, there is no existing contractual obligation of KVK or its Subsidiaries or Affiliates is with or for the direct benefit of (i) any party owning, or formerly owning, beneficially or of record, directly or indirectly, in excess of five percent (5%) of the outstanding capital stock of KVK and/or KemPharm, (ii) any director, officer or similar representative of KVK or KemPharm, other than employment agreements, (iii) any natural person related by blood, adoption or marriage to any party described in (i) or (ii), or (iv) any entity in which any of the foregoing parties has, directly or indirectly, at least a five percent (5%) beneficial interest (a "Related Party"). Without limiting the generality of the foregoing, no Related Party, directly or indirectly, owns or controls any material assets or material properties which are used in the KVK's business and to the knowledge of KVK, no Related Party, directly or indirectly, engages in or has any significant interest in or connection with any business which is, or has been within the last two years, a competitor, customer or supplier of KVK or has done business with the KVK or which currently sells or provides products or services which are similar or related to the products or services sold or provided in connection with the Business.

(j) KVK represents and warrants to KemPharm that there is no action, suit or proceeding pending or, to KVK's Knowledge, threatened against KVK or Affiliates which, if adversely determined, would, individually or together with all such other actions, reasonably be expected to have a Material Adverse Effect or otherwise affect KVK's performance of its obligations and responsibilities pursuant to this Agreement. As of the Effective Date, there is no action, suit or proceeding pending or, to KVK's Knowledge, threatened against KVK or any of their Subsidiaries or Affiliates which challenges or impairs the ability of KVK or any of their Subsidiaries or Affiliates to manufacture and sell the Licensed Product herein, or otherwise execute, deliver or perform its obligations under this Agreement.")

10.4 Compliance with Laws.

(a) Each Party shall, and shall ensure that its Affiliates and their respective sublicensees will, and KemPharm shall, and take all reasonable actions to ensure KemPharm Partner(s)'s shall, comply in all respects with Proper Conduct Practices and all applicable Laws in the conduct of Regulatory Activities with respect to, and Commercialization of, Licensed Products and performance of its obligations under this Agreement, including the GCP, GLP and any Regulatory Authority and Government Authority health care programs having jurisdiction in such Party's respective territory, each as may be amended from time to time.

(b) Each Party shall immediately notify the other Party if it has any information or suspicion that there may be a violation of any applicable Laws in connection with its performance under this Agreement or the conduct of Regulatory Activities with respect to, or Commercialization of, any Licensed Product hereunder. In the event that either Party has violated or been suspected of violating any of its obligations, representations, warranties or covenants in Section 10.4(a), such Party will take reasonable actions to remedy such breach and to prevent further such breaches from occurring.

10.5 Additional KVK Covenants. In addition to any covenants made by KVK elsewhere in this Agreement, KVK hereby covenants to KemPharm as follows:

(a) neither KVK nor any of its Affiliates will employ or use the services of any Person who is debarred or disqualified under the Act, or comparable applicable Laws outside the U.S., in connection with activities relating to any Licensed Product; and in the event that KVK becomes aware of the debarment or disqualification or threatened debarment or disqualification of any Person providing services to KVK or any of its Affiliates with respect to any activities relating to any Licensed Product, KVK will promptly notify KemPharm in writing and KVK will cease, or cause its Affiliate to cease, as applicable, employing, contracting with, or retaining any such Person to perform any services relating to any Licensed Product; and

(b) neither it nor its Affiliates, or its or their sublicensees, shall exploit in any manner any Licensed Product outside of the scope of the licenses expressly granted to KVK under this Agreement.

10.6 No Other Representations or Warranties. EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, NO REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NON-INFRINGEMENT OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS, ARE MADE OR GIVEN BY OR ON BEHALF OF A PARTY OR ITS AFFILIATE, AND ALL REPRESENTATIONS AND WARRANTIES, WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, ARE HEREBY EXPRESSLY EXCLUDED. For clarity and without limiting the foregoing, KemPharm makes no representation or warranty concerning the Licensed Products or Licensed IP except as expressly set forth in this Article 10.

Article 11
Indemnification

11.1 Indemnification by KemPharm. KemPharm shall defend, indemnify, and hold KVK and its Affiliates and their respective officers, directors, employees, and agents (the "**KVK Indemnitees**") harmless from and against any and all losses, damages, liabilities, expenses and costs, including reasonable legal expense and attorneys' fees ("**Losses**") to which any KVK Indemnitee may become subject as a result of any claim, demand, action or other proceeding by any Third Party (collectively, "**Claims**") arising out of, based on, or resulting from (a) the Development of Licensed Products in the Field in the Collaboration Territory by or on behalf of KemPharm, its Affiliates or KemPharm Partner(s) including, without limitation, the formulation of the Licensed Products or failure to warn regarding same, but excluding manufacture of said formulation or Licensed Products, (b) the breach of any of KemPharm's obligations under this Agreement, including KemPharm's representations and warranties set forth herein, (c) the willful misconduct or negligent acts of any KemPharm Indemnitee or KemPharm Partner(s) or such KemPharm Partner(s)'s respective officers, directors, employees, and agents, (d) any Infringement Actions. The foregoing indemnity obligation shall not apply to the extent that (i) the KVK Indemnitees fail to materially comply with the indemnification procedures set forth in Section 11.3 and KemPharm's defense of the relevant Claim is prejudiced by such failure, or (ii) any Claim arises from, is based on, or results from any activity or occurrence for which KVK is obligated to indemnify the KemPharm Indemnitees under Section 11.2.

11.2 Indemnification by KVK. KVK shall defend, indemnify, and hold KemPharm and its Affiliates and their respective officers, directors, employees, and agents (the "**KemPharm Indemnitees**") harmless from and against any and all Losses to which any KemPharm Indemnitee may become subject as a result of any Claims by any Third Party arising out of, based on, or resulting from (a) the conduct of Regulatory Activities with respect to, or Commercialization of, Licensed Products by or on behalf of KVK or its Affiliates or sublicensees (excluding (x) any Infringement Actions, (y) the conduct of Commercialization activities by or on behalf of KemPharm in accordance with the Commercialization Plan or otherwise performed at the request or under the direction of KVK, and (z) any action done at the request or demand of KemPharm or the JSC), (b) the breach of any of KVK's obligations under this Agreement, including KVK's representations and warranties set forth herein, (c) the manufacture of the Licensed Product and or formulations thereof or (d) the willful misconduct or negligent acts of any KVK Indemnitee. The foregoing indemnity obligation shall not apply to the extent that (i) the KemPharm Indemnitees fail to materially comply with the indemnification procedures set forth in Section 11.3 and KVK's defense of the relevant Claim is prejudiced by such failure, or (ii) any Claim arises from, is based on, or results from any activity or occurrence for which KemPharm is obligated to indemnify the KVK Indemnitees under Section 11.1.

11.3 Indemnification Procedures. The Party claiming indemnity under this Article 11 (the "**Indemnified Party**") shall give written notice to the Party from whom indemnity is being sought (the "**Indemnifying Party**") promptly after learning of such Claim and shall offer control of the defense of such Claim to the Indemnifying Party. The Indemnified Party shall provide the Indemnifying Party with reasonable assistance, at the Indemnifying Party's expense, in connection with the defense of the Claim for which indemnity is being sought. The Indemnified Party may participate in and monitor such defense with counsel of its own choosing at its sole expense; *provided, however,* the Indemnifying Party shall have the right to assume and conduct the defense of the Claim with counsel of its choice. The Indemnifying Party shall not settle any Claim without the prior written consent of the Indemnified Party, not to be unreasonably withheld, unless the settlement involves only the payment of money. So long as the Indemnifying Party is actively defending the Claim in good faith, the Indemnified Party shall not settle or compromise any such Claim without the prior written consent of the Indemnifying Party. If the Indemnifying Party does not assume and conduct the defense of the Claim as provided above, (a) the Indemnified Party may defend against, consent to the entry of any judgment, or enter into any settlement with respect to such Claim in any manner the Indemnified Party may deem reasonably appropriate, and the Indemnified Party need not consult with, or obtain any consent from, the Indemnifying Party in connection therewith, and (b) the Indemnifying Party shall remain responsible to indemnify the Indemnified Party as provided in this Article 11. Notwithstanding anything contained in the foregoing to the contrary, the provisions of Section 9.4 shall govern the defense of any Infringement Actions. Additionally, KVK shall not be obligated to indemnify KemPharm for any Claims related to such Infringement Action.

11.4 Limitation of Liability. NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, PUNITIVE, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 11.4 IS INTENDED TO OR SHALL LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER SECTIONS 11.1, 11.2 or 11.3, OR DAMAGES AVAILABLE FOR A PARTY'S BREACH OF CONFIDENTIALITY OBLIGATIONS IN ARTICLE 12 OR FOR EITHER PARTY'S BREACH OF ITS OBLIGATIONS IN SECTION 2.5.

11.5 Insurance. Each Party shall procure and maintain insurance, including product liability insurance, adequate to cover obligations for which it is liable hereunder and consistent with normal business practices of prudent companies similarly situated. It is understood that such insurance shall not be construed to create a limit of either Party's liability with respect to its indemnification obligations under this Article 11. Each Party shall provide the other Party with written evidence of such insurance upon request. Each Party shall provide the other Party with written notice at least [*] days prior to the cancellation, non-renewal or material change in such insurance.

Article 12
Confidentiality

12.1 Confidentiality. Each Party agrees that, during the Term and for a period of [*] years thereafter, it shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement or any other Transaction Agreement (which includes the exercise of any rights or the performance of any obligations hereunder or thereunder) any Confidential Information of the other Party, except to the extent expressly authorized by any Transaction Agreement or otherwise agreed in writing by the Parties. The foregoing confidentiality and non-use obligations shall not apply to any portion of the other Party's Confidential Information that the receiving Party can demonstrate by competent written proof:

(a) was already known to the receiving Party or its Affiliate, other than under an obligation of confidentiality, at the time of disclosure by the other Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party or its Affiliate in breach of this Agreement;

(d) was disclosed to the receiving Party or its Affiliate by a Third Party who has a legal right to make such disclosure and who did not obtain such information directly or indirectly from the other Party; or

(e) was independently discovered or developed by the receiving Party or its Affiliate without access to or aid, application, use of the other Party's Confidential Information, as evidenced by a contemporaneous writing.

12.2 Authorized Disclosure. Notwithstanding the obligations set forth in Section 12.1, a Party may disclose the other Party's Confidential Information and the terms of this Agreement to the extent:

(a) such disclosure is reasonably necessary (i) for the filing or prosecuting Patent rights as contemplated by any of the Transaction Agreements; (ii) to comply with the requirements of Regulatory Authorities with respect to obtaining and maintaining Regulatory Approval of Licensed Product; or (iii) for the prosecuting or defending litigation as contemplated by any of the Transaction Agreements;

(b) such disclosure is reasonably necessary to its or its Affiliate's employees, agents, consultants, contractors, licensees or sublicensees on a need-to-know basis for the sole purpose of performing its obligations or exercising its rights under any of the Transaction Agreements; provided that in each case, the disclosees are bound by written obligations of confidentiality and non-use at least as restrictive as those contained in this Agreement;

(c) such disclosure is reasonably necessary to any bona fide potential or actual investor, acquiror, merger partner, or other financial or commercial partner for the sole purpose of evaluating or carrying out an actual or potential investment, acquisition or other business relationship; provided that in connection with such disclosure, such Party shall inform each disclosee of the confidential nature of such Confidential Information and require each disclosee to treat such Confidential Information as confidential; or

(d) such disclosure is reasonably necessary to comply with applicable Laws, including regulations promulgated by applicable security exchanges, court order, administrative subpoena or order.

Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Sections 12.2(a) or 12.2(d), such Party shall promptly notify the other Party of such required disclosure and shall use reasonable efforts to obtain, or to assist the other Party in obtaining, a protective order preventing or limiting the required disclosure.

12.3 Publicity; Terms of Agreement.

(a) The Parties agree that the terms of this Agreement are the Confidential Information of both Parties, subject to the special authorized disclosure provisions set forth in this Section 12.3.

(b) If either Party desires to make a public disclosure concerning the terms of this Agreement, such Party shall give reasonable prior advance notice of the proposed text of such disclosure to the other Party for its prior review and approval, except as otherwise provided herein, which approval shall not be unreasonably withheld or delayed. A Party commenting on such a proposed disclosure shall provide its comments, if any, within [*] Business Days after receiving the proposed disclosure for review, or such shorter period of time as necessitated by regulatory requirements. In addition, where required by applicable Law, including regulations promulgated by applicable security exchanges, either Party shall have the right to make a press release or other public disclosure regarding the achievement of each sales milestone under this Agreement as it is achieved, the achievements of Regulatory Approval in the Collaboration Territory as they occur, or the occurrence of other events that affect either Party's rights or obligations under this Agreement, in each case subject only to the review procedure set forth in the preceding sentences. In relation to the other Party's review of such an announcement, such other Party may make specific, reasonable comments on such proposed press release within the prescribed time for commentary. Neither Party shall be required to seek the permission of the other Party to repeat any information regarding the terms of this Agreement that has already been publicly disclosed by such Party, or by the other Party, in accordance with this Section 12.3.

(c) The Parties acknowledge that either or both Parties or their Affiliates may be obligated to file under applicable Laws a copy of this Agreement with Governmental Authorities. Each Party and its Affiliates shall be entitled to make such a required filing, provided that it requests confidential treatment of the commercial terms and sensitive technical terms hereof and thereof to the extent such confidential treatment is reasonably available. In the event of any such filing, each Party will provide the other Party with a copy of this Agreement marked to show provisions for which such Party or its Affiliate intends to seek confidential treatment and shall reasonably consider and incorporate the other Party's timely comments thereon to the extent consistent with the legal requirements, with respect to the filing Party or Affiliate, governing disclosure of material agreements and material information that must be publicly filed.

12.4 Technical Publication. KVK may not publish peer reviewed manuscripts or provide other forms of public disclosure, including abstracts and presentations, pertaining to the Licensed Products or Licensed Know-How, without the prior written consent of KemPharm.

12.5 Equitable Relief. Each Party acknowledges that its breach of this Article 12 will cause irreparable harm to the other Party, which cannot be reasonably or adequately compensated in damages in an action at law. By reasons thereof, each Party agrees that the other Party shall be entitled, in addition to any other remedies it may have under this Agreement or otherwise, to preliminary and permanent injunctive and other equitable relief to prevent or curtail any actual or threatened breach of the obligations relating to Confidential Information set forth in this Article 12 by the other Party.

Article 13
Term And Termination

13.1 Term. The term of this Agreement (the "**Term**") shall commence upon the Effective Date and, unless earlier terminated pursuant to this Article 13, shall expire on the later of (a) expiration of the last claim of a Licensed Patent in the Collaboration Territory and (b) KVK's cessation of all Commercialization of Licensed Products in the Collaboration Territory.

13.2 Termination by KVK.

(a) KVK may terminate this Agreement in its entirety for convenience upon eighteen (18) months prior written notice given to KemPharm at any time after the third (3rd) anniversary of the Effective Date; *provided, however,* that the Parties may, upon mutual written consent, accelerate the effectiveness of such termination to the extent permitted by applicable Law in the Collaboration Territory.

(b) KVK may terminate this Agreement upon ninety (90) days prior written notice to KemPharm if a Regulatory Authority in the Collaboration Territory has ordered KVK to stop all sales of Licensed Products in the Collaboration Territory due to a safety concern; *provided, however,* that KVK has, for a period of ninety (90) days prior to the provision of such notice by KVK, used Commercially Reasonable Efforts to resolve such safety concern.

13.3 Termination by KemPharm.

(a) KemPharm may terminate this Agreement upon written notice to KVK, if KVK stops conducting Regulatory Activities with respect to, or Commercializing, Licensed Products in the Collaboration Territory for a period of six (6) months or more, unless the conduct of Regulatory Activities or Commercialization of Licensed Products was prevented throughout such period by a force majeure for which KVK provided notice pursuant to Section 15.2 prior to or at the start of such period and that persisted throughout such period despite KVK's reasonable efforts to remove or mitigate it. Such termination shall go into effect on the date specified in the applicable termination notice.

(b) KemPharm may terminate this Agreement in its entirety upon written notice to KVK, if KVK or its Affiliates or their respective sublicensees, directly or indirectly, individually or in association with any other person or entity, challenges the validity, enforceability or scope of any Licensed Patent. Such termination shall go into effect on the date specified in the applicable termination notice.

13.4 Termination for Breach. Each Party shall have the right to terminate this Agreement in its entirety immediately upon written notice to the other Party if the other Party materially breaches its obligations under any Transaction Agreement and, after receiving written notice identifying such material breach in reasonable detail, fails to cure such material breach within thirty (30) days from the date of such notice.

13.5 Termination Due to Bankruptcy. Either Party may terminate this Agreement if, at any time, the other Party files in any court or agency pursuant to any statute or regulation of any state, country or jurisdiction, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of that Party or of its assets, or if the other Party proposes a written agreement of composition or extension of its debts, or if the other Party is served with an involuntary petition against it, filed in any insolvency proceeding, and such petition is not dismissed within sixty (60) days after the filing thereof, or if the other Party proposes or becomes a Party to any dissolution or liquidation, or if the other Party makes an assignment for the benefit of its creditors.

13.6 Proof of Market Viability Termination. Either Party may terminate this Agreement in accordance with Section 6.9. In the event that KemPharm terminates this Agreement pursuant to Section 6.9 and continues to Commercialize Licensed Products in the Field in the Collaboration Territory, in addition to the effects of termination described in Section 13.7, [*] prior to the effective date of termination.

13.7 Effect of Termination or Expiration. Upon the any termination or expiration of this Agreement, the following shall apply, in addition to any other rights and obligations under this Agreement with respect to such termination:

(a) Licenses. All licenses and other rights granted by KemPharm to KVK under this Agreement shall terminate, including all sublicenses granted by KVK unless such sublicenses are assumed by KemPharm as contemplated by Section 2.1(c)(vi), which shall survive expiration or termination. KemPharm shall have a reversion of all rights previously licensed to KVK hereunder for which the relevant licenses have terminated on a fully paid-up and royalty-free basis, itself or with or through an Affiliate or Third Party, to conduct Regulatory Activities with respect to, and Commercialize, the Licensed Products in the Field in the Collaboration Territory at KemPharm's discretion.

(b) Regulatory Materials; Data. KVK shall transfer or assign to KemPharm or its designee all Regulatory Materials, including Regulatory Approvals, for the Licensed Products to the extent possible under applicable Law in the Collaboration Territory. KVK shall also promptly transfer or assign to KemPharm all Data, to the extent not already provided to KemPharm, including pharmacovigilance data, generated by or on behalf of KVK. In addition, each Party shall promptly return or destroy, at the other Party's election, all Confidential Information of such Party. If this Agreement is terminated by KVK pursuant to Sections 13.4 or 13.5, KemPharm shall bear the cost arising out of this subsection. If this Agreement is terminated by KVK pursuant to Sections 13.2(a) or if this Agreement is terminated by KemPharm pursuant to Sections 13.3(a), 13.3(b), 13.4, or 13.5, [*]. If this Agreement is terminated by KVK pursuant to Section 13.2(b) or by either Party pursuant to Section 13.6, [*].

(c) Transition Assistance. Upon KemPharm's request, KVK shall provide such assistance as may be reasonably necessary or useful for KemPharm to continue the Commercialization of Licensed Products in the Collaboration Territory, to the extent KVK or its Affiliate or sublicensee is then performing or having performed such activities, including upon request of KemPharm, assigning or amending as appropriate any agreements or arrangements with any Third Party for the distribution, sale or otherwise Commercialization of Licensed Products. If this Agreement is terminated by KVK pursuant to Sections 13.4 or 13.5, [*]. If this Agreement is terminated by KVK pursuant to Sections 13.2(a) or if this Agreement is terminated by KemPharm pursuant to Sections 13.3(a), 13.3(b), 13.4, or 13.5, [*]. If this Agreement is terminated by KVK pursuant to Sections 13.2(b) or by either Party pursuant to Section 13.6, [*]. Without limiting KVK's obligations pursuant to Section 2.1(c)(vi), to the extent that any such contract between KVK or its Affiliate or sublicensee and a Third Party is not assignable to KemPharm, KVK shall reasonably cooperate with KemPharm, at KemPharm's request [*], to arrange to continue to provide such services for a reasonable time after termination and to facilitate KemPharm's entry into a replacement agreement with such Third Party for such services. Additionally, KVK shall provide KemPharm with copies of any promotional and marketing materials generated by or on behalf of KVK with respect to Licensed Products prior to the effective date of expiration or termination. Upon KemPharm's request, KVK shall continue to Commercialize the Licensed Products in the Collaboration Territory for up to [*] after the effective date of expiration or termination of this Agreement, subject to [*].

(d) Inventory. In the event that this Agreement is terminated in its entirety, KemPharm shall have the right, but not the obligation to purchase any and all of the inventory of Licensed Products, including any samples and/or ingredients, held by KVK or its Affiliates or sublicensees as of the date of termination, at a price equal to (i) in the event that KVK is not the manufacturer of the Licensed Products, [*], or (ii) in the event that KVK is the manufacturer of the Licensed Products, [*]. Notwithstanding the above, if this Agreement is terminated by KVK pursuant to Sections 13.4 or 13.5, KVK shall have the right, at its sole discretion, to continue to be permitted to sell such inventory for up to at least [*] months after the effective date of termination of this Agreement.

13.8 Survival. Termination or expiration of this Agreement shall not affect rights or obligations of the Parties under this Agreement that have accrued prior to the date of termination or expiration. Notwithstanding anything to the contrary, the following provisions shall survive any expiration or termination of this Agreement: Articles 1 and 9 through 13, and Sections 2.1, 2.3, 2.4, 5.1, 5.3, 5.9, 5.10, 6.6, 6.7, 8.4 through 8.9, and 14.2.

13.9 Termination Not Sole Remedy. Termination is not the sole remedy under this Agreement and, whether or not termination is affected and notwithstanding anything contained in this Agreement to the contrary, all other remedies shall remain available except as agreed to otherwise herein.

Article 14
Dispute Resolution

14.1 Disputes; Internal Resolution. The Parties recognize that disputes as to certain matters may from time to time arise that relate to either Party's rights and/or obligations hereunder. It is the objective of the Parties to establish procedures to facilitate the resolution of disputes arising under this Agreement in an expedient manner by mutual cooperation. To accomplish this objective, the Parties agree that, if a dispute arises under this Agreement with respect to which a Party does not have final decision-making authority pursuant to Section 3.3, and the Parties are unable to resolve such dispute within [*] days after such dispute is first identified by either Party in writing to the other, the Parties shall refer such dispute to the respective Chief Executive Officer of KemPharm, or one of its Affiliates, and KVK (the "**Executive Officers**") for attempted resolution by good faith negotiations within [*] days after such notice is received, which shall include at least one (1) in person meeting of the Executive Officers within [*] days after such notice is received. If the dispute is not resolved within such [*] days, either Party may resolve such dispute in accordance with Section 14.2.

14.2 Governing Law. Resolution of all disputes and any remedies relating thereto, shall be governed by and construed under the laws of the State of Delaware, U.S., without giving effect to any choice of law principles that would require the application of the laws of a different state. Each of the Parties hereby irrevocably and unconditionally consents to submit to the exclusive jurisdiction of the courts of the State of Delaware for any matter arising out of or relating to this Agreement and the transactions contemplated hereby, and agrees not to commence any litigation relating thereto except in such courts. Each of the Parties hereby irrevocably and unconditionally waives any objection to the laying of venue of any matter arising out of this Agreement or the transactions contemplated hereby in the courts of the State of Delaware and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such matter brought in any such court has been brought in an inconvenient forum.

Article 15
Miscellaneous

15.1 Entire Agreement; Amendment. This Agreement, including the Exhibits hereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Effective Date, all prior and contemporaneous agreements and understandings between the Parties with respect to the subject matter hereof, including the Confidentiality Agreement. The foregoing shall not be interpreted as a waiver of any remedies available to either Party as a result of any breach, prior to the Effective Date, by the other Party of its obligations under the Confidentiality Agreement. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth in this Agreement. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

15.2 Force Majeure. Both Parties shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by force majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure shall include conditions beyond the reasonable control of the applicable Party, which may include an act of God, war, civil commotion, terrorist act, labor strike or lock-out, epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, and failure of plant or machinery. Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a force majeure affecting such Party. If a force majeure persists for more than ninety (90) days, then the Parties will discuss in good faith the modification of the Parties' obligations under this Agreement in order to mitigate the delays caused by such force majeure.

15.3 Notices. Any notice required or permitted to be given under this Agreement shall be in writing, shall specifically refer to this Agreement, and shall be addressed to the appropriate Party at the address specified below or such other address as may be specified by such Party in writing in accordance with this Section 15.3, and shall be deemed to have been given for all purposes (a) when received, if hand-delivered or sent by a reputable courier service, or (b) [*] Business Days after mailing, if mailed by first class certified or registered airmail, postage prepaid, return receipt requested.

If to KemPharm:
KemPharm Inc.
2500 Crosspark Road, Suite E126
Coralville, IA 52241
Attn: R. LaDuane Clifton, CFO, Secretary and Treasurer

with copies to, which shall not constitute notice:

Cooley LLP
One Freedom Square
Reston, VA 20190-5656
Attn: Brent Siler, Esq.

If to KVK:
110 Terry Drive
KVK Tech, Inc.
Newtown, PA 18940
Attn: Anthony P. Tabasso, CEO

with copies to, which shall not constitute notice:

Klehr Harrison Harvey Branzburg LLP
1835 Market Street
Philadelphia, PA 19103
Attn: Francis M. Correll, Jr., Esq.

15.4 No Strict Construction; Headings. This Agreement has been prepared jointly by the Parties and shall not be strictly construed against either Party. Ambiguities, if any, in this Agreement shall not be construed against any Party, irrespective of which Party may be deemed to have authored the ambiguous provision. The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section. Except where the context otherwise requires, the use of any gender shall be applicable to all genders, and the word "or" is used in the inclusive sense (and/or). The term "including" as used herein means including, without limiting the generality of any description preceding such term.

15.5 Assignment; Change of Control.

(a) Neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other Party, except that either Party may make such an assignment without the other Party's express written consent to its Affiliates.

(b) Notwithstanding Section 15.5(a), either Party may without such consent but with prior written notice to the other Party, assign this Agreement and its rights and obligations hereunder in connection with a Change of Control, provided further that if the said assignee is engaged in a business that competes with the Licensed Product and/or the notified Party's business, the notified Party shall have the right to terminate this Agreement without any obligation to the other Party, by providing written notice thereof within [*] after the receipt of such notice from the assigning Party. Any permitted assignee shall assume all obligations of its assignor under this Agreement. Any assignment or attempted assignment by either Party in violation of the terms of this Section 15.5 shall be null, void and of no legal effect.

15.6 Performance by Affiliates. Each Party may discharge any obligations and exercise any right hereunder through any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

15.7 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

15.8 Severability. If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

15.9 No Waiver. Any delay in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement, except with respect to an express written and signed waiver relating to a particular matter for a particular period of time.

15.10 Independent Contractors. Each Party shall act solely as an independent contractor, and nothing in this Agreement shall be construed to give either Party the power or authority to act for, bind, or commit the other Party in any way. Nothing herein shall be construed to create the relationship of partners, principal and agent, or joint-venture partners between the Parties.

15.11 English Language. This Agreement was prepared in the English language, which language shall govern the interpretation of, and any dispute regarding, the terms of this Agreement.

15.12 Counterparts. This Agreement may be executed in one (1) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

{Signature Page Follows}

In Witness Whereof, the Parties have executed this License, Development and Commercialization Agreement in duplicate originals by their duly authorized officers as of the Effective Date.

KemPharm, Inc.

By: /s/ R. LaDuane Clifton
Name: R. LaDuane Clifton
Title: CFO, Secretary and Treasurer

KVK Tech, Inc.

By: /s/ Anthony P. Tabasso
Name: Anthony P. Tabasso
Title: CEO and General Counsel

LIST OF EXHIBITS

Exhibit A: Licensed Patents
Exhibit A-1: Limited Licensed Priority Patents
Exhibit B: Initial Commercialization Plan
Exhibit C: Licensed Product Label
Exhibit D: [*]
Exhibit E: Net Profit Share Example

Exhibit A
Licensed Patents and Patent Applications

Title: [*]

Inventors: [*]

	Application #	Filing Date	Patent #	Grant Date
1	[*]	[*]	[*]	[*]
2	[*]	[*]	[*]	[*]
3	[*]	[*]		

Exhibit A-1
Limited Licensed Priority Patents and Patent Applications

Title: [*]

Inventors: [*]

	Application #	Filing Date	Patent #	Grant Date
1	[*]	[*]		
2	[*]	[*]	[*]	[*]
3	[*]	[*]	[*]	[*]
4	[*]	[*]	[*]	[*]
5	[*]	[*]	[*]	[*]
6	[*]	[*]		

Exhibit B
Initial Commercialization Plan

[*]

Exhibit C
Licensed Product Label

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **APADAZ™ safely and effectively. See full prescribing information for APADAZ.**

APADAZ (benzhydrocodone and acetaminophen) tablets, for oral use, CII
Initial U.S. Approval: 1982

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; HEPATOTOXICITY, CYTOCHROME P450 3A4 INTERACTION, and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

See full prescribing information for complete boxed warning.

- **APADAZ exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions. (5.1)**
- **Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. (5.2)**
- **Accidental ingestion of APADAZ, especially by children, can result in a fatal overdose of hydrocodone. (5.2)**
- **Prolonged use of APADAZ during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.3)**
- **Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of hydrocodone from APADAZ. (5.4, 7, 12.3)**
- **APADAZ contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product. (5.5)**
- **Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation. (5.6, 7)**

INDICATIONS AND USAGE

APADAZ is a combination of benzhydrocodone, a prodrug of the opioid agonist hydrocodone, and acetaminophen, and is indicated 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. (1)

Limitations of Use (1)
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve APADAZ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

DOSAGE AND ADMINISTRATION

- Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. (2.1)
- Individualize dosing based on the severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. (2.1)
- Initiate treatment with APADAZ at 1 or 2 tablets every 4 to 6 hours as needed for pain. Dosage should not exceed 12 tablets in a 24- hour period. (2.2)
- 6.12 mg benzhydrocodone is equivalent to 4.54 mg hydrocodone or 7.5 mg hydrocodone bitartrate. If switching from immediate-release hydrocodone bitartrate/acetaminophen, substitute 6.12 mg/325 mg APADAZ for 7.5 mg/325 mg hydrocodone bitartrate/acetaminophen. Dosage of APADAZ should be adjusted according to the severity of the pain and the response of the patient.
- Do not stop APADAZ abruptly in a physically-dependent patient. (2.5)

DOSAGE FORMS AND STRENGTHS

Immediate-release tablets: 6.12 mg benzhydrocodone (equivalent to 6.67 mg benzhydrocodone hydrochloride) and 325 mg acetaminophen (3)

CONTRAINDICATIONS

- Significant respiratory depression (4)
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment (4)
- Known or suspected gastrointestinal obstruction, including paralytic ileus (4)

- Hypersensitivity to hydrocodone or acetaminophen (4)

WARNINGS AND PRECAUTIONS

- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration. (5.7)
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.8)
- Severe Hypotension: Monitor during dosage initiation and titration. Avoid use of APADAZ in patients with circulatory shock. (5.9)
- Serious Skin Reactions: Discontinue APADAZ immediately at the first appearance of skin rash and if symptoms associated with allergy or hypersensitivity occur. Do not use in patients with acetaminophen allergy. (5.10)
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of APADAZ in patients with impaired consciousness or coma. (5.11)

ADVERSE REACTIONS

Most common adverse reactions (>5%) are nausea, somnolence, vomiting, constipation, pruritus, dizziness, and headache. (6)

To report SUSPECTED ADVERSE REACTIONS, contact KemPharm, Inc. at 1-321-939-3416 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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---------- **DRUG INTERACTIONS** ----------

- Serotonergic Drugs: Concomitant use may result in serotonin syndrome. Discontinue APADAZ if serotonin syndrome is suspected. (7)
- Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics: Avoid use with APADAZ because they may reduce analgesic effect of APADAZ or precipitate withdrawal symptoms. (7)
- Monoamine Oxidase Inhibitors (MAOIs): Can potentiate the effects of hydrocodone. Avoid concomitant use in patients receiving MAOIs or within 14 days of stopping treatment with an MAOI. (7)

USE IN SPECIFIC POPULATIONS

Pregnancy: May cause fetal harm (8.1).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 02/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; HEPATOTOXICITY; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

APADAZ exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing APADAZ, and monitor all patients regularly for the development of these behaviors and conditions [*see Warnings and Precautions (5.1)*].

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of APADAZ. Monitor for respiratory depression, especially during initiation of APADAZ or following a dose increase [*see Warnings and Precautions (5.2)*].

Accidental Ingestion

Accidental ingestion of even one dose of APADAZ, especially by children, can result in a fatal overdose of hydrocodone [*see Warnings and Precautions (5.2)*].

Neonatal Opioid Withdrawal Syndrome

Prolonged use of APADAZ during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available [*see Warnings and Precautions (5.3)*].

Cytochrome P450 3A4 Interaction

The concomitant use of APADAZ with all cytochrome P450 3A4 inhibitors may result in an increase in hydrocodone plasma concentrations, which could increase or prolong adverse reactions and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in hydrocodone plasma concentration. Monitor patients receiving APADAZ and any CYP3A4 inhibitor or inducer [*see Warnings and Precautions (5.4), Drug Interactions (7), Clinical Pharmacology (12.3)*].

Hepatotoxicity

APADAZ contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product [*see Warnings and Precautions (5.5)*].

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory
depression, coma, and death *[see Warnings and Precautions (5.6), Drug Interactions (7)]*.

•Reserve concomitant prescribing of APADAZ and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.

- **•Limit dosages and durations to the minimum required.**
- **•Follow patients for signs and symptoms of respiratory depression and sedation.**

1 INDICATIONS AND USAGE

APADAZ is indicated 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.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses *[see Warnings and Precautions (5.1)]*, reserve APADAZ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals *[see Warnings and Precautions (5)]*. The total dosage of APADAZ and any concomitant acetaminophen-containing products should not exceed 4000 mg of acetaminophen in a 24-hour period.
- Initiate the dosing regimen for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse *[see Warnings and Precautions (5.1)]*.
- Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy and following dosage increases with APADAZ and adjust the dosage accordingly *[see Warnings and Precautions (5.2)]*.

2.2 Initial Dosage

Use of APADAZ as the First Opioid Analgesic

Initiate treatment with APADAZ at 1 to 2 tablets every 4 to 6 hours as needed for pain. Dosage should not exceed 12 tablets in a 24-hour period.

2.3 Conversion from Other Opioids to APADAZ

There is inter-patient variability in the potency of opioid drugs and opioid formulations. Therefore, a conservative approach is advised when determining the total daily dosage of APADAZ. It is safer to underestimate a patient's 24-hour APADAZ dosage than to overestimate the 24-hour APADAZ dosage and manage an adverse reaction due to overdose.

Conversion from Hydrocodone Bitartrate/Acetaminophen to APADAZ

Hydrocodone content in 6.12 mg benzhydrocodone is 4.54 mg hydrocodone or is equivalent to 7.5 mg hydrocodone bitartrate. If switching from immediate-release hydrocodone bitartrate/acetaminophen, substitute 6.12 mg/325 mg APADAZ for 7.5 mg/325 mg hydrocodone bitartrate/acetaminophen.

2.4 Titration and Maintenance of Therapy

Individually titrate APADAZ to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving APADAZ to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse, or misuse [*see Warnings and Precautions (5.1)*]. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration.

If the level of pain increases after dosage stabilization, attempt to identify the source of increased pain before increasing the APADAZ dosage. If unacceptable opioid-related adverse reactions are observed, consider reducing the dosage. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

Total dosage of APADAZ and any concomitant acetaminophen-containing products should not exceed 4000 mg of acetaminophen in a 24-hour period.

2.5 Discontinuation of APADAZ

When a patient who has been taking APADAZ regularly and may be physically dependent no longer requires therapy with APADAZ, taper the dose gradually, by 25% to 50% every 2 to 4 days, while monitoring carefully for signs and symptoms of withdrawal. If the patient develops these signs or symptoms, raise the dose to the previous level and taper more slowly, either by increasing the interval between decreases, decreasing the amount of change in dose, or both. Do not abruptly discontinue APADAZ in a physically dependent patient [*see Warnings and Precautions (5.15), Drug Abuse and Dependence (9.3)*].

3 DOSAGE FORMS AND STRENGTHS

Immediate-release tablet. Each capsule-shaped white tablet debossed with "KP201" on one side contains 6.12 mg benzhydrocodone (equivalent to 6.67 mg benzhydrocodone hydrochloride) and 325 mg acetaminophen.

4 CONTRAINDICATIONS

APADAZ is contraindicated in patients with:

- Significant respiratory depression [*see Warnings and Precautions (5.2)*]

- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment *[see Warnings and Precautions (5.7)]*
- Known or suspected gastrointestinal obstruction, including paralytic ileus *[see Warnings and Precautions (5.13)]*
- Hypersensitivity to hydrocodone or acetaminophen, or any other component of this product (e.g., anaphylaxis) *[see Warnings and Precautions (5.12), Adverse Reactions (6)]*

5 WARNINGS AND PRECAUTIONS

5.1 Addiction, Abuse, and Misuse

APADAZ contains benzhydrocodone, a Schedule II controlled substance. As an opioid, APADAZ exposes users to the risks of addiction, abuse, and misuse *[see Drug Abuse and Dependence (9)]*.

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed APADAZ. Addiction can occur at recommended dosages and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing APADAZ, and monitor all patients receiving APADAZ for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as APADAZ, but use in such patients necessitates intensive counseling about the risks and proper use of APADAZ along with intensive monitoring for signs of addiction, abuse, and misuse.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing APADAZ. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug *[see Patient Counseling Information (17)]*. Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

5.2 Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status [see Overdosage (10)]. Carbon dioxide (CO_2) retention from opioid- induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of APADAZ, the risk is greatest during the initiation of therapy or following a dosage increase.

Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy with and following dosage increases of APADAZ.

To reduce the risk of respiratory depression, proper dosing and titration of APADAZ are essential *[see Dosage and Administration (2)]*. Overestimating the APADAZ dosage when converting patients from another opioid product can result in a fatal overdose with the first dose.

Accidental ingestion of even one dose of APADAZ, especially by children, can result in respiratory depression and death due to an overdose of hydrocodone.

5.3 Neonatal Opioid Withdrawal Syndrome

Prolonged use of APADAZ during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Use in Specific Populations (8.1), Patient Counseling Information(17)]*.

5.4 Risks of Concomitant Use or Discontinuation of Cytochrome P450 CYP3A4 Inhibitors and Inducers

Concomitant use of APADAZ with a CYP3A4 inhibitor, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir), may increase plasma concentrations of hydrocodone and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression *[see Warnings and Precautions (5.2)]*, particularly when an inhibitor is added after a stable dose of APADAZ is achieved. Similarly, discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, in APADAZ-treated patients may increase hydrocodone plasma concentrations and prolong opioid adverse reactions. When using APADAZ with CYP3A4 inhibitors or discontinuing CYP3A4 inducers in APADAZ-treated patients, monitor patients closely at frequent intervals and consider dosage reduction of APADAZ until stable drug effects are achieved *[see Drug Interactions (7)]*.

Concomitant use of APADAZ with CYP3A4 inducers or discontinuation of an CYP3A4 inhibitor could decrease hydrocodone plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to hydrocodone. When using APADAZ with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, monitor patients closely at frequent intervals and consider increasing the opioid dosage if needed to maintain adequate analgesia or if symptoms of opioid withdrawal occur *[see Drug Interactions (7)]*.

5.5 Acetaminophen Hepatotoxicity

APADAZ contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and

often involve more than one acetaminophen-containing product *[see Overdosage (10)]*. The excessive intake of acetaminophen may be intentional to cause self-harm or unintentional as patients attempt to obtain more pain relief or unknowingly take other acetaminophen-containing products.

The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen.

Instruct patients to look for acetaminophen or APAP on package labels and not to use more than one product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

5.6 Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of APADAZ with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics [*see Drug Interactions (7)*].

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Advise both patients and caregivers about the risks of respiratory depression and sedation when APADAZ is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs [*see Drug Interactions (7), Patient Counseling Information (17)*].

5.7 Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of APADAZ in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: APADAZ-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of APADAZ [*see Warnings and Precautions (5.2)*].

Elderly, Cachetic, or Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients [*see Warnings and Precautions (5.2)*].

Monitor such patients closely, particularly when initiating and titrating APADAZ and when APADAZ is given concomitantly with other drugs that depress respiration [*see Warnings and Precautions (5.2)*]. Alternatively, consider the use of non-opioid analgesics in these patients.

5.8 Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

5.9 Severe Hypotension

APADAZ may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics) [*see Drug Interactions (7)*]. Monitor these patients for signs of hypotension after initiating or titrating the dosage of APADAZ. In patients with circulatory shock, APADAZ may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of APADAZ in patients with circulatory shock.

5.10 Serious Skin Reactions

Rarely, acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Inform patients about the signs of serious skin reactions and discontinue use at the first appearance of skin rash or any other sign of hypersensitivity.

5.11 Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

In patients who may be susceptible to the intracranial effects of CO2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), APADAZ may reduce respiratory drive, and the resultant CO2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with APADAZ.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of APADAZ in patients with impaired consciousness or coma.

5.12 Hypersensitivity/Anaphylaxis

There have been post-marketing reports of hypersensitivity and anaphylaxis associated with use of acetaminophen. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, pruritus, and vomiting. There were infrequent reports of life-threatening anaphylaxis requiring emergency medical attention. Instruct patients to discontinue APADAZ tablets immediately and seek medical care if they experience these symptoms. Do not prescribe APADAZ tablets for patients with acetaminophen allergy.

5.13 Risks of Use in Patients with Gastrointestinal Conditions

APADAZ is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The hydrocodone from APADAZ may cause spasm of the sphincter of Oddi. Opioids may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis for worsening symptoms.

5.14 Increased Risk of Seizures in Patients with Seizure Disorders

The hydrocodone from APADAZ may increase the frequency of seizures in patients with seizure disorders, and may increase the risk of seizures occuring in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during APADAZ therapy.

5.15 Withdrawal

Avoid the use of mixed agonist/antagonist (e.g, pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving a full opioid agonist

analgesic, including APADAZ [see Drug Interactions (7)]. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or precipitate withdrawal symptoms.

When discontinuing APADAZ, gradually taper the dosage [*see Dosage and Administration (2.5)*]. Do not abruptly discontinue APADAZ [*see Drug Abuse and Dependence (9.3)*].

5.16 Risks of Driving and Operating Machinery

APADAZ may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of APADAZ and know how they will react to the medication [*see Patient Counseling Information (17)*].

6 ADVERSE REACTIONS

The following serious adverse reactions are described, or described in greater detail, in other sections:

- Addiction, Abuse, and Misuse *[see Warnings and Precautions (5.1)]*
- Life-Threatening Respiratory Depression *[see Warnings and Precautions (5.2)]*
- Neonatal Opioid Withdrawal Syndrome *[see Warnings and Precautions (5.3)]*
- Hepatotoxicity *[see Warnings and Precautions (5.5)]*
- Interactions with Benzodiazepines and other CNS Depressants *[see Warnings and Precautions (5.6)]*
- Adrenal Insufficiency *[see Warnings and Precautions (5.8)]*
- Severe Hypotension *[see Warnings and Precautions (5.9)]*
- Serious Skin Reactions *[see Warnings and Precautions (5.10)]*
- Anaphylaxis and Other Hypersensitivity Reactions *[see Warnings and Precautions (5.12)]*
- Gastrointestinal Adverse Reactions *[see Warnings and Precautions (5.13)]*
- Seizures *[see Warnings and Precautions (5.14)]*
- Withdrawal *[see Warnings and Precautions (5.15)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of APADAZ was evaluated in six Phase 1 studies in which a total of 200 healthy adult subjects receive at least one oral dose of APADAZ. The most common AEs (>5%) reported across these studies were: nausea (21.5%), somnolence (18.5%), vomiting (13.0%), constipation (12.0%), pruritus (11.5%), dizziness (7.5%), and headache (6.0%).

The following adverse reactions occurred with an incidence of 1% to 5% in single-dose or repeated-dose clinical trials of APADAZ.

Gastrointestinal disorder: abdominal distension, abdominal pain, flatulence

General disorders and administration site conditions: asthenia

Nervous system disorders: presyncope, tremor

Respiratory, thoracic and mediastinal disorders: dyspnea

Vascular disorders: hot flush, hypotension

Adverse reactions occurring at less than 1%: the following lists clinically relevant adverse reactions that occurred with an incidence of less than 1% in APADAZ clinical trials.

Eye disorders: eye pruritus

Gastrointestinal disorders: diarrhea, gastrooesophageal reflux disease, haematemesis

General disorders and administration site conditions: chest discomfort

Infections and infestations: rhinitis

Nervous system disorders: hypoesthesia, syncope

Psychiatric disorders: agitation, euphoric mood, nightmare

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of hydrocodone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Serotonin syndrome: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.

Adrenal insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.

Anaphylaxis: Anaphylaxis has been reported with ingredients contained in APADAZ.

Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids *[see Clinical Pharmacology (12.2)]*.

7 DRUG INTERACTIONS

Table 1 includes clinically significant drug interactions with APADAZ.

Table 1. Clinically Significant Drug Interactions with APADAZ

CYP3A4 and 2D6 Inhibitors	
Clinical Impact:	The concomitant use of APADAZ and CYP3A4 inhibitors can increase the plasma concentration of hydrocodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of APADAZ and CYP2D6 and CYP3A4 inhibitors, particularly when an inhibitor is added after a stable dose of APADAZ is achieved [*see Warnings and Precautions (5.4)*]. After stopping a CYP3A4 inhibitor, as the effects of the inhibitor decline, the hydrocodone plasma concentration will decrease [*see Clinical Pharmacology (12.3)*], resulting in decreased opioid efficacy or a withdrawal syndrome in patients who had developed physical dependence to hydrocodone.
Intervention:	If concomitant use is necessary, consider dosage reduction of APADAZ until stable drug effects are achieved. Monitor patients for respiratory depression and sedation at frequent intervals. If a CYP3A4 inhibitor is discontinued, consider increasing the APADAZ dosage until stable drug effects are achieved. Monitor for signs of opioid withdrawal.
Examples:	Macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), protease inhibitors (e.g., ritonavir) etc.
CYP3A4 Inducers	
Clinical Impact:	The concomitant use of APADAZ and CYP3A4 inducers can decrease the plasma concentration of hydrocodone [*see Clinical Pharmacology (12.3)*], resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to hydrocodone [*see Warnings and Precautions (5.15)*]. After stopping a CYP3A4 inducer, as the effects of the inducer decline, the hydrocodone plasma concentration will increase [*see Clinical Pharmacology (12.3)*], which could increase or prolong both the therapeutic effects and adverse reactions, and may cause serious respiratory depression.
Intervention:	If concomitant use is necessary, consider increasing the APADAZ dosage until stable drug effects are achieved [*see Dosage and Administration (2)*]. Monitor for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider APADAZ dosage reduction and monitor for signs of respiratory depression.
Examples:	Rifampin, carbamazepine, phenytoin etc.
Benzodiazepines and Other Central Nervous System (CNS) Depressants	
Clinical Impact:	Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants, including alcohol, increases the risk of hypotension, respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation [*see Dosage and Administration (2.5), Warnings and Precautions (5.6)*].
Examples:	Benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Intervention:	If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue APADAZ if serotonin syndrome is suspected.
Examples:	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Impact:	MAOI interactions with opioids may manifest as serotonin syndrome or opioid toxicity (e.g., respiratory depression, coma) [*see Warnings and Precauitons (5.2)*]. If urgent use of an opioid is necessary, use test doses and frequent titration of small doses to treat pain while closely monitoring blood pressure and signs and symptoms of CNS and respiratory depression.
Intervention:	The use of APADAZ is not recommended for patients taking MAOIs or within 14 days of stopping such treatment.
Examples:	phenelzine, tranylcypromine, linezolid
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reduce the analgesic effect of APADAZ and/or precipitate withdrawal symptoms.
Intervention:	Avoid concomitant use.
Examples:	butorphanol, nalbuphine, pentazocine, buprenorphine
Muscle Relaxants	
Clinical Impact:	Hydrocodone may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Intervention:	Monitor patients for signs of respiratory depression that may be greater than otherwise expected and decrease the dosage of APADAZ and/or the muscle relaxant as necessary.
Diuretics	
Clinical Impact:	Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.

	Intervention: Monitor patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.
Anticholinergic Drugs	
	Clinical Impact: The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
	Intervention: Monitor patients for signs of urinary retention or reduced gastric motility when APADAZ is used concomitantly with anticholinergic drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome [*see Warnings and Precautions (5.3)*]. There are no available human data on hydrocodone or APADAZ use during pregnancy to inform any drug associated risks. However, neonatal opioid withdrawal and other adverse reactions during pregnancy and labor can occur with use of APADAZ [*see Clinical Considerations*].

Published studies with oral acetaminophen use during pregnancy have not reported an association with major congenital malformations. No reproductive or developmental toxicology studies in animals have been conducted with benzhydrocodone or the combination of benzhydrocodone and acetaminophen. Reproductive and developmental studies in rats and mice from the published literature identified adverse events at clinically relevant doses with acetaminophen. Treatment of pregnant rats with doses of acetaminophen approximately equal to the maximum human daily dose (MHDD) showed evidence of fetotoxicity and increases in bone variations in the fetuses. In another study, necrosis was observed in the liver and kidney of both pregnant rats and fetuses at doses approximately equal to the MHDD. In mice and rats treated with acetaminophen at doses within the clinical dosing range, cumulative adverse effects on reproductive capacity were reported. In mice, a reduction in number of litters of the parental mating pair was observed as well as retarded growth, abnormal sperm in their offspring, and reduced birth weight in the next generation. In rats, female fertility was decreased following in utero exposure to acetaminophen [*see DATA*].

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes can result in physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth.

Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly [*see Warnings and Precautions (5.3)*].

Labor or Delivery

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone, must be available for reversal of opioid-induced respiratory depression in the neonate. APADAZ is not recommended for use in pregnant women during or immediately prior to labor, when other analgesic techniques are more appropriate. Opioid analgesics, including APADAZ, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine contractions. However, this effect is not consistent and may be offset by an increased rate of cervical dilation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Data

Human Data

Acetaminophen:

Published data from a large population-based prospective cohort study and a population-based, case-control study do not clearly report an association with oral acetaminophen and major birth defects, miscarriage, or adverse maternal or fetal outcomes when acetaminophen is used during pregnancy. However, these studies cannot definitely establish the absence of any risk because of methodological limitations including recall bias.

Animal Data

No reproductive or developmental toxicology studies were conducted with benzhydrocodone or the combination of benzhydrocodone and acetaminophen. The following data are based on findings from studies performed with acetaminophen alone.

Studies in pregnant rats that received oral acetaminophen during organogenesis at doses up to 0.88 the maximum human daily dose (MHDD) of 3.9 grams/day based on a body surface area comparison showed evidence of fetotoxicity (reduced fetal weight and length) and a dose-related

increase in bone variations (reduced ossification and rudimentary rib changes). Offspring had no evidence of external, visceral, or skeletal malformations. When pregnant rats received oral acetaminophen throughout gestation at doses of 1.2 times the MHDD (based on a body surface area comparison), areas of necrosis occurred in both the liver and kidney of pregnant rats and fetuses. These effects did not occur in animals that received oral acetaminophen at doses 0.3 times the MHDD, based on a body surface area comparison. In a continuous breeding study, pregnant mice received 0.25, 0.5, or 1.0% acetaminophen via the diet (357, 715, or 1430 mg/kg/day). These doses are approximately 0.45, 0.89, and 1.78 times the MHDD, respectively, based on a body surface area comparison. A dose-related reduction in body weights of fourth and fifth litter offspring of the treated mating pair occurred during lactation and post-weaning at all doses. Animals in the high dose group had a reduced number of litters per mating pair, male offspring with an increased percentage of abnormal sperm, and reduced birth weights in the next generation pups.

8.2 Lactation

Risk Summary

Hydrocodone is present in human milk. A published lactation study reports variable concentrations of hydrocodone and hydromorphone (an active metabolite) in breast milk with administration of hydrocodone to nursing mothers in the early post-partum period. This lactation study did not assess breastfed infants for potential adverse drug reactions. There is potential for sedation and respiratory depression resulting from infant exposure to hydrocodone and its metabolites in breast milk.

Acetaminophen is present in human milk in small quantities after oral administration. Based on data from more than 15 nursing mothers, the calculated infant daily dose of acetaminophen is approximately 1 to 2% of the maternal dose. There is one well-documented report of a rash in a breast-fed infant that resolved when the mother stopped acetaminophen use and recurred when she resumed acetaminophen use.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for APADAZ and any potential adverse effects on the breastfed child from APADAZ or from the underlying maternal condition.

Clinical Considerations

Infants exposed to APADAZ through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.

8.3 Females and Males of Reproductive Potential

Infertility

Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible [*see Adverse Reactions (6.2),*

Clinical Pharmacology (12.2)].

Published animal studies report that oral acetaminophen treatment of male animals at doses that are 1.2 times the MHDD and greater (based on a body surface area comparison) result in decreased testicular weights, reduced spermatogenesis, reduced fertility, and reduced implantation sites in females given the same doses. Additional published animal studies indicate that acetaminophen exposure in utero adversely impacts reproductive capacity of both male and female offspring at clinically relevant exposures [*see Nonclinical Toxicology (13.1)*].

8.4 Pediatric Use

Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

8.5 Geriatric Use

Elderly patients (aged 65 years or older) may have increased sensitivity to hydrocodone. In general, use caution when selecting a dosage for an elderly patient, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

Respiratory depression is the chief risk for elderly patients treated with opioids, and has occurred after large initial doses were administered to patients who were not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of APADAZ slowly in geriatric patients and monitor closely for signs of respiratory depression [*see Warnings and Precautions (5.2)*].

Hydrocodone and acetaminophen are known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of APADAZ has not been determined. Patients with hepatic impairment may have higher plasma concentrations than those with normal function. Use a low initial dose of APADAZ in patients with hepatic impairment or active liver disease and monitor closely for adverse events such as respiratory depression and hepatotoxicity [*see Warnings and Precautions (5.2 and 5.5)*].

8.7 Renal Impairment

The effect of renal impairment on the pharmacokinetics of APADAZ has not been determined. Patients with renal impairment may have higher plasma concentrations than those with normal function. Use a low initial dose of APADAZ in patients with renal impairment and monitor closely for adverse events such as respiratory depression.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

APADAZ contains benzhydrocodone, a Schedule II controlled substance.

9.2 Abuse

APADAZ contains benzhydrocodone, a substance with a high potential for abuse similar to other opioids including fentanyl, hydromorphone, methadone, morphine, oxycodone, oxymorphone, and tapentadol. APADAZ can be abused and is subject to misuse, addiction, and criminal diversion [*see Warnings and Precautions (5.1)*].

All patients treated with opioids require careful monitoring for signs of abuse and addiction, because use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, even once, for its rewarding psychological or physiological effects.

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

“Drug-seeking” behavior is very common in persons with substance use disorders. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing, or referral, repeated “loss” of prescriptions, tampering with prescriptions, and reluctance to provide prior medical records or contact information for other treating healthcare provider(s). “Doctor shopping” (visiting multiple prescribers to obtain additional prescriptions) is common among drug abusers and people suffering from untreated addiction. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Health care providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

APADAZ, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Risks Specific to Abuse of APADAZ

APADAZ is for oral use only. Abuse of APADAZ poses a risk of overdose and death. The risk is increased with concurrent use of APADAZ with alcohol and other central nervous system depressants.

With intravenous abuse, the inactive ingredients in APADAZ can result in local tissue necrosis, infection, pulmonary granulomas, embolism and death, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases, such as hepatitis and HIV.

Abuse Deterrent Studies

In vitro and human abuse potential studies comparing APADAZ to an immediate-release hydrocodone/acetaminophen tablet control were conducted to assess the potential abuse deterrent properties of APADAZ.

In Vitro Testing

In vitro physical and chemical manipulation studies were performed to evaluate the ability of different methods to extract and convert benzyhydrocodone to hydrocodone for the purpose of preparing APADAZ for abuse by the intravenous route or by smoking. The efficiency of extracting benzhydrocodone from APADAZ was similar compared to the efficiency of extracting hydrocodone from the non-abuse-deterrent hydrocodone/acetaminophen control. Further conversion (hydrolysis) of benzhydrocodone to hydrocodone in vitro is a difficult process. Overall, these studies showed no advantage for APADAZ over the hydrocodone/acetaminophen control.

Oral Clinical Abuse Potential Study

In an oral, single-center, randomized, double-blind, active- and placebo-controlled, 7-period, crossover, human abuse potential study, 71 recreational opioid users were randomized into the Treatment Phase; 62 subjects completed the study. Treatment arms included APADAZ (4, 8, and 12 tablets, each containing 6.12 mg benzhydrocodone and 325 mg acetaminophen), hydrocodone/acetaminophen (4, 8 and 12 tablets, each containing 4.54 mg hydrocodone and 325 mg acetaminophen), and placebo. The respective dosage strengths for APADAZ and hydrocodone/acetaminophen contained equimolar amounts of hydrocodone. The rate (Cmax) and extent (AUClast, AUCinf) of hydrocodone exposure following APADAZ administration was comparable to that for hydrocodone/acetaminophen across all 3 dosage strengths. There were no statistically significant differences nor any clinically meaningful differences between APADAZ and the hydrocodone/acetaminophen control for the pre-specified primary endpoint of maximal score (Emax) for Drug Liking VAS or secondary endpoints of Emax for High VAS and Take Drug Again VAS. The results do not support a finding that APADAZ can be expected to deter abuse by the oral route of administration.

Intranasal Clinical Abuse Potential Study

In an intranasal single-center, randomized, double-blind, double-dummy, two-part human abuse potential study, 46 recreational opioid users were randomized into the Treatment Phase; 42

subjects completed the study. Five treatment arms included intranasal crushed and oral APADAZ (2 tablets, each containing 6.12 mg benzhydrocodone and 325 mg acetaminophen), intranasal crushed and oral hydrocodone/acetaminophen (2 tablets, each containing 4.54 mg hydrocodone and 325 mg acetaminophen), and intranasal placebo powder. The respective dosage strengths for APADAZ and hydrocodone/acetaminophen contained equimolar amounts of hydrocodone.

The pharmacokinetic data showed that overall (AUClast, AUCinf, and Cmax) hydrocodone exposure was comparable between intranasal crushed APADAZ and intranasal crushed hydrocodone/acetaminophen. These treatments were also comparable with cumulative hydrocodone exposure at the timepoints of 4, 8, and 24 hours (AUC0-4, AUC0-8, AUC0-24). Over the first 2 hours post-dosing (AUC0-0.5, AUC0-1, and AUC0-2), the cumulative hydrocodone exposure was lower following intranasal APADAZ compared to intranasal hydrocodone/ acetaminophen.

There were numerically small but not statistically significant differences between APADAZ and the hydrocodone/acetaminophen control observed for the pre-specified primary endpoint, maximum effect on Drug Liking VAS (Emax), and the secondary endpoints of Emax for High VAS and Take Drug Again VAS.

Table 2: Summary Statistics of Maximum Scores (Emax) on Drug Liking, High and Take Drug Again, Following Intranasal Administration of Apadaz, Hydrocodone/APAP, and Placebo

VAS Scale (100 point) *intranasal* (n=42)	Apadaz Crushed	Hydrocodone/APAP Crushed	Placebo
Drug Liking *			
Mean (SE)	75.9 (2.3)	79.0 (2.7)	53.0 (1.2)
Median (Range)	74.0 (50-100)	80.0 (50-100)	51.0 (50-85)
High**			
Mean (SE)	61.8 (4.6)	59.1 (5.1)	8.8 (3.8)
Median (Range)	68.5 (0-100)	67.5 (0-100)	0.0 (0-100)
Take Drug Again*			
Mean (SE)	69.5 (3.9)	74.5 (3.9)	48.2 (2.2)
Median (Range)	68.0 (0-100)	81.5 (0-100)	50.0 (0-100)

*Bipolar scale (0=maximum negative response, 50=neutral response, 100=maximum positive response)
** Unipolar scale (0=maximum negative response, 100=maximum positive response)

Additional secondary analyses of Drug Liking based on area under the effect curve analyses (AUE) for the first half hour, hour, and 2 hours post-dosing, demonstrated numerically small differences between intranasal APADAZ and intranasal hydrocodone/acetaminophen. However, there were no differences between these two treatments with respect to the cumulative High experienced over the first 2 hours post-dosing using similar AUE analyses. There are no data to support that small differences in the early Drug Liking experience over the first 2 hours are clinically relevant findings consistent with possible abuse-deterrent effects, particularly in the

setting of the Emax analyses for Drug Liking, Take Drug Again, and High that do not support a deterrent effect. Based on the overall results, APADAZ cannot be expected to deter abuse by the intranasal route of administration.

Summary

The in vitro studies that evaluated physical manipulation and extraction for the purpose of preparing APADAZ for abuse by the intravenous route or by smoking did not find an advantage for APADAZ over the hydrocodone/acetaminophen control.

The results of the oral and intranasal human abuse potential studies do not support a finding that APADAZ can be expected to deter abuse by the oral or nasal routes of administration.

9.3 Dependence

Both tolerance and physical dependence can develop during chronic opioid therapy. Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different rates for different effects.

Physical dependence results in withdrawal symptoms after abrupt discontinuation or a significant dosage reduction of a drug. Withdrawal also may be precipitated through the administration of drugs with opioid antagonist activity (e.g., naloxone, nalmefene), mixed agonist/antagonist analgesics (e.g., pentazocine, butorphanol, nalbuphine), or partial agonists (e.g., buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued opioid usage.

APADAZ should not be abruptly discontinued in a physically-dependent patient [*see Dosage and Administration (2.5)*]. If APADAZ is abruptly discontinued in a physically-dependent patient, a withdrawal syndrome may occur. Some or all of the following can characterize this syndrome: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs [*see Use in Specific Populations (8.1)*].

10 OVERDOSAGE

Clinical Presentation

Following an acute overdosage, toxicity may result from hydrocodone or acetaminophen.

Hydrocodone

Acute overdose with APADAZ can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted

pupils, and, in some cases, pulmonary edema, bradycardia, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations [*see Clinical Pharmacology (12.2)*].

Acetaminophen

In acute acetaminophen overdosage, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia also occur. Plasma acetaminophen levels > 300 mcg/mL at 4 hours after oral ingestion were associated with hepatic damage in 90% of patients; minimal hepatic damage is anticipated if plasma levels at 4 hours are < 150 mcg/mL or < 37.5 mcg/mL at 12 hours after ingestion. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Treatment of Overdose

A single or multiple drug overdose with hydrocodone and acetaminophen is a potentially lethal polydrug overdose, and consultation with a regional poison control center is recommended. Immediate treatment includes support of cardiorespiratory function and measures to reduce drug absorption. Oxygen, intravenous fluids, vasopressors, assisted ventilation, and other supportive measures should be employed as indicated.

Hydrocodone

In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support techniques.

The opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to hydrocodone overdose, administer an opioid antagonist. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to hydrocodone overdose.

Because the duration of opioid reversal is expected to be less than the duration of action of hydrocodone from APADAZ, carefully monitor the patient until spontaneous respiration is reliably re-established. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product’s prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be begun with care and by titration with smaller than usual doses of the antagonist.

Acetaminophen

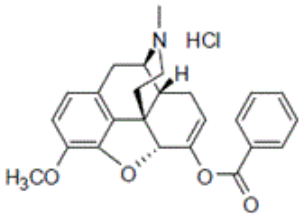
If an acetaminophen overdose is suspected, obtain a serum acetaminophen assay as soon as possible, but no sooner than 4 hours following oral ingestion. Obtain liver function studies initially and repeat at 24-hour intervals. Administer the antidote N-acetylcysteine (NAC) as early as possible. As a guide to treatment of acute ingestion, the acetaminophen level can be plotted against time since oral ingestion on a nomogram (Rumack-Matthew). The lower toxic line on the nomogram is equivalent to 150 mcg/mL at 4 hours and 37.5 mcg/mL at 12 hours. If serum level is above the lower line, administer the entire course of NAC treatment. Withhold NAC therapy if the acetaminophen level is below the lower line.

Gastric decontamination with activated charcoal should be administered just prior to N- acetylcysteine (NAC) to decrease systemic absorption if acetaminophen ingestion is known or suspected to have occurred within a few hours of presentation. Serum acetaminophen levels should be obtained immediately if the patient presents 4 hours or more after ingestion to assess potential risk of hepatotoxicity; acetaminophen levels drawn less than 4 hours post-ingestion may be misleading. To obtain the best possible outcome, NAC should be administered as soon as possible where impending or evolving liver injury is suspected. Intravenous NAC may be administered when circumstances preclude oral administration.

Vigorous supportive therapy is required in severe intoxication. Procedures to limit the continuing absorption of the drug must be readily performed since the hepatic injury is dose-dependent and occurs early in the course of intoxication.

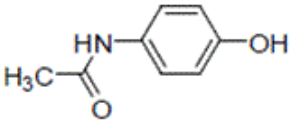
11 DESCRIPTION

APADAZ (benzhydrocodone and acetaminophen) tablet is an immediate-release, fixed-dose combination of an opioid agonist and acetaminophen. APADAZ tablets are white to off-white, capsule shaped tablets with KP201 debossed on one side and contain 6.12 mg of benzhydrocodone (equivalent to 6.67 mg benzhydrocodone hydrochloride) and 325 mg of acetaminophen for oral administration.



Benzhydrocodone hydrochloride is a prodrug of hydrocodone. It occurs as a fine white powder and is not affected by light. The chemical name is 6,7-didehydro-4,5á-epoxy-3-methoxy-17- methylmorphinan-6-yl benzoate hydrochloride. The molecular formula is C25H26ClNO4, which corresponds to a molecular weight of 439.93 g/mol. It has the following chemical structure:

Acetaminophen, 4’-hydroxyacetanilide, a slightly bitter, white, odorless, crystalline powder, is a non-opiate, non-salicylate analgesic and antipyretic. The molecular formula for acetaminophen is



C8H9NO2, which corresponds to a molecular weight of 151.16 g/mol. It has the following structural

formula:

APADAZ tablets contain 6.12 mg of benzhydrocodone (equivalent to 6.67 mg benzhydrocodone hydrochloride) and 325 mg of acetaminophen and are white to off-white in color. In addition, each tablet contains the following inactive ingredients: crospovidone, microcrystalline cellulose, pregelatinized starch, Povidone K30, and stearic acid.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Benzhydrocodone

Benzhydrocodone is a prodrug of hydrocodone.

Hydrocodone

Hydrocodone is a full opioid agonist with relative selectivity for the mu-opioid receptor, although it can interact with other opioid receptors at higher doses. The principal therapeutic action of hydrocodone is analgesia. Like all full opioid agonists, there is no ceiling effect for analgesia with hydrocodone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug.

Acetaminophen

Acetaminophen is a non-opioid, non-salicylate analgesic. The site and mechanism for the analgesic effect of acetaminophen has not been determined but is thought to primarily involve central actions.

12.2 Pharmacodynamics

Hydrocodone

Effects on the Central Nervous System

Hydrocodone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves a reduction in the responsiveness of the brain stem respiratory centers to both increases in carbon dioxide tension and electrical stimulation.

Hydrocodone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origins may produce similar findings). Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Effects on the Gastrointestinal Tract and Other Smooth Muscle

Hydrocodone causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm, resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System

Hydrocodone produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or orthostatic hypotension.

Caution must be used in hypovolemic patients, such as those suffering acute myocardial infarction, because hydrocodone may cause or further aggravate their hypotension. Caution must also be used in patients with cor pulmonale who have received therapeutic doses of opioids.

Effects on the Endocrine System

Opioids inhibit the secretion of adrenocorticotropic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans [*see Adverse Reactions (6.2)*]. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon.

Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation [*see Adverse Reactions (6.2)*].

Effects on the Immune System

Opioids have been shown to have a variety of effects on components of the immune system in in vitro and animal models. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

Concentration–Efficacy Relationships

The minimum effective analgesic concentration will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. The minimum effective analgesic concentration of hydrocodone for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome, and/or the development of analgesic tolerance [*see Dosage and Administration (2.1, 2.5)*].

Concentration–Adverse Reaction Relationships

There is a relationship between increasing hydrocodone plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions [*see Dosage and Administration (2.1, 2.2, 2.4)*].

12.3 Pharmacokinetics

APADAZ has met the bioequivalence criteria for hydrocodone AUC and Cmax to other immediate- release hydrocodone combination products. Benzhydrocodone was not detectable in plasma after oral administration in clinical studies, indicating that exposure to benzhydrocodone was minimal and transient. Steady state with APADAZ is attained within 24 to 36 hours of dosing. The systemic exposure to hydrocodone from APADAZ increases linearly after administration of single and multiple doses of 2 tablets of APADAZ.

Absorption

Single–Dose Studies

In 2 comparative bioavailability studies following oral administration of single dose to healthy subjects under fasted conditions, 6.67 mg/325 mg APADAZ tablet met the bioequivalence criteria for hydrocodone AUC and Cmax to immediate-release tablet of 7.5 mg hydrocodone/200 mg ibuprofen (N = 28); and the bioequivalence criteria for acetaminophen AUC and Cmax to immediate-release tablet of 37.5 mg tramadol/325 mg acetaminophen (N = 27)

In a comparative bioavailability study following oral administration of single dose under fasted conditions in 24 healthy subjects comparing 6.67 mg/325 mg APADAZ to immediate-release tablet of 7.5 mg hydrocodone/325 mg acetaminophen, APADAZ met the bioequivalence criteria for hydrocodone Cmax and AUC; and met the bioequivalence criteria for acetaminophen AUC, with comparable acetaminophen Cmax.

In a study to assess the effect of food on the bioavailability and pharmacokinetics of APADAZ in 38 healthy subjects, compared to fasted condition, coadministration of APADAZ with a high-fat, high-calorie meal showed a slight decrease in the rate but no change in the extent of hydrocodone absorption; and no difference in rate and extent of acetaminophen absorption. The effect of a high-fat, high-calorie meal on pharmacokinetics is similar between APADAZ and immediate- release tablet of 7.5 mg hydrocodone/325 mg acetaminophen. APADAZ can be administered without regard to food. The PK parameters for hydrocodone and acetaminophen after oral administration of APADAZ tablet, 6.67 mg/325 mg under fasted and fed conditions are shown in Table 3 below.

Table 3. PK parameters of hydrocodone and acetaminophen after oral administration of APADAZ tablet, 6.67 mg/325 mg under fasted and fed conditions.

Parameter[a]	Fed	Fasted
Hydrocodone		
Cmax (ng/mL)	16.04 ± 3.60 (40)	19.18 ± 4.84 (38)
Tmax (h)	2.50 (40) [0.50–4.00]	1.25 (38) [0.50–3.00]
AUCinf (h●ng/mL)	130.91 ± 29.45 (40)	125.73 ± 36.78 (38)
t½ (h)	4.53 ± 0.70 (40)	4.33 ± 0.67 (38)
Acetaminophen		
Cmax (“g/mL)	3.34 ± 1.01 (39)	4.05 ± 1.30 (38)
Tmax (h)	1.50 (39) [0.50–4.00]	1.00 (38) [0.50–3.00]
AUCinf (h●“g/mL)	15.0 ± 3.53 (36)	14.7 ± 3.87 (36)
t½ (h)	5.64 ± 1.58 (36)	4.78 ± 1.30 (36)

[a] Arithmetic mean ± standard deviation (N) except Tmax for which the median (N) [Range] is reported

Multiple-Dose Study

A multiple-dose study in 24 healthy subjects showed no measurable exposure to benzhydrocodone, when 2 tablets of APADAZ, 6.67 mg/325 mg, was administered orally every 4 hours for a total of 13 doses. Steady state for hydrocodone and acetaminophen was achieved after 24 hours and between 24 and 36 hours, respectively. The accumulation ratios for hydrocodone Cmax and AUC values were 1.85-fold and 2.03-fold, respectively. The accumulation ratios for acetaminophen Cmax and AUC values were 1.38-fold and 1.80-fold, respectively.

Elimination

Hydrocodone is eliminated primarily from the kidneys. Elimination of acetaminophen is principally by liver metabolism and subsequent renal excretion of metabolites.

Metabolism

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by enzymes in the intestinal tract.

Hydrocodone exhibits a complex pattern of metabolism, including O-demethylation, N- demethylation, and 6-keto reduction to the corresponding 6-á-and 6-®-hydroxy metabolites. Hydromorphone, a potent opioid, is formed from the O-demethylation of hydrocodone and contributes to the total analgesic effect of hydrocodone. The O- and N- demethylation processes are mediated by separate P-450 isoenzymes: CYP2D6 and CYP3A4, respectively. [*see Drug Interactions (7)*].

Acetaminophen is primarily metabolized in the liver by first-order kinetics and involves three principal separate pathways:

a) conjugation with glucuronide;

b) conjugation with sulfate; and

c) oxidation via the cytochrome, P450-dependent, mixed-function oxidase enzyme pathway to form a reactive intermediate metabolite, which conjugates with glutathione and is then further metabolized to form cysteine and mercapturic acid conjugates. The principal cytochrome P450 isoenzyme involved appears to be CYP2E1, with CYP1A2 and CYP3A4 as additional pathways.

In adults, the majority of acetaminophen is conjugated with glucuronic acid and, to a lesser extent, with sulfate. These glucuronide-, sulfate-, and glutathione-derived metabolites lack biologic activity. In premature infants, newborns, and young infants, the sulfate conjugate predominates.

Excretion

Hydrocodone and its metabolites are eliminated primarily in the kidneys, with a mean plasma half- life of 4.5 hours.

The half-life of acetaminophen is about 2 to 3 hours in adults. It is somewhat shorter in children and somewhat longer in neonates and in cirrhotic patients. Acetaminophen is eliminated from the body primarily by formation of glucuronide and sulfate conjugates in a dose-dependent manner. Less than 9% of acetaminophen is excreted unchanged in the urine.

Specific Populations

Age

For hydrocodone, no significant pharmacokinetic differences based on age have been demonstrated. For APAP, a population pharmacokinetic analysis of data obtained from a clinical trial in patients with chronic pain treated with immediate-release tablet of 7.5 mg hydrocodone/325 mg acetaminophen, which included 55 patients between 65 and 75 years of age and 19 patients over 75 years of age, showed no significant changes in the pharmacokinetics of acetaminophen in elderly patients with normal renal and hepatic function [*see Use in Specific Populations (8.5)*].

Sex

For hydrocodone, no significant pharmacokinetic differences based on gender have been demonstrated.

Renal Impairment

The effect of renal insufficiency on the pharmacokinetics of APADAZ has not been determined [*see Use in Specific Populations (8.7)*].

Hepatic Impairment

Because acetaminophen is extensively metabolized by the liver, the use of APADAZ in patients with severe hepatic impairment or severe active liver disease is contraindicated. The pharmacokinetics and tolerability of APADAZ in patients with impaired hepatic function have not been studied [*see Contraindications (4), Use in Specific Populations (8.6)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies to evaluate the carcinogenic potential of benzhydrocodone or the combination of benzhydrocodone and acetaminophen have not been conducted.

Long-term studies in mice and rats have been completed by the National Toxicology Program to evaluate the carcinogenic potential of acetaminophen. In 2-year feeding studies, F344/N rats and B6C3F1 mice were fed a diet containing acetaminophen up to 6000 ppm. Female rats demonstrated equivocal evidence of carcinogenic activity based on increased incidences of mononuclear cell leukemia at 0.8 times the maximum human daily dose (MHDD) of 3.9 grams/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats (0.7 times) or mice (1.3-1.5 times the MHDD, based on a body surface area comparison).

Mutagenesis

Benzhydrocodone was positive in an in vitro mammalian cell chromosome aberration assay in the presence of a metabolic activation (S9 mix) and negative in the absence of metabolic activation. Benzhydrocodone was negative in an in vitro bacterial mutation assay as well as in the in vivo rat micronucleus and comet assays.

Acetaminophen was not mutagenic in the bacterial reverse mutation assay (Ames test). In contrast, acetaminophen tested positive in the in vitro mouse lymphoma assay and the in vitro chromosomal aberration assay using human lymphocytes. In the published literature, acetaminophen has been reported to be clastogenic when administered at 1500 mg/kg/day to the rat model (3.7-times the MHDD, based on a body surface area comparison). In contrast, no clastogenicity was noted at a dose of 750 mg/kg/day (1.9-times the MHDD, based on a body surface area comparison), suggesting a threshold effect.

Impairment of Fertility

No nonclinical fertility studies have been conducted with benzhydrocodone or the combination of benzhydrocodone and acetaminophen.

In studies conducted by the National Toxicology Program, fertility assessments with acetaminophen have been completed in Swiss CD-1 mice via a continuous breeding study. There were no effects on fertility parameters in mice consuming up to 1.8 times the MHDD of acetaminophen, based on a body surface area comparison. Although there was no effect on sperm motility or sperm density in the epididymis, there was a significant increase in the percentage of abnormal sperm in mice consuming 1.8 times the MHDD (based on a body surface comparison) and there was a reduction in the number of mating pairs producing a fifth litter at this dose, suggesting the potential for cumulative toxicity with chronic administration of acetaminophen near the upper limit of daily dosing.

Published studies in rodents report that oral acetaminophen treatment of male animals at doses that are 1.2 times the MHDD and greater (based on a body surface comparison) result in decreased testicular weights, reduced spermatogenesis, reduced fertility, and reduced implantation sites in females given the same doses. These effects appear to increase with the duration of treatment.

In a published mouse study, oral administration of 50 mg/kg acetaminophen to pregnant mice from Gestation Day 7 to delivery (0.06 times the MHDD) reduced the number of primordial follicles in female offspring and reduced the percentage of full term pregnancies and number of pups born to these females exposed to acetaminophen in utero.

In a published study, pregnant rats oral administration of 350 mg/kg acetaminophen (0.9 times the MHDD) from Gestation Day 13 to 21 (dams), reduced the number of germ cells in the fetal ovary and decreased ovary weight and reduced number of pups per litter in F1 females as well as reduced ovary weights in F2 females.

16 HOW SUPPLIED/STORAGE AND HANDLING

APADAZ (benzhydrocodone and acetaminophen) is a capsule-shaped white tablet debossed with “KP201” on one side. Each tablet contains 6.12 mg benzhydrocodone and 325 mg acetaminophen.

The tablets are supplied as:

NDC 70040-0167-1: Bottles of 100 Tablets

NDC 70040-0167-3: Blister Wallet Pack of 18 Tablets

Flush expired or unused APADAZ tablets that are no longer needed down the toilet or contact the Drug Enforcement Agency (DEA) to find the location of an authorized collector (1-800-882-9539).

Storage

Store at 20°C to 25°C (68°F to 77°F). Excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Important Administration Instructions

Instruct patients how to properly take APADAZ [*see Dosage and Administration (2), Warnings and Precautions (5)*].

- Do not take more than 4,000 milligrams of acetaminophen per day. Call your doctor if you took more than the recommended dose.
- Use APADAZ exactly as prescribed to reduce the risk of life-threatening adverse reactions (e.g., respiratory depression)
- Do not discontinue APADAZ without first discussing the need for a tapering regimen with your doctor.

Addiction, Abuse, and Misuse

Inform patients that the use of APADAZ, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death [*see Warnings and Precautions (5.1)*]. Instruct patients not to share APADAZ with others and to take steps to protect APADAZ from theft or misuse.

Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting APADAZ or when the dosage is increased, and that it can occur even at recommended dosages [*see Warnings and Precautions (5.2)*]. Advise patients how to recognize respiratory depression and to seek medical attention if breathing difficulties develop.

Accidental Ingestion

Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death [*see Warnings and Precautions (5.2)*]. Instruct patients to take steps to store APADAZ securely and to dispose of unused APADAZ by flushing the tablets down the toilet.

Maximum Daily Acetaminophen Use

Advise patients not to take more than 4,000 milligrams of acetaminophen per day and call their doctor if they have taken more than the recommended dose. Advise patients not to take APADAZ in combination with other tramadol or acetaminophen-containing products, including over-the- counter preparations (*see Warnings and Precautions (5.5)*].

Interactions with Benzodiazepines and Other CNS Depressants

Inform patients that potentially fatal additive effects may occur if APADAZ is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these unless supervised by a healthcare provider [*see Warnings and Precautions (5.6), Drug Interactions (7)*].

Serotonin Syndrome

Inform patients that opioids could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their healthcare providers if they are taking, or plan to take serotonergic medications. [*see Drug Interactions (7)*].

MAOI Interaction

Inform patients to avoid taking APADAZ while using any drugs that inhibit monoamine oxidase. Patients should not start MAOIs while taking APADAZ [*see Drug Interactions (7)*].

Adrenal Insufficiency

Inform patients that opioids could cause adrenal insufficiency, a potentially life-threatening condition. Adrenal insufficiency may present with non-specific symptoms and signs such as nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. Advise patients to seek medical attention if they experience a constellation of these symptoms [*see Warnings and Precautions (5.8)*].

Hypotension

Inform patients that APADAZ may cause orthostatic hypotension and syncope. Instruct patients how to recognize symptoms of low blood pressure and how to reduce the risk of serious consequences should hypotension occur (e.g., sit or lie down, carefully rise from a sitting or lying position) [*see Warnings and Precautions (5.9)*].

Serious Skin Reactions

Advise patients to stop APADAZ immediately if they develop any type of rash and to contact their healthcare provider as soon as possible [*see Warnings and Precautions (5.10)*].

Anaphylaxis

Inform patients that anaphylaxis have been reported with ingredients contained in APADAZ. Advise patients how to recognize such a reaction and when to seek medical attention [*see Contraindications (4), Warnings and Precautions (5.12), Adverse Reactions (6)*].

Pregnancy

Neonatal Opioid Withdrawal Syndrome

Inform female patients of reproductive potential that prolonged use of APADAZ during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated [*see Warnings and Precautions (5.3), Use in Specific Populations (8.1)*].

Embryo-Fetal Toxicity

Inform female patients of reproductive potential that APADAZ can cause fetal harm and to inform their healthcare provider of a known or suspected pregnancy [*see Use in Specific Populations (8.1*)].

Lactation

Advise nursing mothers to monitor infants for increased sleepiness (more than usual), breathing difficulties, or limpness. Instruct nursing mothers to seek immediate medical care if they notice

these signs [*see Use in Specific Populations (8.2)*].

Infertility

Inform patients that chronic use of opioids may cause reduced fertility. It is not known whether these effects on fertility are reversible [*see Use in Specific Populations (8.3)*].

Driving or Operating Heavy Machinery

Inform patients that APADAZ may impair the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication [*see Warnings and Precautions (5.16)*].

Constipation

Advise patients of the potential for severe constipation, including management instructions and when to seek medical attention [*see Adverse Reactions (6)*].

Disposal of Unused APADAZ

Advise patients to flush the unused tablets down the toilet when APADAZ is no longer needed or to contact the Drug Enforcement Agency (DEA) to find the location of an authorized collector (1-800-882-9539).

Manufactured for:
KemPharm, Inc.
2500 Crosspark Road
Coralville, IA 52241

PI-0167-01 R.02/18

Exhibit D
[*]

Exhibit E
Example Net Profit Share Computation

[*]

Exhibit 10.29

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

THIS WARRANT AND THE UNDERLYING SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"). THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT AS TO SUCH SECURITIES UNDER THE ACT OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED.

KEMPHARM, INC.

WARRANT TO PURCHASE COMMON STOCK

No. CS-1 **October 25, 2018**

Void After October 24, 2023

THIS CERTIFIES THAT, FOR VALUE RECEIVED, **KVK TECH, INC.** (OR ITS PERMITTED ASSIGNS, THE "***HOLDER***"), IS ENTITLED TO SUBSCRIBE FOR AND PURCHASE AT THE EXERCISE PRICE (AS DEFINED BELOW) FROM **KEMPHARM, INC.**, A DELAWARE CORPORATION, A DELAWARE CORPORATION (THE "***COMPANY***"), UP TO THE EXERCISE NUMBER (AS DEFINED BELOW) OF SHARES OF COMMON STOCK OF THE COMPANY (THE "***COMMON STOCK***") ON THE TERMS AND SUBJECT TO THE CONDITIONS SET FORTH BELOW.

This warrant (this "***Warrant***") is being issued pursuant in connection with the License Agreement (as defined below).

The number of shares of Common Stock that the Holder may purchase by exercising this Warrant is the Exercise Number, subject to adjustment pursuant to the terms herein, including but not limited to adjustment pursuant to Section 5 below.

1. DEFINITIONS. AS USED HEREIN, THE FOLLOWING TERMS SHALL HAVE THE FOLLOWING RESPECTIVE MEANINGS:

(a) "***Exercise Number***" shall initially mean zero shares of Common Stock. The Exercise Number shall (i) increase by 125,000 shares of Common Stock on the first date when Net Sales (as defined in the License Agreement) under the License Agreement is equal to or greater than [*] in a Rolling Year (as defined in the License Agreement); (ii) increase by 125,000 shares of Common Stock on the first date when Net Sales (as defined in the License Agreement) under the License Agreement is equal to or greater than [*] in a Rolling Year (as defined in the License Agreement); (iii) increase by 125,000 shares of Common Stock on the first date when Net Sales (as defined in the License Agreement) under the License Agreement is equal to or greater than [*] in a Rolling Year (as defined in the License Agreement); and (iv) increase by 125,000 shares of Common Stock on the first date when Net Sales (as defined in the License Agreement) under the License Agreement is equal to or greater than [*] in a Rolling Year (as defined in the License Agreement). The achievement of any milestone under the terms of this Warrant shall be determined in accordance with the terms of the License Agreement in the sole discretion of the Company's board of directors. Notwithstanding anything herein to the contrary, the Exercise Number shall increase only once for each milestone described in clauses (i) through (iv) of this definition and the aggregate number of shares of Common Stock issuable under this Warrant shall not be greater than 500,000 shares, subject to adjustment described herein.

(b) "***Exercise Period***" shall mean the period commencing with October 25, 2018 and ending upon the earlier to occur of (i) five (5) years from the date hereof; or (ii) the date that is 60 days following the termination of the License Agreement, unless sooner terminated as provided below.

(c) "***Exercise Price***" shall mean $2.30 per share, subject to adjustment pursuant to the terms herein, including but not limited to adjustment pursuant to Section 5 below.

(d) "***Exercise Shares***" shall mean the shares of the Common Stock issuable upon exercise of the Warrant, subject to adjustment pursuant to the terms herein, including but not limited to adjustment pursuant to Section 5 below.

(e) "***License Agreement***" shall mean that certain collaboration and license agreement, dated as of October 25, 2018, by and between the Company and the Holder, as the same may be amended and restated from time to time.

2. Exercise of Warrant. The rights represented by the Warrant may be exercised in whole or in part at any time during the Exercise Period, by delivery of the following to the Company at its address set forth above (or at such other address as it may designate by notice in writing to the Holder):

(a) An executed Notice of Exercise in the form attached hereto;

(b) Payment of the Exercise Price in cash or by check; and

(c) The Warrant.

Upon the exercise of the rights represented by the Warrant, a certificate or certificates for or evidence of book entry of the Exercise Shares so purchased, registered in the name of the Holder or persons affiliated with the Holder, if the Holder so designates, shall be issued and delivered to the Holder within a reasonable time after the rights represented by the Warrant shall have been so exercised.

The person in whose name any certificate or certificates for Exercise Shares are to be issued upon exercise of the Warrant shall be deemed to have become the holder of record of such shares on the date on which the Warrant was surrendered and payment of the Exercise Price was made, irrespective of the date of delivery of such certificate or certificates, except that, if the date of such surrender and payment is a date when the stock transfer books of the Company are closed, such person shall be deemed to have become the holder of such shares at the close of business on the next succeeding date on which the stock transfer books are open.

2.1 Net Exercise. Notwithstanding any provisions herein to the contrary, if the fair market value of one share of the Common Stock is greater than the Exercise Price (at the date of calculation as set forth below), in lieu of exercising the Warrant by payment of cash, the Holder may elect to receive shares equal to the value (as determined below) of the Warrant (or the portion thereof being canceled) by surrender of the Warrant at the principal office of the Company together with the properly endorsed Notice of Exercise in which event the Company shall issue to the Holder a number of shares of Common Stock computed using the following formula:

$$X = \frac{Y\,(A-B)}{A}$$

Where X = the number of shares of Common Stock to be issued to the Holder

Y = the number of shares of Common Stock purchasable under the Warrant or, if only a portion of the Warrant is being exercised, the portion of the Warrant being canceled (at the date of such calculation)

A = the fair market value of one share of the Common Stock (at the date of such calculation)

B = Exercise Price (as adjusted to the date of such calculation)

For purposes of the above calculation, the fair market value of one share of Common Stock shall equal the closing sale price of the Common Stock on the Nasdaq Stock Market, or such exchange upon which the Company's Common Stock is sold, on (i), if the date of exercise of the Warrant is a trading day on such market, the date of exercise; or (ii) if the date of exercise of the Warrant is not a trading day on such market, the last trading day prior to such exercise. If the Company's Common Stock is not sold on any such exchange, then the fair market value shall be determined by the Company's Board of Directors in good faith.

3. Covenants of the Company.

3.1 Covenants as to Exercise Shares. The Company covenants and agrees that all Exercise Shares that may be issued upon the exercise of the rights represented by the Warrant will, upon issuance, be validly issued and outstanding, fully paid and nonassessable, and free from all taxes, liens and charges with respect to the issuance thereof. The Company further covenants and agrees that the Company will at all times during the Exercise Period, have authorized and reserved, free from preemptive rights, a sufficient number of shares of its Common Stock to provide for the exercise of the rights represented by the Warrant. If at any time during the Exercise Period the number of authorized but unissued shares of Common Stock shall not be sufficient to permit exercise of the Warrant, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes.

3.2 Notices of Record Date. In the event of any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend (other than a cash dividend which is the same as cash dividends paid in previous quarters) or other distribution, the Company shall mail to the Holder, at least ten (10) days prior to the date specified herein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend or distribution.

4. REPRESENTATIONS OF HOLDER.

4.1 Satisfaction of Obligations. The Holder represents and warrants that the Company's issuance of the Warrant to the Holder satisfies in full any and all obligations of the Company to issue to the Holder any equity securities prior to and as of the date hereof, whether in connection with the0 License Agreement or otherwise, and that this Warrant represents in full any and all equity securities of the Company to which the Holder is, or may be, entitled to receive pursuant to or in connection with the License Agreement or any other arrangement with the Company as of the date hereof.

4.2 Acquisition of Warrant for Personal Account. The Holder represents and warrants that it is acquiring the Warrant and the Exercise Shares solely for its account for investment and not with a view to or for sale or distribution of said Warrant or Exercise Shares or any part thereof. The Holder also represents that the entire legal and beneficial interests of the Warrant and Exercise Shares the Holder is acquiring is being acquired for, and will be held for, its account only.

4.3 Securities Are Not Registered.

(a) The Holder understands that the Warrant and the Exercise Shares have not been registered under the Securities Act of 1933, as amended (the "***Act***") on the basis that no distribution or public offering of the stock of the Company is to be effected. The Holder realizes that the basis for the exemption may not be present if, notwithstanding its representations, the Holder has a present intention of acquiring the securities for a fixed or determinable period in the future, selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the securities. The Holder has no such present intention.

(b) The Holder recognizes that the Warrant and the Exercise Shares must be held indefinitely unless they are subsequently registered under the Act or an exemption from such registration is available. The Holder recognizes that the Company has no obligation to register the Warrant or the Exercise Shares of the Company, or to comply with any exemption from such registration.

(c) The Holder is aware that neither the Warrant nor the Exercise Shares may be sold pursuant to Rule 144 adopted under the Act unless certain conditions are met, including, among other things, the existence of a public market for the shares, the availability of certain current public information about the Company, the resale following the required holding period under Rule 144 and the number of shares being sold during any three month period not exceeding specified limitations.

(d) The Holder hereby represents and warrants that it constitutes an accredited investor, as such term is defined under Regulation D promulgated under the Act.

4.4 Disposition of Warrant and Exercise Shares.

(a) The Holder further agrees not to make any disposition of all or any part of the Warrant or Exercise Shares in any event unless and until:

(i) [Intentionally omitted.]

(ii) There is then in effect a registration statement under the Act covering such proposed disposition and such disposition is made in accordance with said registration statement; or

(iii) The Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and if reasonably requested by the Company, the Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, for the Holder to the effect that such disposition will not require registration of such Warrant or Exercise Shares under the Act or any applicable state securities laws.

(b) The Holder understands and agrees that all certificates evidencing the shares to be issued to the Holder may bear the following legend:

> THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933 (THE "***ACT***") AND MAY NOT BE OFFERED, SOLD OR OTHERWISE TRANSFERRED, ASSIGNED, PLEDGED OR HYPOTHECATED UNLESS AND UNTIL REGISTERED UNDER THE ACT OR UNLESS THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY AND ITS COUNSEL THAT SUCH REGISTRATION IS NOT REQUIRED.

5. Adjustment of Exercise Price. In the event of changes in the outstanding Common Stock by reason of stock dividends, split-ups, recapitalizations, reclassifications, combinations or exchanges of shares, separations, reorganizations, liquidations, or the like, the number and class of shares available under the Warrant in the aggregate and the Exercise Price shall be correspondingly adjusted to give the Holder of the Warrant, on exercise for the same aggregate Exercise Price, the total number, class, and kind of shares as the Holder would have owned had the Warrant been exercised prior to the event and had the Holder continued to hold such shares until after the event requiring adjustment; *provided*, *however*, that such adjustment shall not be made with respect to, and the Warrant shall terminate if not exercised prior to, the events set forth in Section 7 below. The form of the Warrant need not be changed because of any adjustment in the number of Exercise Shares subject to the Warrant.

6. Fractional Shares. No fractional shares shall be issued upon the exercise of the Warrant as a consequence of any adjustment pursuant hereto. All Exercise Shares (including fractions) issuable upon exercise of the Warrant may be aggregated for purposes of determining whether the exercise would result in the issuance of any fractional share. If, after aggregation, the exercise would result in the issuance of a fractional share, the Company shall, in lieu of issuance of any fractional share, pay the Holder otherwise entitled to such fraction a sum in cash equal to the product resulting from multiplying the then current fair market value of an Exercise Share by such fraction.

7. Early Termination. In the event of, at any time during the Exercise Period the Company effects any capital reorganization, or any reclassification of the capital stock of the Company (other than a change in par value or from par value to no par value or no par value to par value or as a result of a stock dividend or subdivision, split-up or combination of shares), or the consolidation or merger of the Company with or into another corporation (other than a merger solely to effect a reincorporation of the Company into another state), the sale (whether by tender offer or otherwise) of a majority of the then outstanding shares of capital stock of the Company by its stockholders to a single entity, or group of affiliated entities, or the sale or other disposition of all or substantially all the properties and assets of the Company in its entirety to any other person (any such transaction, a "***Corporate Transaction***"), the Company shall provide to the Holder written notice of such Corporate Transaction at the same time that the Company's provides notice of such Corporate Transaction to the holders of its Common Stock, and the Warrant shall terminate unless exercised prior to the occurrence of such Corporate Transaction.

8. Reserved.

9. No Stockholder Rights. The Warrant in and of itself shall not entitle the Holder to any voting rights or other rights as a stockholder of the Company.

10. Transfer of Warrant. Subject to applicable laws and the restriction on transfer set forth on the first page of the Warrant, the Warrant and all rights hereunder are transferable, by the Holder in person or by duly authorized attorney, upon delivery of the Warrant and the form of assignment attached hereto to any transferee designated by Holder. The transferee shall sign an investment letter in form and substance satisfactory to the Company.

11. Lost, Stolen, Mutilated or Destroyed Warrant. If the Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as the Warrant so lost, stolen, mutilated or destroyed. Any such new Warrant shall constitute an original contractual obligation of the Company, whether or not the allegedly lost, stolen, mutilated or destroyed Warrant shall be at any time enforceable by anyone.

12. Notices, etc. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed email or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications in connection with this Warrant and each other warrant previously issued by the Company to the Holder shall be sent to the Company at its Corporate headquarters and to Holder at the address set forth on the signature page hereto or at such other address as the Company or Holder may designate by ten (10) days advance written notice to the other.

13. Governing Law. The Warrant and all rights, obligations and liabilities hereunder shall be governed by the laws of the State of Delaware.

[signature page follows]

In Witness Whereof, the Company and the Holder have caused the Warrant to be executed as of October 25, 2018.

KemPharm, Inc.

By: /s/ R. LaDuane Clifton

Name: R. LaDuane Clifton

Title: Chief Financial Officer, Secretary and Treasurer

Holder:

KVK Tech, Inc.

Signature: /s/ Anthony P. Tabasso

Printed name: Anthony P. Tabasso

Title: Chief Executive Officer and General Counsel

Address: KVK Tech, Inc.
110 Terry Drive
Newtown, PA 18940
Attn: Anthony P. Tabasso, CEO

NOTICE OF EXERCISE

TO: KEMPHARM, INC.

(1) ☐ The undersigned hereby elects to purchase _____ shares of the Common Stock of **KemPharm, Inc.** (the "***Company***") pursuant to the terms of the attached Warrant, and tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any.

☐ The undersigned hereby elects to purchase _____ shares of the Common Stock of **KemPharm, Inc.** (the "***Company***") pursuant to the terms of the net exercise provisions set forth in Section 2.1 of the attached Warrant, and shall tender payment of all applicable transfer taxes, if any.

(2) Please register said shares of Common Stock in the name of the undersigned or in such other name as is specified below:

_____
(Name)

_____
_____
(Address)

(3) By executing below, the undersigned hereby represents, warrants and covenants, as provided in Section 4 of the Warrant, effective as of the date hereof, which Section 4 is incorporated herein by reference.

_____ _____
(Date) (Signature)

_____
(Print name)

ASSIGNMENT FORM

(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, THE FOREGOING WARRANT AND ALL RIGHTS EVIDENCED THEREBY ARE HEREBY ASSIGNED TO

Name: _____
(Please Print)

Address: _____
(Please Print)

Dated: _____, 20__

Holder's
Signature: _____

Holder's
Address: _____

NOTE: The signature to this Assignment Form must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Exhibit 10.30

PURCHASE AGREEMENT

THIS PURCHASE AGREEMENT (the "Agreement"), dated as of February 28, 2019 (the "Execution Date"), is entered into by and between **KEMPHARM, INC.**, a Delaware corporation (the "Company"), and **LINCOLN PARK CAPITAL FUND, LLC**, an Illinois limited liability company (the "Investor"). Capitalized terms used herein and not otherwise defined herein are defined in Section 1 hereof.

WHEREAS:

Subject to the terms and conditions set forth in this Agreement, the Company wishes to sell to the Investor, and the Investor wishes to buy from the Company, up to Fifteen Million Dollars ($15,000,000) (the "Commitment Amount") of the Company's common stock, par value $0.0001 per share (the "Common Stock"). The shares of Common Stock to be purchased hereunder are referred to herein as the "Purchase Shares".

NOW THEREFORE, in consideration of the mutual covenants contained in this Agreement, and for other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Company and the Investor hereby agree as follows:

1. CERTAIN DEFINITIONS.

For purposes of this Agreement, the following terms shall have the following meanings:

(a) "Accelerated Purchase Date" means, with respect to any Accelerated Purchase (as defined below) made pursuant to Section 2(b) hereof, the Business Day immediately following the applicable Purchase Date with respect to the corresponding Regular Purchase referred to in clause (i) of the second sentence of Section 2(a) hereof.

(b) "Accelerated Purchase Floor Price" means $1.50, which shall be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction and, effective upon the consummation of any such reorganization, recapitalization, non-cash dividend, stock split or other similar transaction, the Accelerated Purchase Floor Price shall mean the lower of (i) the adjusted price and (ii) $1.00.

(c) "Accelerated Purchase Minimum Price Threshold" means, with respect to any Accelerated Purchase made pursuant to Section 2(b) hereof, any minimum per share price threshold set forth in the applicable Accelerated Purchase Notice.

(d) "Accelerated Purchase Notice" means, with respect to an Accelerated Purchase made pursuant to Section 2(b) hereof, an irrevocable written notice from the Company to the Investor directing the Investor to purchase the applicable Accelerated Purchase Share Amount at the Accelerated Purchase Price on the Accelerated Purchase Date for such Accelerated Purchase in accordance with this Agreement, and specifying any Accelerated Purchase Minimum Price Threshold determined by the Company.

(e) "Accelerated Purchase Price" means, with respect to an Accelerated Purchase made pursuant to Section 2(b) hereof, the lower of (i) ninety-seven percent (97%) of the VWAP for the period beginning at 9:30:01 a.m., Eastern time, on the applicable Accelerated Purchase Date, or such other time publicly announced by Principal Market as the official open (or commencement) of trading on the Principal Market on such applicable Accelerated Purchase Date (the "Accelerated Purchase Commencement Time"), and ending at the earliest of (A) 4:00:00 p.m., Eastern time, on such applicable Accelerated Purchase Date, or such other time publicly announced by Principal Market as the official close of trading on the Principal Market on such applicable Accelerated Purchase Date, (B) such time, from and after the Accelerated Purchase Commencement Time for such Accelerated Purchase, that total number (or volume) of shares of Common Stock traded on the Principal Market has exceeded the applicable Accelerated Purchase Share Volume Maximum, and (C) such time, from and after the Accelerated Purchase Commencement Time for such Accelerated Purchase, that the Sale Price has fallen below the applicable Accelerated Purchase Minimum Price Threshold (such earliest of (i)(A), (i)(B) and (i)(C) above, the "Accelerated Purchase Termination Time"), and (ii) the Closing Sale Price of the Common Stock on such applicable Accelerated Purchase Date (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction).

(f) "Accelerated Purchase Share Amount" means, with respect to an Accelerated Purchase made pursuant to Section 2(b) hereof, the number of Purchase Shares directed by the Company to be purchased by the Investor in an Accelerated Purchase Notice, which number of Purchase Shares shall not exceed the lesser of (i) 300% of the number of Purchase Shares directed by the Company to be purchased by the Investor pursuant to the corresponding Regular Purchase Notice for the corresponding Regular Purchase referred to in clause (i) of the second sentence of Section 2(b) hereof (subject to the Purchase Share limitations contained in Section 2(b) hereof) and (ii) an amount equal to (A) the Accelerated Purchase Share Percentage multiplied by (B) the total number (or volume) of shares of Common Stock traded on the Principal Market during the period on the applicable Accelerated Purchase Date beginning at the Accelerated Purchase Commencement Time for such Accelerated Purchase and ending at the Accelerated Purchase Termination Time for such Accelerated Purchase.

(g) "Accelerated Purchase Share Percentage" means, with respect to an Accelerated Purchase made pursuant to Section 2(b) hereof, thirty percent (30%).

(h) "Accelerated Purchase Share Volume Maximum" means, with respect to an Accelerated Purchase made pursuant to Section 2(b) hereof, a number of shares of Common Stock equal to (i) the applicable Accelerated Purchase Share Amount to be purchased by the Investor pursuant to the applicable Accelerated Purchase Notice for such Accelerated Purchase, divided by (ii) the Accelerated Purchase Share Percentage (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction).

(i) "Additional Accelerated Purchase Date" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, the Business Day (i) that is the Accelerated Purchase Date with respect to the corresponding Accelerated Purchase referred to in Section 2(b) hereof and (ii) on which the Investor receives, prior to 1:00 p.m., Eastern time, on such Business Day, a valid Additional Accelerated Purchase Notice for such Additional Accelerated Purchase in accordance with this Agreement.

(j) "Additional Accelerated Purchase Floor Price" means $1.50, which shall be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction and, effective upon the consummation of any such reorganization, recapitalization, non-cash dividend, stock split or other similar transaction, the Additional Accelerated Purchase Floor Price shall mean the lower of (i) the adjusted price and (ii) $1.00.

(k) "Additional Accelerated Purchase Minimum Price Threshold" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, any minimum per share price threshold set forth in the applicable Additional Accelerated Purchase Notice.

(l) "Additional Accelerated Purchase Notice" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, an irrevocable written notice from the Company to the Investor directing the Investor to purchase the applicable Additional Accelerated Purchase Share Amount at the Additional Accelerated Purchase Price for such Additional Accelerated Purchase in accordance with this Agreement.

(m) "Additional Accelerated Purchase Price" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(b) hereof, the lower of (i) ninety-seven percent (97%) of the VWAP for the period on the applicable Additional Accelerated Purchase Date, beginning at the latest of (A) the applicable Accelerated Purchase Termination Time with respect to the corresponding Accelerated Purchase referred to in Section 2(b) hereof on such Additional Accelerated Purchase Date, (B) the applicable Additional Accelerated Purchase Termination Time with respect to the most recently completed prior Additional Accelerated Purchase on such Additional Accelerated Purchase Date, as applicable, and (C) the time at which all Purchase Shares subject to all prior Accelerated Purchases and Additional Accelerated Purchases (as applicable), including, without limitation, those that have been effected on the same Business Day as the applicable Additional Accelerated Purchase Date with respect to which the applicable Additional Accelerated Purchase relates, have theretofore been received by the Investor as DWAC Shares in accordance with this Agreement (such latest of (i)(A), (i)(B) and (i)(C) above, the "Additional Accelerated Purchase Commencement Time"), and ending at the earliest of (X) 4:00 p.m., Eastern time, on such Additional Accelerated Purchase Date, or such other time publicly announced by Principal Market as the official close of trading on the Principal Market on such Additional Accelerated Purchase Date, (Y) such time, from and after the Additional Accelerated Purchase Commencement Time for such Additional Accelerated Purchase, that total number (or volume) of shares of Common Stock traded on the Principal Market has exceeded the applicable Additional Accelerated Purchase Share Volume Maximum, and (Z) such time, from and after the Additional Accelerated Purchase Commencement Time for such Additional Accelerated Purchase, that the Sale Price has fallen below the applicable Additional Accelerated Purchase Minimum Price Threshold (if any) (such earliest of (i)(X), (i)(Y) and (i)(Z) above, the "Additional Accelerated Purchase Termination Time"), and (ii) the Closing Sale Price of the Common Stock on such Additional Accelerated Purchase Date (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction).

(n) "Additional Accelerated Purchase Share Amount" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, the number of Purchase Shares directed by the Company to be purchased by the Investor on an Additional Accelerated Purchase Notice, which number of Purchase Shares shall not exceed the lesser of (i) 300% of the number of Purchase Shares directed by the Company to be purchased by the Investor pursuant to the corresponding Regular Purchase Notice for the corresponding Regular Purchase referred to in Section 2(c) hereof (subject to the Purchase Share limitations contained in Section 2(a) hereof) and (ii) an amount equal to (A) the Additional Accelerated Purchase Share Percentage multiplied by (B) the total number (or volume) of shares of Common Stock traded on the Principal Market during the period on the applicable Additional Accelerated Purchase Date beginning at the Additional Accelerated Purchase Commencement Time for such Additional Accelerated Purchase and ending at the Additional Accelerated Purchase Termination Time for such Additional Accelerated Purchase.

(o) "Additional Accelerated Purchase Share Percentage" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, thirty percent (30%).

(p) "Additional Accelerated Purchase Share Volume Maximum" means, with respect to an Additional Accelerated Purchase made pursuant to Section 2(c) hereof, a number of shares of Common Stock equal to (i) the applicable Additional Accelerated Purchase Share Amount properly directed by the Company to be purchased by the Investor in the applicable Additional Accelerated Purchase Notice for such Additional Accelerated Purchase, divided by (ii) the Additional Accelerated Purchase Share Percentage (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction)

(q) "Alternate Adjusted Regular Purchase Share Limit" means, with respect to a Regular Purchase made pursuant to Section 2(a) hereof, the maximum number of Purchase Shares which, taking into account the applicable per share Purchase Price therefor calculated in accordance with this Agreement, would enable the Company to deliver to the Investor, on the applicable Purchase Date for such Regular Purchase, a Regular Purchase Notice for a Purchase Amount equal to, or as closely approximating without exceeding, One Hundred Fifty Thousand Dollars ($150,000).

(r) "Available Amount" means, initially, Fifteen Million Dollars ($15,000,000) in the aggregate, which amount shall be reduced by the Purchase Amount each time the Investor purchases Purchase Shares pursuant to Section 2 hereof.

(s) "Average Price" means a price per Purchase Share (rounded to the nearest tenth of a cent) equal to the quotient obtained by dividing (i) the aggregate gross purchase price paid by the Investor for all Purchase Shares purchased pursuant to this Agreement, by (ii) the aggregate number of Purchase Shares issued pursuant to this Agreement.

(t) "Bankruptcy Law" means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors.

(u) "Base Prospectus" means the Company's final base prospectus, dated October 3, 2016, a preliminary form of which is included in the Registration Statement, including the documents incorporated by reference therein.

(v) "Business Day" means any day on which the Principal Market is open for trading, including any day on which the Principal Market is open for trading for a period of time less than the customary time.

(w) "Common Stock Equivalents" means any securities of the Company or its Subsidiaries which entitle the holder thereof to acquire at any time Common Stock, including, without limitation, any debt, preferred stock, rights, options, warrants or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Stock.

(x) "Closing Sale Price" means, for any security as of any date, the last closing sale price for such security on the Principal Market as reported by the Principal Market.

(y) "Commencement" means the satisfaction of the conditions set forth in Sections 7 and 8 hereof.

(z) "Commencement Date" means the date on which the satisfaction of the conditions set forth in Sections 7 and 8 hereof has taken place.

(aa) "Confidential Information" means any information disclosed by either party to the other party, either directly or indirectly, in writing, orally or by inspection of tangible objects (including, without limitation, documents, prototypes, samples, plant and equipment), which is designated as "Confidential," "Proprietary" or some similar designation. Information communicated orally shall be considered Confidential Information if such information is confirmed in writing as being Confidential Information within ten (10) Business Days after the initial disclosure. Confidential Information may also include information disclosed to a disclosing party by third parties. Confidential Information shall not, however, include any information which (i) was publicly known and made generally available in the public domain prior to the time of disclosure by the disclosing party; (ii) becomes publicly known and made generally available after disclosure by the disclosing party to the receiving party through no action or inaction of the receiving party; (iii) is already in the possession of the receiving party without confidential restriction at the time of disclosure by the disclosing party as shown by the receiving party's files and records immediately prior to the time of disclosure; (iv) is obtained by the receiving party from a third party without a breach of such third party's obligations of confidentiality; (v) is independently developed by the receiving party without use of or reference to the disclosing party's Confidential Information, as shown by documents and other competent evidence in the receiving party's possession; or (vi) is required by law to be disclosed by the receiving party, provided that the receiving party gives the disclosing party prompt written notice of such requirement prior to such disclosure and assistance in obtaining an order protecting the information from public disclosure.

(bb) "Custodian" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

(cc) "DTC" means The Depository Trust Company, or any successor performing substantially the same function for the Company.

(dd) "DWAC Shares" means shares of Common Stock that are (i) issued in electronic form, (ii) freely tradable and transferable and without restriction on resale and (iii) timely credited by the Company, once a DWAC notice is received, to the Investor's or its designee's specified Deposit/Withdrawal at Custodian (DWAC) account with DTC under its Fast Automated Securities Transfer (FAST) Program, or any similar program hereafter adopted by DTC performing substantially the same function.

(ee) "Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(ff) "Floor Price" means $1.00, which shall be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction and, effective upon the consummation of any such reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction, the Floor Price shall mean the lower of (i) the adjusted price and (ii) $1.00.

(gg) "Fully Adjusted Regular Purchase Share Limit" means, with respect to any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction from and after the date of this Agreement, the Regular Purchase Share Limit (as defined in Section 2(a) hereof) in effect on the applicable date of determination, after giving effect to the full proportionate adjustment thereto made pursuant to Section 2(a) hereof for or in respect of such reorganization, recapitalization, non-cash dividend, stock split or other similar transaction.

(hh) "Initial Prospectus Supplement" means the prospectus supplement of the Company relating to the Securities, including the accompanying Base Prospectus, to be prepared and filed by the Company with the SEC pursuant to Rule 424(b) under the Securities Act and in accordance with Section 5(a) hereof, together with all documents and information incorporated therein by reference.

(ii) "Material Adverse Effect" means any material adverse effect on (i) the enforceability of any Transaction Document, (ii) the results of operations, assets, business or financial condition of the Company and its Subsidiaries, taken as a whole, other than any material adverse effect that resulted exclusively from (A) any change in the United States or foreign economies or securities or financial markets in general that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, (B) any change that generally affects the industry in which the Company and its Subsidiaries operate that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, (C) any change arising in connection with earthquakes, hostilities, acts of war, sabotage or terrorism or military actions or any escalation or material worsening of any such hostilities, acts of war, sabotage or terrorism or military actions existing as of the date hereof, (D) any action taken by the Investor, its affiliates or its or their successors and assigns with respect to the transactions contemplated by this Agreement, (E) the effect of any change in applicable laws or accounting rules that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, or (F) any change resulting from compliance with terms of this Agreement or the consummation of the transactions contemplated by this Agreement, or (iii) the Company's ability to perform in any material respect on a timely basis its obligations under any Transaction Document to be performed as of the date of determination.

(jj) "Maturity Date" means the first day of the month immediately following the thirty-six (36) month anniversary of the Commencement Date.

(kk) "PEA Period" means the period commencing at 9:30 a.m., Eastern time, on the fifth (5^{th}) Business Day immediately prior to the filing of any post-effective amendment to the Registration Statement (as defined herein) or New Registration Statement (as such term is defined in the Registration Rights Agreement), and ending at 9:30 a.m., Eastern time, on the Business Day immediately following, the effective date of any post-effective amendment to the Registration Statement (as defined herein) or New Registration Statement (as such term is defined in the Registration Rights Agreement).

(ll) "Person" means an individual or entity including but not limited to any limited liability company, a partnership, a joint venture, a corporation, a trust, an unincorporated organization and a government or any department or agency thereof.

(mm) "Principal Market" means The Nasdaq Global Market (or any nationally recognized successor thereto); provided, however, that in the event the Company's Common Stock is ever listed or traded on the Nasdaq Global Select Market, The Nasdaq Capital Market, the New York Stock Exchange, the NYSE American, the NYSE Arca, the OTC Bulletin Board, or the OTCQX or OTCQB operated by the OTC Markets Group, Inc. (or any nationally recognized successor to any of the foregoing), then the "Principal Market" shall mean such other market or exchange on which the Company's Common Stock is then listed or traded.

(nn) "Prospectus" means the Base Prospectus, as supplemented by any Prospectus Supplement (including the Initial Prospectus Supplement), including the documents and information incorporated by reference therein.

(oo) "Prospectus Supplement" means any prospectus supplement to the Base Prospectus (including the Initial Prospectus Supplement) filed with the SEC pursuant to Rule 424(b) under the Securities Act in connection with the transactions contemplated by this Agreement, including the documents and information incorporated by reference therein.

(pp) "Purchase Amount" means, with respect to any Regular Purchase, any Accelerated Purchase or any Additional Accelerated Purchase made hereunder, as applicable, the portion of the Available Amount to be purchased by the Investor pursuant to Section 2 hereof.

(qq) "Purchase Date" means, with respect to a Regular Purchase made pursuant to Section 2(a) hereof, the Business Day on which the Investor receives, after 4:00 p.m., Eastern time, but prior to 7:00 p.m., Eastern time, on such Business Day, a valid Regular Purchase Notice for such Regular Purchase in accordance with this Agreement.

(rr) "Purchase Price" means, with respect to any Regular Purchase made pursuant to Section 2(a) hereof, the lower of: (i) the lowest Sale Price on the applicable Purchase Date for such Regular Purchase and (ii) the arithmetic average of the three (3) lowest Closing Sale Prices for the Common Stock during the ten (10) consecutive Business Days prior to the Purchase Date for such Regular Purchase (in each case, to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction that occurs on or after the date of this Agreement).

(ss) "Registration Rights Agreement" means that certain Registration Rights Agreement, of even date herewith between the Company and the Investor.

(tt) "Registration Statement" has the meaning set forth in the Registration Rights Agreement.

(uu) "Regular Purchase Notice" means, with respect to any Regular Purchase pursuant to Section 2(a) hereof, an irrevocable written notice from the Company to the Investor directing the Investor to buy such applicable amount of Purchase Shares at the applicable Purchase Price as specified by the Company therein on the applicable Purchase Date for such Regular Purchase.

(vv) "Sale Price" means any trade price for the shares of Common Stock on the Principal Market as reported by the Principal Market.

(ww) "SEC" means the U.S. Securities and Exchange Commission.

(xx) "Securities" means, collectively, the Purchase Shares and the Commitment Shares (as defined below).

(yy) "Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

(zz) "Subsidiary" means any Person the Company wholly owns or controls, or in which the Company, directly or indirectly, owns a majority of the voting stock or similar voting interest, in each case that would be disclosable pursuant to Item 601(b)(21) of Regulation S-K promulgated under the Securities Act.

(aaa) "Transaction Documents" means, collectively, this Agreement and the schedules and exhibits hereto, the Registration Rights Agreement and the schedules and exhibits thereto, and each of the other agreements, documents, certificates and instruments entered into or furnished by the parties hereto in connection with the transactions contemplated hereby and thereby.

(bbb) "Transfer Agent" means Computershare Trust Company, N.A., or such other Person who is then serving as the transfer agent for the Company in respect of the Common Stock.

(ccc) "VWAP" means in respect of an Accelerated Purchase Date and an Additional Accelerated Purchase Date, as applicable, the volume weighted average price of the Common Stock on the Principal Market, as reported on the Principal Market or by another reputable source such as Bloomberg, L.P.

2. PURCHASE OF COMMON STOCK.

Subject to the terms and conditions set forth in this Agreement, the Company has the right, but not the obligation, to sell to the Investor, in the Company's sole and absolute discretion, and the Investor has the obligation to purchase from the Company, Purchase Shares as follows:

(a) Commencement of Regular Sales of Common Stock. Beginning one (1) Business Day following the Commencement Date and thereafter, the Company shall have the right, but not the obligation, to direct the Investor, by its delivery to the Investor of a Regular Purchase Notice from time to time, to purchase up to One Hundred Thousand (100,000) Purchase Shares, subject to adjustment as set forth below in this Section 2(a) (such maximum number of Purchase Shares, as may be adjusted from time to time, the "Regular Purchase Share Limit"), at the Purchase Price on the Purchase Date (each such purchase a "Regular Purchase"); provided, however, that (i) the Regular Purchase Share Limit shall be increased to One Hundred Fifty Thousand (150,000) Purchase Shares, if the Closing Sale Price of the Common Stock on the applicable Purchase Date is not below $3.00 and (ii) the Regular Purchase Share Limit shall be increased to Two Hundred Thousand (200,000) Purchase Shares, if the Closing Sale Price of the Common Stock on the applicable Purchase Date is not below $5.00 (all of which share and dollar amounts shall be appropriately proportionately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction; provided that if, after giving effect to the full proportionate adjustment to the Regular Purchase Share Limit therefor, the Fully Adjusted Regular Purchase Share Limit then in effect would preclude the Company from delivering to the Investor a Regular Purchase Notice hereunder for a Purchase Amount (calculated by multiplying (X) the number of Purchase Shares equal to the Fully Adjusted Regular Purchase Share Limit, by (Y) the Purchase Price per Purchase Share covered by such Regular Purchase Notice on the applicable Purchase Date therefor) equal to or greater than One Hundred Fifty Thousand Dollars ($150,000), the Regular Purchase Share Limit for such Regular Purchase Notice shall not be fully adjusted to equal the applicable Fully Adjusted Regular Purchase Share Limit, but rather the Regular Purchase Share Limit for such Regular Purchase Notice shall be adjusted to equal the applicable Alternate Adjusted Regular Purchase Share Limit as of the applicable Purchase Date for such Regular Purchase Notice); and provided, further, however, that the Investor's committed obligation under any single Regular Purchase, other than any Regular Purchase with respect to which an Alternate Adjusted Regular Purchase Share Limit shall apply, shall not exceed Two Million Dollars ($2,000,000) and provided, further, however, that the parties may mutually agree to increase the Regular Purchase Share Limit. If the Company delivers any Regular Purchase Notice for a Purchase Amount in excess of the limitations contained in the immediately preceding sentence, such Regular Purchase Notice shall be void *ab initio* to the extent of the amount by which the number of Purchase Shares set forth in such Regular Purchase Notice exceeds the number of Purchase Shares which the Company is permitted to include in such Regular Purchase Notice in accordance herewith, and the Investor shall have no obligation to purchase such excess Purchase Shares in respect of such Regular Purchase Notice; provided, however, that the Investor shall remain obligated to purchase the number of Purchase Shares which the Company is permitted to include in such Regular Purchase Notice. The Company may deliver multiple Regular Purchase Notices to the Investor in a day as often as every Business Day, so long as the Company has not failed to deliver Purchase Shares for the most recent prior Regular Purchase. Notwithstanding the foregoing, the Company shall not deliver a Regular Purchase Notice to the Investor (i) on any Purchase Date that the Closing Sale Price of the Common Stock is less than the Floor Price or (ii) during the PEA Period.

(b) Accelerated Purchases. Subject to the terms and conditions of this Agreement, from and after the Commencement Date, in addition to purchases of Purchase Shares as described in Section 2(a) above, the Company shall also have the right, but not the obligation, to direct the Investor, by its delivery to the Investor of an Accelerated Purchase Notice from time to time in accordance with this Agreement, to purchase the applicable Accelerated Purchase Share Amount at the Accelerated Purchase Price on the Accelerated Purchase Date therefor in accordance with this Agreement (each such purchase, an "Accelerated Purchase"). The Company may deliver an Accelerated Purchase Notice to the Investor only on a Purchase Date on which (i) the Company also properly submitted a Regular Purchase Notice providing for a Regular Purchase of a number of Purchase Shares not less than the Regular Purchase Share Limit then in effect on such Purchase Date in accordance with this Agreement (including, without limitation, giving effect to any automatic increase to the Regular Purchase Share Limit as a result of the Closing Sale Price of the Common Stock exceeding certain thresholds set forth in Section 2(b) above on such Purchase Date and any other adjustments to the Regular Purchase Share Limit, in each case pursuant to Section 2(b) above) and (ii) the Closing Sale Price of the Common Stock is not less than the Accelerated Purchase Floor Price. If the Company delivers any Accelerated Purchase Notice directing the Investor to purchase an amount of Purchase Shares that exceeds the Accelerated Purchase Share Amount that the Company is then permitted to include in such Accelerated Purchase Notice, such Accelerated Purchase Notice shall be void *ab initio* to the extent of the amount by which the number of Purchase Shares set forth in such Accelerated Purchase Notice exceeds the Accelerated Purchase Share Amount that the Company is then permitted to include in such Accelerated Purchase Notice (which shall be confirmed in an Accelerated Purchase Confirmation), and the Investor shall have no obligation to purchase such excess Purchase Shares in respect of such Accelerated Purchase Notice; provided, however, that the Investor shall remain obligated to purchase the Accelerated Purchase Share Amount which the Company is permitted to include in such Accelerated Purchase Notice; and provided, further, however, that the parties may mutually agree to increase the Accelerated Purchase Share Amount applicable to any Accelerated Purchase, and all of the Purchase Shares subject to such increased Accelerated Purchase shall be purchased by the Investor at the Accelerated Purchase Price for such increased Accelerated Purchase in accordance with this Agreement. Within one (1) Business Day after completion of each Accelerated Purchase Date for an Accelerated Purchase, the Investor will provide to the Company a written confirmation of such Accelerated Purchase setting forth the applicable Accelerated Purchase Share Amount and Accelerated Purchase Price for such Accelerated Purchase (each, an "Accelerated Purchase Confirmation"). Notwithstanding the foregoing, the Company shall not deliver any Accelerated Purchase Notices during the PEA Period.

(c) Additional Accelerated Purchases. Subject to the terms and conditions of this Agreement, beginning one (1) Business Day following the Commencement Date and thereafter, in addition to purchases of Purchase Shares as described in Section 2(a) and Section 2(b) above, the Company shall also have the right, but not the obligation, to direct the Investor, by its timely delivery to the Investor of an Additional Accelerated Purchase Notice on an Additional Accelerated Purchase Date in accordance with this Agreement, to purchase the applicable Additional Accelerated Purchase Share Amount at the applicable Additional Accelerated Purchase Price therefor in accordance with this Agreement (each such purchase, an "Additional Accelerated Purchase"). The Company may deliver multiple Additional Accelerated Purchase Notices to the Investor on an Additional Accelerated Purchase Date; provided, however, that the Company may deliver an Additional Accelerated Purchase Notice to the Investor only (i) on a Business Day that is also the Accelerated Purchase Date for an Accelerated Purchase with respect to which the Company properly submitted to the Investor an Accelerated Purchase Notice in accordance with this Agreement on the applicable Purchase Date for a Regular Purchase of a number of Purchase Shares not less than the Regular Purchase Share Limit then in effect in accordance with this Agreement (including, without limitation, giving effect to any automatic increase to the Regular Purchase Share Limit as a result of the Closing Sale Price of the Common Stock exceeding certain thresholds set forth in Section 2(b) above on such Purchase Date and any other adjustments to the Regular Purchase Share Limit, in each case pursuant to Section 2(b) above), (ii) if the Closing Sale Price of the Common Stock on the Business Day immediately preceding the Business Day on which such Additional Accelerated Purchase Notice is delivered is not less than the Additional Accelerated Purchase Floor Price, and (iii) if all Purchase Shares subject to all prior Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases, including, without limitation, those that have been effected on the same Business Day as the applicable Additional Accelerated Purchase Date with respect to which the applicable Additional Accelerated Purchase relates, have theretofore been received by the Investor as DWAC Shares in accordance with this Agreement. If the Company delivers any Additional Accelerated Purchase Notice directing the Investor to purchase an amount of Purchase Shares that exceeds the Additional Accelerated Purchase Share Amount that the Company is then permitted to include in such Additional Accelerated Purchase Notice in accordance with the terms of this Agreement, such Additional Accelerated Purchase Notice shall be void *ab initio* to the extent of the amount by which the number of Purchase Shares set forth in such Additional Accelerated Purchase Notice exceeds the Additional Accelerated Purchase Share Amount that the Company is then permitted to include in such Additional Accelerated Purchase Notice in accordance with the terms of this Agreement (which shall be confirmed in an Additional Accelerated Purchase Confirmation (defined below)), and the Investor shall have no obligation to purchase such excess Purchase Shares in respect of such Additional Accelerated Purchase Notice; provided, however, that the Investor shall remain obligated to purchase the Additional Accelerated Purchase Share Amount which the Company is permitted to include in such Additional Accelerated Purchase Notice; and provided, further, however, that the parties may mutually agree to increase the Additional Accelerated Purchase Share Amount applicable to any Additional Accelerated Purchase, and all of the Purchase Shares subject to such increased Additional Accelerated Purchase shall be purchased by the Investor at the Additional Accelerated Purchase Price for such increased Additional Accelerated Purchase in accordance with this Agreement. Within one (1) Business Day after completion of each Additional Accelerated Purchase Date, the Investor will provide to the Company a written confirmation of each Additional Accelerated Purchase on such Additional Accelerated Purchase Date setting forth the applicable Additional Accelerated Purchase Share Amount and Additional Accelerated Purchase Price for each such Additional Accelerated Purchase on such Additional Accelerated Purchase Date (each, an "Additional Accelerated Purchase Confirmation").

(d) Payment for Purchase Shares. For each Regular Purchase, the Investor shall pay to the Company an amount equal to the Purchase Amount with respect to such Regular Purchase as full payment for such Purchase Shares via wire transfer of immediately available funds on the same Business Day that the Investor receives such Purchase Shares, if such Purchase Shares are received by the Investor before 1:00 p.m., Eastern time, or, if such Purchase Shares are received by the Investor after 1:00 p.m., Eastern time, the next Business Day. For each Accelerated Purchase and each Additional Accelerated Purchase, the Investor shall pay to the Company an amount equal to the Purchase Amount with respect to such Accelerated Purchase and Additional Accelerated Purchase, respectively, as full payment for such Purchase Shares via wire transfer of immediately available funds on the second Business Day following the date that the Investor receives such Purchase Shares. If the Company or the Transfer Agent shall fail for any reason or for no reason to electronically transfer any Purchase Shares as DWAC Shares submitted by the Investor or its agent in respect of any Regular Purchase, Accelerated Purchase or Additional Accelerated Purchase (as applicable) within two (2) Business Days following the receipt by the Company of the Purchase Price, Accelerated Purchase Price or Additional Accelerated Purchase Price, respectively, therefor in compliance with this Section 2(d), and if on or after such two (2) Business Days the Investor purchases (in an open market transaction or otherwise) shares of Common Stock to deliver in satisfaction of a sale by the Investor of such Purchase Shares that the Investor anticipated receiving from the Company in respect of such Regular Purchase, Accelerated Purchase or Additional Accelerated Purchase (as applicable), then the Company shall, within two (2) Business Days after the Investor's request, either (i) pay cash to the Investor in an amount equal to the Investor's total purchase price (including customary brokerage commissions, if any) for the shares of Common Stock so purchased (the "Cover Price"), at which point the Company's obligation to deliver such Purchase Shares as DWAC Shares shall terminate, or (ii) promptly honor its obligation to deliver to the Investor such Purchase Shares as DWAC Shares and pay cash to the Investor in an amount equal to the excess (if any) of the Cover Price over the total Purchase Amount paid by the Investor pursuant to this Agreement for all of the Purchase Shares to be purchased by the Investor in connection with such purchases. The Company shall not issue any fraction of a share of Common Stock upon any Regular Purchase, Accelerated Purchase or Additional Accelerated Purchase. If the issuance would result in the issuance of a fraction of a share of Common Stock, the Company shall round such fraction of a share of Common Stock down to the nearest whole share. All payments made under this Agreement shall be made in lawful money of the United States of America or wire transfer of immediately available funds to such account as the Company may from time to time designate by written notice in accordance with the provisions of this Agreement. Whenever any amount expressed to be due by the terms of this Agreement is due on any day that is not a Business Day, the same shall instead be due on the next succeeding day that is a Business Day.

(e) Compliance with Rules of Principal Market.

(i) Exchange Cap. Subject to Section 2(e)(ii) below, the Company shall not issue or sell any shares of Common Stock pursuant to this Agreement, and the Investor shall not purchase or acquire any shares of Common Stock pursuant to this Agreement, to the extent that after giving effect thereto, the aggregate number of shares of Common Stock that would be issued pursuant to this Agreement and the transactions contemplated hereby would exceed 5,288,425 shares of Common Stock, representing 19.99% of the shares of Common Stock outstanding on the date of this Agreement (which number of shares shall be reduced, on a share-for-share basis, by the number of shares of Common Stock issued or issuable pursuant to any transaction or series of transactions that may be aggregated with the transactions contemplated by this Agreement under applicable rules of the Nasdaq Global Market or any other Principal Market on which the Common Stock may be listed or quoted) (the "Exchange Cap"), unless and until the Company elects to solicit stockholder approval of the issuance of Common Stock as contemplated by this Agreement and the stockholders of the Company have in fact approved such issuance in accordance with the applicable rules and regulations of the Nasdaq Global Market, any other Principal Market on which the Common Stock may be listed or quoted, and the Company's Certificate of Incorporation, as amended (the "Certificate of Incorporation"), and the Company's Amended and Restated Bylaws, as amended (the "Bylaws"). For the avoidance of doubt, the Company may, but shall be under no obligation to, request its stockholders to approve the issuance of Common Stock as contemplated by this Agreement; provided, that if stockholder approval is not obtained in accordance with this Section 2(e)(i), the Exchange Cap shall be applicable for all purposes of this Agreement and the transactions contemplated hereby at all times during the term of this Agreement (except as set forth in Section 2(e)(ii) below).

(ii) At-the-Market Transaction. Notwithstanding Section 2(e)(i) above and subject to the prior approval of the Nasdaq Global Market or any other Principal Market on which the Common Stock may be listed or quoted (to the extent required), the Exchange Cap shall not be applicable for any purposes of this Agreement and the transactions contemplated hereby, solely to the extent that (and only for so long as) the Average Price shall equal or exceed the Base Price and in accordance with any other applicable rules of the Nasdaq Global Market or any other Principal Market on which the Common Stock may be listed or quoted (it being hereby acknowledged and agreed that the Exchange Cap shall be applicable for all purposes of this Agreement and the transactions contemplated hereby at all other times during the term of this Agreement, unless the stockholder approval referred to in Section 2(e)(i) is obtained). "Base Price" means a price per Purchase Share equal to the sum of (i) the Signing Market Price and (ii) $0.0524 (subject to adjustment for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction that occurs on or after the date of this Agreement). "Signing Market Price" means $2.2540, representing the lower of (i) the closing price of the Common Stock on the Nasdaq Global Market immediately preceding the date of this Agreement or (ii) the average of the closing price of the Common Stock on the Nasdaq Global Market for the five Business Days immediately preceding the signing of this Agreement.

(iii) General. The Company shall not issue any Securities pursuant to this Agreement if such issuance would reasonably be expected to result in (A) a violation of the Securities Act or (B) a breach of the rules and regulations of the Principal Market. The provisions of this Section 2(e) shall be implemented in a manner otherwise than in strict conformity with the terms hereof only if necessary to ensure compliance with the Securities Act and the rules and regulations of the Principal Market.

(f) Beneficial Ownership Limitation. Notwithstanding anything to the contrary contained in this Agreement, the Company shall not issue or sell, and the Investor shall not purchase or acquire, any Common Stock under this Agreement which, when aggregated with all other shares of Common Stock then beneficially owned by the Investor and its affiliates (as calculated pursuant to Section 13(d) of the Exchange Act and Rule 13d-3 promulgated thereunder) would result in the beneficial ownership by the Investor and its affiliates of more than 9.99% of the then issued and outstanding Common Stock (the "Beneficial Ownership Limitation"). Upon the written or oral request of the Investor, the Company shall promptly (but not later than 24 hours) confirm orally or in writing to the Investor the amount of Common Stock then outstanding. The Investor and the Company shall each cooperate in good faith in the determinations required hereby and the application hereof. Upon the oral or written request of the Company, the Investor shall promptly (but not later than 24 hours) confirm orally or in writing to the Company whether the total number of shares beneficially held by it and its affiliates exceeds 9.0% of the total outstanding amount of Common Stock then outstanding.

3. INVESTOR'S REPRESENTATIONS AND WARRANTIES.

The Investor represents and warrants to the Company that as of the Execution Date and as of the Commencement Date:

(a) Organization, Authority. Investor is an entity duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization, with the requisite power and authority to enter into and to consummate the transactions contemplated by this Agreement and otherwise to carry out its obligations hereunder and thereunder.

(b) Accredited Investor Status. The Investor is an "accredited investor" as that term is defined in Rule 501(a)(3) of Regulation D promulgated under the Securities Act.

(c) Information. The Investor understands that its investment in the Securities involves a high degree of risk. The Investor (i) is able to bear the economic risk of an investment in the Securities including a total loss thereof, (ii) has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risks of the proposed investment in the Securities and (iii) has had an opportunity to ask questions of and receive answers from the officers of the Company concerning the financial condition and business of the Company and others matters related to an investment in the Securities. Neither such inquiries nor any other due diligence investigations conducted by the Investor or its representatives shall modify, amend or affect the Investor's right to rely on the Company's representations and warranties contained in Section 4 below. The Investor has sought such accounting, legal and tax advice from its own independent advisors as it has considered necessary to make an informed investment decision with respect to its acquisition of the Securities and is not relying on any accounting, legal, tax or other advice from the Company or its officers, employees, representatives or advisors.

(d) No Governmental Review. The Investor understands that no federal, state or any other government or governmental agency has passed on or made any recommendation or endorsement of the Securities or the fairness or suitability of an investment in the Securities nor have such authorities passed upon or endorsed the merits of the offering of the Securities.

(e) Validity; Enforcement. This Agreement has been duly and validly authorized, executed and delivered on behalf of the Investor and is a valid and binding agreement of the Investor enforceable against the Investor in accordance with its terms, subject as to enforceability to general principles of equity and to applicable bankruptcy, insolvency, reorganization, moratorium, liquidation and other similar laws relating to, or affecting generally, the enforcement of applicable creditors' rights and remedies.

(f) Residency. The Investor's principal place of business is in the State of Illinois.

(g) No Short Selling. The Investor represents and warrants to the Company that at no time prior to the date of this Agreement has any of the Investor, its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any (i) "short sale" (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of the Common Stock or (ii) hedging transaction, which establishes a net short position with respect to the Common Stock.

4. REPRESENTATIONS AND WARRANTIES OF THE COMPANY.

The Company represents and warrants to the Investor that as of the Execution Date and as of the Commencement Date:

(a) Organization and Qualification. The Company and each of its Subsidiaries is an entity duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization, with the requisite corporate power and authority to own and use its properties and assets and to carry on its business as currently conducted. Neither the Company nor any of its Subsidiaries is in violation or default of any of the provisions of its respective certificate of incorporation, bylaws or other organizational or charter documents. Each of the Company and its Subsidiaries is duly qualified to conduct business and is in good standing as a foreign corporation or other entity in each jurisdiction in which the nature of the business conducted or property owned by it makes such qualification necessary, except where the failure to be so qualified or in good standing, as the case may be, could not have or reasonably be expected to result in a Material Adverse Effect and no proceeding has been instituted in any such jurisdiction revoking, limiting or curtailing or seeking to revoke, limit or curtail such power and authority or qualification. The Company currently has no Subsidiaries.

(b) Authorization; Enforcement; Validity. (i) The Company has the requisite corporate power and authority to enter into and perform its obligations under this Agreement and each of the other Transaction Documents to which it is a party, and to issue the Securities in accordance with the terms hereof and thereof, (ii) the execution and delivery of the Transaction Documents by the Company to which it is a party and the consummation by it of the transactions contemplated hereby and thereby, including without limitation, the issuance of the Commitment Shares and the reservation for issuance and the issuance of the Purchase Shares issuable under this Agreement, have been duly authorized by the Company's Board of Directors, or a validly authorized committee thereof (collectively, the "Board of Directors"), and no further consent or authorization is required by the Company, its Board of Directors or its stockholders, (iii) this Agreement has been, and each other Transaction Document shall be on the Commencement Date, duly executed and delivered by the Company and (iv) this Agreement constitutes, and each other Transaction Document upon its execution on behalf of the Company, shall constitute, the valid and binding obligations of the Company enforceable against the Company in accordance with their terms, except as such enforceability may be limited by general principles of equity or applicable bankruptcy, insolvency, reorganization, moratorium, liquidation or similar laws relating to, or affecting generally, the enforcement of creditors' rights and remedies. The Board of Directors has passed all applicable resolutions (the "Resolutions") to authorize this Agreement and the transactions contemplated hereby. The Resolutions are valid, in full force and effect and have not been modified or supplemented in any respect. The Company has delivered to the Investor a certified copy of the Resolutions passed by the Board of Directors. Except as set forth in this Agreement, no other approvals or consents of the Board of Directors and/or stockholders is necessary under applicable laws, and the Certificate of Incorporation and Bylaws of the Company, to authorize the execution and delivery of this Agreement or any of the transactions contemplated hereby, including, but not limited to, the issuance of the Commitment Shares and the issuance of the Purchase Shares.

(c) Capitalization. As of the date hereof, the authorized capital stock of the Company is set forth in the Company's Quarterly Report on Form 10-Q filed on November 9, 2018 for the quarter ended September 30, 2018. Except as disclosed in the SEC Documents (as defined below) or on Schedule 4(c), (i) no shares of the Company's capital stock are subject to preemptive rights or any other similar rights or any liens or encumbrances suffered or permitted by the Company, (ii) there are no outstanding debt securities, (iii) there are no outstanding options, warrants, scrip, rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities or rights convertible into, any shares of capital stock of the Company or any of its Subsidiaries, or contracts, commitments, understandings or arrangements by which the Company or any of its Subsidiaries is or may become bound to issue additional shares of capital stock of the Company or any of its Subsidiaries or options, warrants, scrip, rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities or rights convertible into, any shares of capital stock of the Company or any of its Subsidiaries, (iv) there are no agreements or arrangements under which the Company or any of its Subsidiaries is obligated to register the sale of any of their securities under the Securities Act (except the Registration Rights Agreement), (v) there are no outstanding securities or instruments of the Company or any of its Subsidiaries which contain any redemption or similar provisions, and there are no contracts, commitments, understandings or arrangements by which the Company or any of its Subsidiaries is or may become bound to redeem a security of the Company or any of its Subsidiaries, (vi) there are no securities or instruments containing anti-dilution or similar provisions that will be triggered by the issuance of the Securities as described in this Agreement and (vii) the Company does not have any stock appreciation rights or "phantom stock" plans or agreements or any similar plan or agreement. The Company has furnished to the Investor true and correct copies of (A) the Company's certificate of incorporation, as amended and as in effect on the date hereof (the "Certificate of Incorporation"), (B) the Company's Bylaws, as amended and as in effect on the date hereof (the "Bylaws"), and (C) summaries of the material terms of all securities convertible into or exercisable for Common Stock, if any, and copies of any documents containing the material rights of the holders thereof in respect thereto, which in the case of these clauses (A), (B) and (C), are not disclosed in any SEC Document or filed as an exhibit thereto.

(d) Issuance of Securities. Upon issuance and payment therefor in accordance with the terms and conditions of this Agreement, the Purchase Shares shall be validly issued, fully paid and nonassessable and free from all taxes, liens, charges, restrictions, rights of first refusal and preemptive rights with respect to the issue thereof, with the holders being entitled to all rights accorded to a holder of Common Stock. Upon issuance in accordance with the terms and conditions of this Agreement, the Commitment Shares shall be validly issued, fully paid and nonassessable and free from all taxes, liens, charges, restrictions, rights of first refusal and preemptive rights with respect to the issue thereof, with the holders being entitled to all rights accorded to a holder of Common Stock. 15,000,000 shares of Common Stock (the "Reserve Amount") have been duly authorized and reserved for issuance upon purchase under this Agreement as Purchase Shares.

(e) No Conflicts. The execution, delivery and performance of the Transaction Documents by the Company and the consummation by the Company of the transactions contemplated hereby and thereby (including, without limitation, the reservation for issuance and issuance of the Purchase Shares and the Commitment Shares) will not (i) result in a violation of the Certificate of Incorporation, any Certificate of Designations, Preferences and Rights of any outstanding series of preferred stock of the Company or the Bylaws or (ii) conflict with, or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any agreement, indenture or instrument to which the Company or any of its Subsidiaries is a party, or result in a violation of any law, rule, regulation, order, judgment or decree (including federal and state securities laws and regulations and the rules and regulations of the Principal Market applicable to the Company or any of its Subsidiaries) or by which any property or asset of the Company or any of its Subsidiaries is bound or affected, except in the case of conflicts, defaults, terminations, amendments, accelerations, cancellations and violations under clause (ii), which could not reasonably be expected to result in a Material Adverse Effect. Neither the Company nor its Subsidiaries is in violation of any term of or in default under its Certificate of Incorporation, any Certificate of Designation, Preferences and Rights of any outstanding series of preferred stock of the Company or Bylaws or their organizational charter or bylaws, respectively. Neither the Company nor any of its Subsidiaries is in violation of any term of or is in default under any material contract, agreement, mortgage, indebtedness, indenture, instrument, judgment, decree or order or any statute, rule or regulation applicable to the Company or its Subsidiaries, except for possible conflicts, defaults, terminations or amendments that could not reasonably be expected to have a Material Adverse Effect. The business of the Company and its Subsidiaries is not being conducted, and shall not be conducted, in violation of any law, ordinance or regulation of any governmental entity, except for possible violations, the sanctions for which either individually or in the aggregate could not reasonably be expected to have a Material Adverse Effect. Except as specifically contemplated by this Agreement and as required under the Securities Act or applicable state securities laws and the rules and regulations of the Principal Market, the Company is not required to obtain any consent, authorization or order of, or make any filing or registration with, any court or governmental agency or any regulatory or self-regulatory agency in order for it to execute, deliver or perform any of its obligations under or contemplated by the Transaction Documents in accordance with the terms hereof or thereof. Except as set forth elsewhere in this Agreement, all consents, authorizations, orders, filings and registrations which the Company is required to obtain pursuant to the preceding sentence shall be obtained or effected on or prior to the Commencement Date. Except as disclosed in the SEC Documents (as defined below), since one year prior to the date hereof, the Company has not received nor delivered any notices or correspondence from or to the Principal Market, other than notices with respect to listing of additional shares of Common Stock and other routine correspondence. Except as disclosed in the SEC Documents, the Principal Market has not commenced any delisting proceedings against the Company.

(f) SEC Documents; Financial Statements. The Company is, and has been during the 12-month period immediately preceding the date of this Agreement, required to file reports, schedules, forms, statements and other documents with the SEC pursuant to Section 13 or 15(d) of the Exchange Act. The Company has filed all reports, schedules, forms, statements and other documents required to be filed by the Company with the SEC under the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof, and under the Securities Act, in each case during the 12-month period immediately preceding the date of this Agreement (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, together with each Prospectus, being collectively referred to herein as the "SEC Documents") on a timely basis or has received a valid extension of such time of filing and has filed any such SEC Documents prior to the expiration of any such extension. As of their respective dates, the SEC Documents complied in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable. None of the SEC Documents, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The financial statements of the Company included in the SEC Documents comply in all material respects with applicable accounting requirements and the rules and regulations of the SEC with respect thereto as in effect at the time of filing. Such financial statements have been prepared in accordance with United States generally accepted accounting principles applied on a consistent basis during the periods involved ("GAAP"), except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP, and fairly present in all material respects the financial position of the Company and its consolidated Subsidiaries as of and for the dates thereof and the results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments. Except as set forth in the SEC Documents, the Company has received no notices or correspondence from the SEC for the one year preceding the date hereof**.** The SEC has not commenced any enforcement proceedings against the Company or any of its Subsidiaries.

(g) Absence of Certain Changes. Except as disclosed in the SEC Documents, since December 31, 2017, there has been no material adverse change in the business, properties, operations, financial condition or results of operations of the Company or its Subsidiaries. The Company is not in violation or default of (i) any provision of the Certificate of Incorporation or Bylaws, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which it is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties, which, in the case of clauses (ii) or (iii), could be reasonably expected to have a Material Adverse Effect. Except as described in the SEC Documents, no dispute between the Company and any third party exists or, to the knowledge of the Company, is threatened or imminent that could reasonably be expected to have a Material Adverse Effect. The Company has not taken any steps, and does not currently expect to take any steps, to seek protection pursuant to any Bankruptcy Law nor does the Company or any of its Subsidiaries have any knowledge or reason to believe that its creditors intend to initiate involuntary bankruptcy or insolvency proceedings. The Company is financially solvent and is generally able to pay its debts as they become due.

(h) Absence of Litigation. Except as disclosed in the SEC Documents, there is no action, suit, proceeding, inquiry or investigation before or by any court, public board, government agency, self-regulatory organization or body pending or, to the knowledge of the Company or any of its Subsidiaries, threatened against or affecting the Company, the Common Stock or any of the Company's or its Subsidiaries' officers or directors in their capacities as such, which could reasonably be expected to have a Material Adverse Effect.

(i) Acknowledgment Regarding Investor's Status. The Company acknowledges and agrees that the Investor is acting solely in the capacity of arm's length purchaser with respect to the Transaction Documents and the transactions contemplated hereby and thereby. The Company further acknowledges that the Investor is not acting as a financial advisor or fiduciary of the Company (or in any similar capacity) with respect to the Transaction Documents and the transactions contemplated hereby and thereby and any advice given by the Investor or any of its representatives or agents in connection with the Transaction Documents and the transactions contemplated hereby and thereby is merely incidental to the Investor's purchase of the Securities. The Company further represents to the Investor that the Company's decision to enter into the Transaction Documents has been based solely on the independent evaluation by the Company and its representatives and advisors.

(j) No Aggregated Offering. Neither the Company, nor any of its affiliates, nor any Person acting on its or their behalf has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under circumstances that would cause this offering of the Securities to be integrated or aggregated with prior offerings by the Company in a manner that would require stockholder approval pursuant to the rules of the Principal Market on which any of the securities of the Company are listed or designated. The issuance and sale of the Securities hereunder does not contravene the rules and regulations of the Principal Market.

(k) Intellectual Property Rights. The Company and its Subsidiaries own or possess adequate rights or licenses to use all material trademarks, trade names, service marks, service mark registrations, service names, patents, patent rights, copyrights, inventions, licenses, approvals, governmental authorizations, trade secrets and rights necessary to conduct their respective businesses as now conducted. None of the Company's material trademarks, trade names, service marks, service mark registrations, service names, patents, patent rights, copyrights, inventions, licenses, approvals, government authorizations, trade secrets or other intellectual property rights have expired or terminated, or, by the terms and conditions thereof, could expire or terminate within two years from the date of this Agreement. The Company and its Subsidiaries do not have any knowledge of any infringement by the Company or its Subsidiaries of any material trademark, trade name rights, patents, patent rights, copyrights, licenses, service names, service marks, service mark registrations, trade secret or other similar rights of others, or of any such development of similar or identical trade secrets or technical information by others, and there is no claim, action or proceeding being made or brought against, or to the Company's knowledge, being threatened against, the Company or its Subsidiaries regarding trademark, trade name, patents, patent rights, invention, copyright, license, service names, service marks, service mark registrations, trade secret or other infringement, which could reasonably be expected to have a Material Adverse Effect.

(l) Environmental Laws. The Company and its Subsidiaries (i) are in compliance with any and all applicable foreign, federal, state and local laws and regulations relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants ("Environmental Laws"), (ii) have received all permits, licenses or other approvals required of them under applicable Environmental Laws to conduct their respective businesses and (iii) are in compliance with all terms and conditions of any such permit, license or approval, except where, in each of the three foregoing clauses, the failure to so comply could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

(m) Title. Except as set forth in the SEC Documents, the Company and its Subsidiaries have good and marketable title in fee simple to all real property owned by them and good and marketable title in all personal property owned by them that is material to the business of the Company and its Subsidiaries, in each case free and clear of all liens, encumbrances and defects ("Liens") and, except for Liens as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and its Subsidiaries and Liens for the payment of federal, state or other taxes, the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company and its Subsidiaries are held by them under valid, subsisting and enforceable leases with which the Company and its Subsidiaries are in compliance with such exceptions as are not material and do not interfere with the use made and proposed to be made of such property and buildings by the Company and its Subsidiaries.

(n) Insurance. The Company and each of its Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as management of the Company believes to be prudent and customary in the businesses in which the Company and its Subsidiaries are engaged. Neither the Company nor any such Subsidiary has been refused any insurance coverage sought or applied for and neither the Company nor any such Subsidiary has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not materially and adversely affect the condition, financial or otherwise, or the earnings, business or operations of the Company and its Subsidiaries, taken as a whole.

(o) Regulatory Permits. Except as set forth in the SEC Documents, the Company and its Subsidiaries possess all material certificates, authorizations and permits issued by the appropriate federal, state, local or foreign regulatory authorities necessary to conduct their respective businesses, and neither the Company nor any such Subsidiary has received any notice of proceedings relating to the revocation or modification of any such certificate, authorization or permit, except, in the case of each of the two foregoing clauses, as could not reasonably be expected to have a Material Adverse Effect.

(p) Tax Status. Except as set forth in the SEC Documents, the Company and each of its Subsidiaries has made or filed all federal and state income and all other material tax returns, reports and declarations required by any jurisdiction to which it is subject (unless and only to the extent that the Company and each of its Subsidiaries has set aside on its books provisions reasonably adequate for the payment of all unpaid and unreported taxes) and has paid all taxes and other governmental assessments and charges that are material in amount, shown or determined to be due on such returns, reports and declarations, except those being contested in good faith and has set aside on its books provision reasonably adequate for the payment of all taxes for periods subsequent to the periods to which such returns, reports or declarations apply, and except as could not reasonably be expected to have a Material Adverse Effect.

(q) Transactions With Affiliates. Except as set forth in the SEC Documents, to the knowledge of the Company, none of the Company's stockholders, officers or directors or any family member or affiliate of any of the foregoing, has either directly or indirectly an interest in, or is a party to, any transaction that is required to be disclosed as a related party transaction pursuant to Item 404 of Regulation S-K promulgated under the Securities Act.

(r) Application of Takeover Protections. The Company and its Board of Directors have taken or will take prior to the Commencement Date all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Certificate of Incorporation, the laws of the state of its incorporation or otherwise which is or could become applicable to the Investor as a result of the transactions contemplated by this Agreement, including, without limitation, the Company's issuance of the Securities and the Investor's ownership of the Securities.

(s) Disclosure. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents that will be timely publicly disclosed by the Company, the Company confirms that neither it nor any other Person acting on its behalf has provided the Investor or its agents or counsel with any information that it believes constitutes or might constitute material, non-public information which is not otherwise disclosed in the Registration Statement or the SEC Documents. The Company understands and confirms that the Investor will rely on the foregoing representation in effecting purchases and sales of securities of the Company. All of the disclosure furnished by or on behalf of the Company to the Investor regarding the Company, its business and the transactions contemplated hereby, including the disclosure schedules to this Agreement, is true and correct and does not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in light of the circumstances under which they were made, not misleading. The Company acknowledges and agrees that the Investor neither makes nor has made any representations or warranties with respect to the transactions contemplated hereby other than those specifically set forth in Section 3 hereof.

(t) Foreign Corrupt Practices; Money Laundering Laws; Sanctions. Neither the Company nor any of the Subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of the Subsidiaries is aware of or has taken any action, directly or indirectly, that would result in a violation by such persons of the Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder (the "FCPA"), including, without limitation, making use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay or authorization of the payment of any money, or other property, gift, promise to give, or authorization of the giving of anything of value to any "foreign official" (as such term is defined in the FCPA) or any foreign political party or official thereof or any candidate for foreign political office, in contravention of the FCPA; and the Company, the Subsidiaries and, to the knowledge of the Company, its affiliates have conducted their businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith. The operations of the Company and the Subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements and the money laundering statutes and the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any applicable governmental agency, including, without limitation, Title 18 U.S. Code section 1956 and 1957, the Patriot Act, the Bank Secrecy Act, and international anti-money laundering principles or procedures by an intergovernmental group or organization, such as the Financial Action Task Force on Money Laundering, of which the United States is a member and with which designation the United States representative to the group or organization continues to concur, all as amended, and any Executive order, directive or regulation pursuant to the authority of any of the foregoing, or any orders or licenses issued thereunder (collectively, the "Money Laundering Laws"), and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its Subsidiaries with respect to the Money Laundering Laws is pending or, to the best knowledge of the Company, threatened. Neither the Company nor any of its Subsidiaries, nor to the knowledge of the Company any of the directors, officers or employees, agents, affiliates or representatives of the Company or its Subsidiaries, is an individual or entity that is, or is owned or controlled by an individual or entity that is: (i) the subject of any sanctions administered or enforced by the U.S. Department of Treasury's Office of Foreign Assets Control, the United Nations Security Council, the European Union, Her Majesty's Treasury, or other relevant sanctions authority (collectively, "Sanctions"), nor (ii) located, organized or resident in a country or territory that is the subject of Sanctions (including, without limitation, Burma/Myanmar, Cuba, Iran, Libya, North Korea, Venezuela, Sudan and Syria). Neither the Company nor any of its Subsidiaries will, directly or indirectly, use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any Subsidiary, joint venture partner or other individual or entity: (i) to fund or facilitate any activities or business of or with any individual or entity or in any country or territory that, at the time of such funding or facilitation, is the subject of Sanctions or (ii) in any other manner that will result in a violation of Sanctions by any individual or entity (including any individual or entity participating in the offering, whether as underwriter, advisor, investor or otherwise). For the past five years, neither the Company nor any of its Subsidiaries has knowingly engaged in, and is not now knowingly engaged in, any dealings or transactions with any individual or entity, or in any country or territory, that at the time of the dealing or transaction is or was the subject of Sanctions.

(u) Registration Statement. The Company has prepared and filed the Registration Statement with the SEC in accordance with the Securities Act. The Registration Statement was declared effective by order of the SEC on October 17, 2016. The Registration Statement is effective pursuant to the Securities Act and available for the issuance of the Securities thereunder. No stop order suspending the effectiveness of the Registration Statement has been issued by the SEC, and no proceeding for that purpose or pursuant to Section 8A of the Securities Act against the Company or related to the offering of the Securities has been initiated or, to the knowledge of the Company, threatened by the SEC. The "Plan of Distribution" section of the Prospectus permits the issuance of the Securities under the terms of this Agreement. At the time the Registration Statement and any amendments thereto became effective, at the date of this Agreement and at each deemed effective date thereof pursuant to Rule 430B(f)(2) of the Securities Act, the Registration Statement and any amendments thereto complied and will comply in all material respects with the requirements of the Securities Act and did not and will not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading; and the Base Prospectus and any Prospectus Supplement thereto, at the time such Base Prospectus or such Prospectus Supplement thereto was issued and on the Commencement Date, complied and will comply in all material respects with the requirements of the Securities Act and did not and will not contain an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading; provided that this representation and warranty does not apply to statements in or omissions from any Prospectus Supplement made in reliance upon and in conformity with information relating to the Investor furnished to the Company in writing by or on behalf of the Investor expressly for use therein. The Company meets all of the requirements for the use of a registration statement on Form S-3 pursuant to the Securities Act for the offering and sale of the Securities contemplated by this Agreement in reliance on General Instruction I.B.1. or General Instruction I.B.6. of Form S-3, and the SEC has not notified the Company of any objection to the use of the form of the Registration Statement pursuant to Rule 401(g)(1) of the Securities Act. The Company hereby confirms that the issuance of the Securities to the Investor pursuant to this Agreement would not result in non-compliance with the Securities Act or any of the General Instructions to Form S-3. The Registration Statement, as of its effective date, meets the requirements set forth in Rule 415(a)(1)(x) pursuant to the Securities Act. At the earliest time after the filing of the Registration Statement that the Company or another offering participant made a bona fide offer (within the meaning of Rule 164(h)(2) of the Securities Act) relating to any of the Securities, the Company was, and as of the date of this Agreement the Company is, not an Ineligible Issuer (as defined in Rule 405 of the Securities Act). The Company has not distributed any offering material in connection with the offering and sale of any of the Securities, other than the Registration Statement or any amendment thereto, the Prospectus or any Prospectus Supplement required pursuant to applicable law or the Transaction Documents. The Company has not made and shall not make an offer relating to the Securities that would constitute a "free writing prospectus" as defined in Rule 405 under the Securities Act.

(v) DTC Eligibility. The Company, through the Transfer Agent, currently participates in the DTC Fast Automated Securities Transfer (FAST) Program and the Common Stock can be transferred electronically to third parties via the DTC Fast Automated Securities Transfer (FAST) Program.

(w) Accounting Controls; Sarbanes-Oxley. The Company maintains a system of internal accounting controls sufficient to provide reasonable assurances that (A) transactions are executed in accordance with management's general or specific authorization; (B) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain accountability for assets; (C) access to assets is permitted only in accordance with management's general or specific authorization; and (D) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company has concluded that its internal control over financial reporting is effective and none of the Company, its board of directors and audit committee is aware of any "significant deficiencies" or "material weaknesses" (each as defined by the rules adopted by the SEC) in its internal control over financial reporting, or any fraud, whether or not material, that involves management or other employees of the Company and its Subsidiaries who have a significant role in the Company's internal controls; and since the end of the latest audited fiscal year, there has been no change in the Company's internal control over financial reporting (whether or not remediated) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting. The Board of Directors has, subject to the exceptions, cure periods and the phase in periods specified in the applicable stock exchange rules of the Principal Market ("Exchange Rules"), validly appointed an audit committee to oversee internal accounting controls whose composition satisfies the applicable independence and other requirements of the Exchange Rules and the rules under the Exchange Act, and the Board of Directors and/or the audit committee has adopted a charter that satisfies the requirements of the Exchange Rules and the rules under the Exchange Act. Neither the Board of Directors nor the audit committee has been informed, nor is any director of the Company or the Company aware, of (A) any significant deficiencies in the design or operation of the Company's internal controls which could adversely affect the Company's ability to record, process, summarize and report financial data or any material weakness in the Company's internal controls; or (B) any fraud, whether or not material, that involves management or other employees of the Company who have a significant role in the Company's internal controls. No relationship, direct or indirect, exists between or among the Company, on the one hand, and the directors, officers, stockholders, customers or suppliers of the Company, on the other hand, which is required to be described in the Registration Statement and the Prospectuses which is not so described. The Company has not, directly or indirectly, extended or maintained credit, or arranged for the extension of credit, or renewed an extension of credit, in the form of a personal loan to or for any of its directors or executive officers in violation of applicable laws, including Section 402 of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the "Sarbanes-Oxley Act").

(x) Certain Fees. Except as disclosed on Schedule 4(x), no brokerage or finder's fees or commissions are or will be payable by the Company to any broker, financial advisor or consultant, finder, placement agent, investment banker, bank or other Person with respect to the transactions contemplated by the Transaction Documents. Except as disclosed on Schedule 4(x), the Investor shall have no obligation with respect to any fees or with respect to any claims made by or on behalf of other Persons for fees of a type contemplated in this Section 4(x) that may be due in connection with the transactions contemplated by the Transaction Documents.

(y) Investment Company. The Company is not, and immediately after receipt of payment for the Securities will not be, an "investment company" within the meaning of the Investment Company Act of 1940, as amended (the "Investment Company Act").

(z) Listing and Maintenance Requirements. The Common Stock is registered pursuant to Section 12(b) of the Exchange Act, and the Company has taken no action designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Common Stock pursuant to the Exchange Act nor has the Company received any notification that the SEC is currently contemplating terminating such registration. The Company has not, in the twelve (12) months preceding the date hereof, received any notice from any Person to the effect that the Company is not in compliance with the listing or maintenance requirements of the Principal Market. The Company is in compliance with all such listing and maintenance requirements.

(aa) Accountants. The Company's accountants are set forth in the SEC Documents and, to the knowledge of the Company, such accountants are an independent registered public accounting firm as required by the Securities Act.

(bb) No Market Manipulation. The Company has not, and to its knowledge no Person acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Securities, (ii) sold, bid for, purchased, or, paid any compensation for soliciting purchases of, any of the Securities, or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company.

(cc) Benefit Plans; Labor Matters. Each benefit and compensation plan, agreement, policy and arrangement that is maintained, administered or contributed to by the Company for current or former employees or directors of, or independent contractors with respect to, the Company has been maintained in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations and the Company has complied in all material respects with all applicable statutes, orders, rules and regulations in regard to such plans, agreements, policies and arrangements. Each stock option granted under any stock option plan of the Company (each, a "Stock Plan") was granted with a per share exercise price no less than the market price per common share on the grant date of such option in accordance with the rules of the Principal Market, and no such grant involved any "back-dating," "forward-dating" or similar practice with respect to the effective date of such grant; each such option (i) was granted in compliance in all material respects with applicable laws and with the applicable Stock Plan(s), (ii) was duly approved by the Board of Directors (or a duly authorized committee thereof) of the Company, and (iii) has been properly accounted for in the Company's financial statements and disclosed, to the extent required, in the Company's filings or submissions with the SEC, and the Principal Market. No labor problem or dispute with the employees of the Company exists or is threatened or imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its principal suppliers or contractors, that could have a Material Adverse Effect.

(dd) Regulatory. Except as described in the SEC Documents, the Company and each of its Subsidiaries: (A) is and at all times has been in material compliance with all applicable U.S. and foreign statutes, rules, regulations, or guidance applicable to Company and its Subsidiaries ("Applicable Laws"), except as could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; (B) have not received any notice of adverse finding, warning letter, untitled letter or other correspondence or notice from any federal, state, or foreign governmental authority having authority over the Company ("Governmental Authority") alleging or asserting noncompliance with any Applicable Laws or any licenses, certificates, approvals, clearances, authorizations, permits and supplements or amendments thereto required by any such Applicable Laws ("Authorizations"); (C) possess all material Authorizations and such material Authorizations are valid and in full force and effect and are not in violation of any term of any such material Authorizations; (D) have not received notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Authority or third party alleging that any product operation or activity is in violation of any Applicable Laws or Authorizations and have no knowledge that any such Governmental Authority or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding; (E) have not received notice that any Governmental Authority has taken, is taking or intends to take action to limit, suspend, modify or revoke any Authorizations and the Company has no knowledge that any such Governmental Authority is considering such action; and (F) have filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or material Authorizations and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and correct in all material respects on the date filed (or were corrected or supplemented by a subsequent submission). To the Company's knowledge, all studies, tests and preclinical and clinical trials conducted by or on behalf of the Company were and, if still pending, are, in all material respects, being conducted in accordance with experimental protocols, procedures and controls pursuant to accepted professional scientific standards and all applicable laws, including, without limitation, the United States Federal Food, Drug and Cosmetic Act; the descriptions of the results of such studies, tests and trials contained in the SEC Documents are accurate and complete in all material respects and fairly present the data derived from such studies, tests and trials; the descriptions in the SEC Documents of the results of such clinical trials are consistent in all material respects with such results and to the Company's knowledge there are no other studies or other clinical trials whose results are materially inconsistent with or otherwise materially call into question the results described or referred to in the SEC Documents; and the Company has not received any notices or correspondence from any Governmental Authority requiring the termination, suspension or material modification of any studies, tests or preclinical or clinical trials conducted by or on behalf of the Company or its Subsidiaries. The Company has concluded that it uses commercially reasonable efforts to review, from time to time, the progress and results of the studies, tests and preclinical and clinical trials and, based upon (i) the information provided to the Company by the third parties conducting such studies, tests, preclinical studies and clinical trials that are described in the SEC Documents and the Company's review of such information, and (ii) the Company's actual knowledge, the Company reasonably believes that the descriptions of the results of such studies, tests, preclinical studies and clinical trials are accurate and complete in all material respects.

(ee) Absence of Schedules. In the event that at Closing, the Company does not deliver any disclosure schedule contemplated by this Agreement, the Company hereby acknowledges and agrees that each such undelivered disclosure schedule shall be deemed to read as follows: "Nothing to Disclose".

5. COVENANTS.

(a) Filing of Current Report and Initial Prospectus Supplement. The Company agrees that it shall, within the time required under the Exchange Act, file with the SEC a Current Report on Form 8-K, or include the disclosure required thereunder within the Company's Annual Report on Form 10-K, relating to the transactions contemplated by, and describing the material terms and conditions of, the Transaction Documents (the "Current Report"). The Company further agrees that it shall, within the time required under Rule 424(b) under the Securities Act, file with the SEC the Initial Prospectus Supplement pursuant to Rule 424(b) under the Securities Act specifically relating to the transactions contemplated by, and describing the material terms and conditions of, the Transaction Documents, containing information previously omitted at the time of effectiveness of the Registration Statement in reliance on Rule 430B under the Securities Act, and disclosing all information relating to the transactions contemplated hereby required to be disclosed in the Registration Statement and the Prospectus as of the date of the Initial Prospectus Supplement, including, without limitation, information required to be disclosed in the section captioned "Plan of Distribution" in the Prospectus. The Investor acknowledges that it will be identified in the Initial Prospectus Supplement as an underwriter within the meaning of Section 2(a)(11) of the Securities Act. The Company shall permit the Investor to review and comment upon the Current Report and the Initial Prospectus Supplement at least two (2) Business Days prior to their filing with the SEC, the Company shall give due consideration to all such comments. The Investor shall use its reasonable best efforts to provide any comments upon the Current Report and the Initial Prospectus Supplement within one (1) Business Day from the date the Investor receives a substantially complete draft thereof from the Company. The Investor shall furnish to the Company such information regarding itself, the Securities held by it and the intended method of distribution thereof, including any arrangement between the Investor and any other Person relating to the sale or distribution of the Securities, as shall be reasonably requested by the Company in connection with the preparation and filing of the Current Report and the Initial Prospectus Supplement, and shall otherwise cooperate with the Company as reasonably requested by the Company in connection with the preparation and filing of the Current Report and the Initial Prospectus Supplement with the SEC.

(b) Blue Sky. The Company shall take all such action, if any, as is reasonably necessary in order to obtain an exemption for or to qualify (i) the issuance of the Commitment Shares and the sale of the Purchase Shares to the Investor under this Agreement and (ii) any subsequent resale of all Commitment Shares and all Purchase Shares by the Investor, in each case, under applicable securities or "Blue Sky" laws of the states of the United States in such states as is reasonably requested by the Investor during the Registration Period, and shall provide evidence of any such action so taken to the Investor.

(c) Listing/DTC. To the extent applicable, the Company shall promptly secure the listing of all of the Purchase Shares and Commitment Shares to be issued to the Investor hereunder on the Principal Market (subject to official notice of issuance) and upon each other national securities exchange or automated quotation system, if any, upon which the Common Stock is then listed, and shall maintain, so long as any shares of Common Stock shall be so listed, such listing of all such Securities from time to time issuable hereunder. The Company shall use reasonable best efforts to maintain the listing of the Common Stock on the Principal Market and shall comply in all respects with the Company's reporting, filing and other obligations under the bylaws or rules and regulations of the Principal Market. Neither the Company nor any of its Subsidiaries shall take any action that would reasonably be expected to result in the delisting or suspension of the Common Stock on the Principal Market. The Company shall promptly, and in no event later than the following Business Day, provide to the Investor copies of any notices it receives from any Person regarding the continued eligibility of the Common Stock for listing on the Principal Market; provided, however, that the Company shall not be required to provide the Investor copies of any such notice that the Company reasonably believes constitutes material non-public information and the Company would not be required to publicly disclose such notice in any report or statement filed with the SEC under the Exchange Act or the Securities Act. The Company shall pay all fees and expenses in connection with satisfying its obligations under this Section 5(c). The Company shall take all action necessary to ensure that its Common Stock can be transferred electronically as DWAC Shares.

(d) Prohibition of Short Sales and Hedging Transactions. The Investor agrees that, beginning on the date of this Agreement and ending on the date of termination of this Agreement as provided in Section 11, the Investor and its agents, representatives and affiliates shall not in any manner whatsoever enter into or effect, directly or indirectly, any (i) "short sale" (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of the Common Stock or (ii) hedging transaction, which establishes a net short position with respect to the Common Stock.

(e) Issuance of Commitment Shares. In consideration for the Investor's execution and delivery of this Agreement, the Company shall cause to be issued to the Investor a total of 120,200 shares of Common Stock (the "Commitment Shares") by the Commencement Date and shall deliver on the Commencement Date, but in any event no later than 5 days after the Execution Date, the Irrevocable Transfer Agent Instructions to the Transfer Agent and cause the Commitment Shares to be issued to the Investor. For the avoidance of doubt, all of the Commitment Shares shall be fully earned as of the Execution Date, whether or not any other Purchase Shares are purchased by the Investor under this Agreement and irrespective of any subsequent termination of this Agreement.

(f) Due Diligence; Non-Public Information. During the term of this Agreement, the Investor shall have the right, from time to time as the Investor may reasonably deem appropriate, and upon reasonable advance notice to the Company, to perform reasonable due diligence on the Company during normal business hours. The Company and its officers and employees shall provide information and reasonably cooperate with the Investor in connection with any reasonable request by the Investor related to the Investor's due diligence of the Company. Each party hereto agrees not to disclose any Confidential Information of the other party to any third party and shall not use the Confidential Information for any purpose other than in connection with, or in furtherance of, the transactions contemplated hereby. Each party hereto acknowledges that the Confidential Information shall remain the property of the disclosing party and agrees that it shall take all reasonable measures to protect the secrecy of any Confidential Information disclosed by the other party. From and after the date of this Agreement, the Company confirms that neither it nor any other Person acting on its behalf shall provide the Investor or its agents or counsel with any information that the Company believes constitutes material, non-public information, unless a simultaneous public announcement thereof is made by the Company in the manner contemplated by Regulation FD under the Exchange Act. In the event of a breach of the foregoing covenant by the Company or any Person acting on its behalf (as determined in the reasonable good faith judgment of the Investor), in addition to any other remedy provided herein or in the other Transaction Documents, the Investor shall have the right to make a public disclosure, in the form of a press release, public advertisement or otherwise, of such material, non-public information without the prior approval by the Company; provided the Investor shall have first provided notice to the Company that it believes it has received information that constitutes material, non-public information, the Company shall have at least 24 hours to publicly disclose such material, non-public information prior to any such disclosure by the Investor, and the Company shall have failed to publicly disclose such material, non-public information within such time period. The Investor shall not have any liability to the Company, any of its Subsidiaries, or any of their respective directors, officers, employees, stockholders or agents, for any such disclosure. The Company understands and confirms that the Investor shall be relying on the foregoing covenants in effecting transactions in securities of the Company.

(g) Purchase Records. The Investor and the Company shall each maintain records showing the remaining Available Amount at any given time and the dates and Purchase Amounts for each Regular Purchase, Accelerated Purchase and Additional Accelerated Purchase or shall use such other method, reasonably satisfactory to the Investor and the Company.

(h) Taxes. The Company shall pay any and all transfer, stamp or similar taxes that may be payable with respect to the issuance and delivery of any Common Stock to the Investor made under this Agreement.

(i) Effective Registration Statement; Current Prospectuses. Without limiting Section 10 of the Registration Rights Agreement, the Company shall use its reasonable best efforts to keep the Registration Statement effective pursuant to Rule 415 promulgated under the Securities Act, and to keep the Registration Statement and the Prospectus current and available for issuances and sales of all of the Securities by the Company to the Investor, at all times until the earlier of (i) the date on which the Investor shall have sold all the Securities and no Available Amount remains under this Agreement and (ii) 180 days following the earlier of (A) the Maturity Date and (B) the date of termination of this Agreement (the "Registration Period"). The Company shall comply with all applicable federal, state and foreign securities laws in connection with the offer, issuance and sale of the Securities contemplated by the Transaction Documents. Without limiting the generality of the foregoing, neither the Company nor any of its officers, directors or affiliates will take, directly or indirectly, any action designed or intended to stabilize or manipulate the price of any security of the Company, or which would reasonably be expected to cause or result in, stabilization or manipulation of the price of any security of the Company.

(j) Compliance with Laws. The Company and each of its Subsidiaries shall maintain, or cause to be maintained, all material permits, licenses and other authorizations required by federal, state and local law in order to conduct their businesses substantially as described in the SEC Documents, and the Company and each of its Subsidiaries shall conduct their businesses, or cause their businesses to be conducted, in substantial compliance with such permits, licenses and authorizations and with applicable laws, except where the failure to maintain or be in compliance with such permits, licenses and authorizations could not reasonably be expected to have a Material Adverse Effect. The Company shall comply with all requirements imposed upon it by the Securities Act and the Exchange Act and applicable U.S. state securities or “Blue Sky” laws as from time to time may be in force in connection with the offer, issuance and sale of the Securities contemplated by the Transaction Documents. Without limiting the generality of the foregoing, neither the Company nor any of its officers, directors or affiliates will take, directly or indirectly, any action designed or intended to stabilize or manipulate the price of any security of the Company, or which would reasonably be expected to cause or result in, stabilization or manipulation of the price of any security of the Company. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor the Subsidiaries will be or become, at any time prior to the termination of this Agreement, an “investment company,” as such term is defined in the Investment Company Act, assuming no change in the SEC’s current interpretation as to entities that are not considered an investment company. The Company and the Subsidiaries will use their best efforts to comply with all effective applicable provisions of the Sarbanes-Oxley Act and The Dodd–Frank Wall Street Reform and Consumer Protection Act.

(k) Use of Proceeds. The Company will use the net proceeds from the offering contemplated hereby in all material respects as described in the Prospectuses in the section entitled "Use of Proceeds."

(l) Aggregation. From and after the date of this Agreement, neither the Company, nor or any of its affiliates will, and the Company shall use its reasonable best efforts to ensure that no Person acting on their behalf will, directly or indirectly, make any offers or sales of any security or solicit any offers to buy any security, under circumstances that would cause this offering of the Securities by the Company to the Investor to be aggregated with other offerings by the Company in a manner that would require stockholder approval pursuant to the rules of the Principal Market on which any of the securities of the Company are listed or designated, unless stockholder approval is obtained before the closing of such subsequent transaction in accordance with the rules of such Principal Market.

(m) Other Transactions. During the term of this Agreement, the Company shall not enter into, announce or recommend to its stockholders any agreement, plan, arrangement or transaction in or of which the terms thereof would restrict, materially delay, conflict with or impair the ability or right of the Company to perform its obligations under the Transaction Documents, including, without limitation, the obligation of the Company to deliver the Purchase Shares and the Commitment Shares to the Investor in accordance with the terms of the Transaction Documents.

(n) Limitation on Variable Rate Transactions. From and after the date of this Agreement until the Maturity Date, the Company and its Subsidiaries shall be prohibited from effecting or entering into an agreement to effect any issuance by the Company or any of its Subsidiaries of Common Stock or Common Stock Equivalents (or a combination of units thereof) involving a Variable Rate Transaction, other than in connection with an Exempt Issuance (as defined below). The Investor shall be entitled to seek injunctive relief against the Company and its Subsidiaries to preclude any such issuance, which remedy shall be in addition to any right to collect damages, without the necessity of showing economic loss and without any bond or other security being required. "Variable Rate Transaction" means a transaction in which the Company (i) issues or sells any equity or debt securities that are convertible into, exchangeable or exercisable for, or include the right to receive additional shares of Common Stock or Common Stock Equivalents either (A) at a conversion price, exercise price, exchange rate or other price that is based upon and/or varies with the trading prices of or quotations for the Common Stock at any time after the initial issuance of such equity or debt securities (including, without limitation, pursuant to any "cashless exercise" provision), or (B) with a conversion, exercise or exchange price that is subject to being reset at some future date after the initial issuance of such equity or debt security or upon the occurrence of specified or contingent events directly or indirectly related to the business of the Company or the market for the Common Stock (including, without limitation, any "full ratchet" or "weighted average" anti-dilution provisions, but not including any standard anti-dilution protection for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction), (ii) issues or sells any equity or debt securities, including without limitation, Common Stock or Common Stock Equivalents, either (A) at a price that is subject to being reset at some future date after the initial issuance of such debt or equity security or upon the occurrence of specified or contingent events directly or indirectly related to the business of the Company or the market for the Common Stock (other than standard anti-dilution protection for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction), or (B) that is subject to or contains any put, call, redemption, buy-back, price-reset or other similar provision or mechanism (including, without limitation, a "Black-Scholes" put or call right) that provides for the issuance of additional equity securities of the Company or the payment of cash by the Company, or (iii) enters into any agreement, including, but not limited to, an "equity line of credit", "at-the-market offering" that is not an Exempt Issuance or other continuous offering or similar offering of Common Stock or Common Stock Equivalents, whereby the Company may sell Common Stock or Common Stock Equivalents at a future determined price. "Exempt Issuance" means the issuance of (a) Common Stock, options or other equity incentive awards to employees, officers, directors or vendors of the Company pursuant to any equity incentive plan duly adopted for such purpose, by the Board of Directors or a majority of the members of a committee of directors established for such purpose, (b) any Securities issued to the Investor pursuant to this Agreement, (c) shares of Common Stock, Common Stock Equivalents or other securities issued to the Investor pursuant to any other existing or future contract, agreement or arrangement between the Company and the Investor, (d) shares of Common Stock, Common Stock Equivalents or other securities upon the exercise, exchange or conversion of any shares of Common Stock, Common Stock Equivalents or other securities held by the Investor at any time, (e) any securities issued upon the exercise or exchange of or conversion of any Common Stock Equivalents issued and outstanding on the date of this Agreement, provided that such securities or Common Stock Equivalents referred to in this clause (e) have not been amended since the date of this Agreement to increase the number of such securities or Common Stock underlying such securities or to decrease the exercise price, exchange price or conversion price of such securities, (f) Common Stock Equivalents that are convertible into, exchangeable or exercisable for, or include the right to receive shares of Common Stock at a conversion price, exercise price, exchange rate or other price (which may be below the then current market price of the Common Stock) that is fixed at the time of initial issuance of such Common Stock Equivalents (subject only to standard anti-dilution protection for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction), which fixed conversion price, exercise price, exchange rate or other price shall not at any time after the initial issuance of such Common Stock Equivalent be based upon or varying with the trading prices of or quotations for the Common Stock or subject to being reset at some future date, (g) securities issued pursuant to acquisitions, divestitures, licenses, partnerships, collaborations or strategic transactions approved by the Board of Directors or a majority of the members of a committee of directors established for such purpose, which acquisitions, divestitures, licenses, partnerships, collaborations or strategic transactions can have a Variable Rate Transaction component, provided that any such issuance shall only be to a Person (or to the equity holders of a Person) which is, itself or through its subsidiaries, an operating company or an asset in a business synergistic with the business of the Company and shall provide to the Company additional benefits in addition to the investment of funds, but shall not include a transaction in which the Company is issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities, (h) Common Stock issued pursuant to an "at-the-market offering" by the Company exclusively through a registered broker-dealer acting as agent of the Company pursuant to a written agreement between the Company and such registered broker-dealer or (i) securities (such as warrants) or Common Stock issued in connection with future financings or offerings of the Company, such as but not limited to, registered direct offerings, rights offerings, and confidentially marketed public offerings; provided such transactions do not involve a Variable Rate Transaction.

6. TRANSFER AGENT INSTRUCTIONS.

(a) On the date of this Agreement, the Company shall issue to the Transfer Agent irrevocable instructions, in the form substantially similar to those used by the Investor in substantially similar transactions and in any case agreed to by the Investor, to issue the Securities in accordance with the terms of this Agreement (the "Irrevocable Transfer Agent Instructions"). The Company warrants to the Investor that no instruction other than as set forth in this Section 6 will be given by the Company to the Transfer Agent with respect to the Securities, and the Securities shall otherwise be freely transferable on the books and records of the Company.

(b) On the earlier of (i) the Commencement Date and (ii) such time that the Investor shall request, provided all conditions of Rule 144 under the Securities Act are met, the Company shall, no later than two (2) Business Days following the delivery by the Investor to the Company or the Transfer Agent of one or more legended certificates or book-entry statements representing the Commitment Shares (which certificates or book-entry statements the Investor shall promptly deliver on or prior to the first to occur of the events described in clauses (i) and (ii) of this sentence), as directed by the Investor, issue and deliver (or cause to be issued and delivered) to the Investor, as requested by the Investor, either: (A) a certificate or book-entry statement representing such Commitment Shares that is free from all restrictive and other legends or (B) a number of shares of Common Stock equal to the number of Commitment Shares represented by the certificate(s) or book-entry statement(s) so delivered by the Investor as DWAC Shares. The Company shall take all actions to carry out the intent and accomplish the purposes of the immediately preceding sentence, including, without limitation, delivering all such legal opinions, consents, certificates, resolutions and instructions to the Transfer Agent, and any successor transfer agent of the Company, as may be requested from time to time by the Investor or necessary or desirable to carry out the intent and accomplish the purposes of the immediately preceding sentence. On the Commencement Date, the Company shall issue to the Transfer Agent, and any subsequent transfer agent, (i) instructions in the form substantially similar to those used by the Investor in substantially similar transactions (the "Commencement Transfer Agent Instructions") and (ii) the notice of effectiveness of the Registration Statement in the form attached as an exhibit to the Registration Rights Agreement (the "Notice of Effectiveness of Registration Statement"), in each case to issue the Commitment Shares and the Purchase Shares in accordance with the terms of this Agreement and the Registration Rights Agreement. All Purchase Shares to be issued from and after Commencement to or for the benefit of the Investor pursuant to this Agreement shall be issued only as DWAC Shares. The Company represents and warrants to the Investor that, while this Agreement is effective, no instruction other than the Commencement Transfer Agent Instructions and the Notice of Effectiveness of Registration Statement referred to in this Section 6(b) will be given by the Company to the Transfer Agent with respect to the Purchase Shares or the Commitment Shares from and after Commencement, and the Purchase Shares and the Commitment Shares covered by the Registration Statement shall otherwise be freely transferable on the books and records of the Company. The Company agrees that if the Company fails to fully comply with the provisions of this Section 6(b) within five (5) Business Days of the Investor providing the deliveries referred to above, the Company shall, at the Investor's written instruction, purchase such shares of Common Stock containing the Restrictive Legend from the Investor at the greater of the (i) purchase price paid for such shares of Common Stock (as applicable) and (ii) the Closing Sale Price of the Common Stock on the date of the Investor's written instruction.

7. CONDITIONS TO THE COMPANY'S RIGHT TO COMMENCE SALES OF COMMON STOCK.

The right of the Company hereunder to commence sales of the Purchase Shares on the Commencement Date is subject to the satisfaction or, where legally permissible, the waiver of each of the following conditions:

(a) The Investor shall have executed each of the Transaction Documents and delivered the same to the Company;

(b) No stop order with respect to the Registration Statement shall be pending or threatened by the SEC; and

(c) The representations and warranties of the Investor shall be true and correct in all material respects as of the Execution Date and as of the Commencement Date as though made at that time.

8. CONDITIONS TO THE INVESTOR'S OBLIGATION TO PURCHASE COMMON STOCK.

The obligation of the Investor to buy Purchase Shares under this Agreement is subject to the satisfaction or, where legally permissible, the waiver of each of the following conditions on or prior to the Commencement Date and, once such conditions have been initially satisfied, there shall not be any ongoing obligation to satisfy such conditions after the Commencement has occurred:

(a) The Company shall have executed each of the Transaction Documents and delivered the same to the Investor;

(b) The Common Stock shall be listed or quoted on the Principal Market and all Securities to be issued by the Company to the Investor pursuant to this Agreement shall have been approved for listing on the Principal Market in accordance with the applicable rules and regulations of the Principal Market, subject only to official notice of issuance;

(c) The Investor shall have received the opinions of the Company's legal counsel dated as of the Commencement Date substantially in the forms agreed to prior to the date of this Agreement by the Company's legal counsel and the Investor's legal counsel;

(d) The representations and warranties of the Company contained in this Agreement shall be true and correct in all material respects (except to the extent that any of such representations and warranties is qualified as to materiality, in which case, any of such representations and warranties shall be true and correct as so qualified) as of the Execution Date and as of the Commencement Date as though made at that time (except for representations and warranties that speak as of a specific date, which shall be true and correct in all material respects as of such date) and the Company shall have performed, satisfied and complied in all material respects with the covenants, agreements and conditions required by the Transaction Documents to be performed, satisfied or complied with by the Company at or prior to the Commencement Date. The Investor shall have received a certificate, executed by the CEO, President or CFO of the Company, dated as of the Commencement Date, to the foregoing effect in the form attached hereto as **Exhibit A**;

(e) The Board of Directors shall have adopted resolutions in connection with this Agreement and the transactions contemplated hereby which shall be in full force and effect without any amendment or supplement thereto as of the Commencement Date;

(f) As of the Commencement Date, the Company shall have reserved out of its authorized and unissued Common Stock the Reserve Amount, solely for the purpose of effecting purchases of Purchase Shares hereunder;

(g) The Irrevocable Transfer Agent Instructions, the Commencement Transfer Agent Instructions and the Notice of Effectiveness of Registration Statement shall have been delivered to the Company's Transfer Agent (or any successor transfer agent) and acknowledged in writing by the Company and the Company's Transfer Agent (or any successor transfer agent), and the Commitment Shares shall have been issued directly to the Investor electronically as DWAC Shares;

(h) The Company shall have delivered to the Investor a certificate evidencing the incorporation and good standing of the Company in the State of Delaware issued by the Secretary of State of the State of Delaware as of a date within ten (10) Business Days of the Commencement Date;

(i) The Company shall have delivered to the Investor a certified copy of the Certificate of Incorporation as certified by the Secretary of State of the State of Delaware within ten (10) Business Days of the Commencement Date;

(j) The Company shall have delivered to the Investor an secretary's certificate executed by the Secretary of the Company, dated as of the Commencement Date, in the form attached hereto as **Exhibit B**;

(k) The Registration Statement shall continue to be effective and no stop order with respect to the Registration Statement shall be pending or threatened by the SEC. The Company shall have a maximum dollar amount certain of Common Stock registered under the Registration Statement which is sufficient to issue to the Investor not less than (i) the full Available Amount worth of Purchase Shares plus (ii) all of the Commitment Shares. The Current Report and the Initial Prospectus Supplement each shall have been filed with the SEC, as required pursuant to Section 5(a), and copies of the Prospectus shall have been delivered to the Investor in accordance with the terms of the Registration Rights Agreement. The Prospectus shall be current and available for issuances and sales of all of the Securities by the Company to the Investor. Any other Prospectus Supplements required to have been filed by the Company with the SEC under the Securities Act at or prior to the Commencement Date shall have been filed with the SEC within the applicable time periods prescribed for such filings under the Securities Act. All reports, schedules, registrations, forms, statements, information and other documents required to have been filed by the Company with the SEC at or prior to the Commencement Date pursuant to the reporting requirements of the Exchange Act shall have been filed with the SEC within the applicable time periods prescribed for such filings under the Exchange Act;

(l) No Event of Default has occurred, or any event which, after notice and/or lapse of time, would become an Event of Default has occurred;

(m) All federal, state and local governmental laws, rules and regulations applicable to the transactions contemplated by the Transaction Documents and necessary for the execution, delivery and performance of the Transaction Documents and the consummation of the transactions contemplated thereby in accordance with the terms thereof shall have been complied with, and all consents, authorizations and orders of, and all filings and registrations with, all federal, state and local courts or governmental agencies and all federal, state and local regulatory or self-regulatory agencies necessary for the execution, delivery and performance of the Transaction Documents and the consummation of the transactions contemplated thereby in accordance with the terms thereof shall have been obtained or made, including, without limitation, in each case those required under the Securities Act, the Exchange Act, applicable state securities or "Blue Sky" laws or applicable rules and regulations of the Principal Market, or otherwise required by the SEC, the Principal Market or any state securities regulators;

(n) No statute, regulation, order, decree, writ, ruling or injunction shall have been enacted, entered, promulgated, threatened or endorsed by any federal, state, local or foreign court or governmental authority of competent jurisdiction which prohibits the consummation of or which would materially modify or delay any of the transactions contemplated by the Transaction Documents;

(o) No action, suit or proceeding before any federal, state, local or foreign arbitrator or any court or governmental authority of competent jurisdiction shall have been commenced or threatened, and no inquiry or investigation by any federal, state, local or foreign governmental authority of competent jurisdiction shall have been commenced or threatened, against the Company, or any of the officers, directors or affiliates of the Company, seeking to restrain, prevent or change the transactions contemplated by the Transaction Documents, or seeking material damages in connection with such transactions; and

(p) The Company shall have provided the Investor with the information requested by the Investor in connection with its due diligence requests in accordance with the terms of Section 5(f) hereof.

9. INDEMNIFICATION.

In consideration of the Investor's execution and delivery of the Transaction Documents and acquiring the Securities hereunder and in addition to all of the Company's other obligations under the Transaction Documents, the Company shall defend, protect, indemnify and hold harmless the Investor and all of its affiliates, stockholders, officers, directors, employees and direct or indirect investors and any of the foregoing Person's agents or other representatives (including, without limitation, those retained in connection with the transactions contemplated by this Agreement) (collectively, the "Indemnitees") from and against any and all actions, causes of action, suits, claims, losses, costs, penalties, fees, liabilities and damages, and expenses in connection therewith (irrespective of whether any such Indemnitee is a party to the action for which indemnification hereunder is sought), and including reasonable attorneys' fees and disbursements (the "Indemnified Liabilities"), incurred by any Indemnitee as a result of, or arising out of, relating to: (a) any misrepresentation or breach of any representation or warranty made by the Company in the Transaction Documents or any other certificate, instrument or document contemplated hereby or thereby, (b) any breach of any covenant, agreement or obligation of the Company contained in the Transaction Documents or any other certificate, instrument or document contemplated hereby or thereby, (c) any cause of action, suit or claim brought or made against such Indemnitee and arising out of or resulting from the execution, delivery, performance or enforcement of the Transaction Documents or any other certificate, instrument or document contemplated hereby or thereby, (d) any violation of the Securities Act, the Exchange Act, state securities or “Blue Sky” laws, or the rules and regulations of the Principal Market in connection with the transactions contemplated by the Transaction Documents by the Company or any of its Subsidiaries, affiliates, officers, directors or employees, (e) any untrue statement or alleged untrue statement of a material fact contained, or incorporated by reference, in the Registration Statement or any amendment thereto or any omission or alleged omission to state therein, or in any document incorporated by reference therein, a material fact required to be stated therein or necessary to make the statements therein not misleading, or (f) any untrue statement or alleged untrue statement of a material fact contained, or incorporated by reference, in the Prospectus, or any omission or alleged omission to state therein, or in any document incorporated by reference therein, a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading; provided, however, that (I) the indemnity contained in clause (c) of this Section 9 shall not apply to any Indemnified Liabilities which directly and primarily result from the fraud, gross negligence or willful misconduct of an Indemnitee, (II) the indemnity contained in clauses (d), (e) and (f) of this Section 9 shall not apply to any Indemnified Liabilities to the extent, but only to the extent, arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by or on behalf of the Investor expressly for use in any Prospectus Supplement (it being hereby acknowledged and agreed that the written information set forth on **Exhibit C** attached hereto is the only written information furnished to the Company by or on behalf of the Investor expressly for use in the Initial Prospectus Supplement), if the Prospectus was timely made available by the Company to the Investor pursuant to terms of the Transaction Documents, (III) the indemnity contained in clauses (d), (e) and (f) of this Section 9 shall not inure to the benefit of the Investor to the extent such Indemnified Liabilities are based on a failure of the Investor to deliver or to cause to be delivered the Prospectus made available by the Company, if such Prospectus was timely made available by the Company pursuant to terms of the Transaction Documents, and if delivery of the Prospectus would have cured the defect giving rise to such Indemnified Liabilities, and (IV) the indemnity in this Section 9 shall not apply to amounts paid in settlement of any claim if such settlement is effected without the prior written consent of the Company, which consent shall not be unreasonably withheld, conditioned or delayed. To the extent that the foregoing undertaking by the Company may be unenforceable for any reason, the Company shall make the maximum contribution to the payment and satisfaction of each of the Indemnified Liabilities which is permissible under applicable law; provided that no seller of Securities guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any seller of Securities who was not guilty of fraudulent misrepresentation. Payment under this indemnification shall be made within thirty (30) days from the date the Investor makes written request for it. A certificate containing reasonable detail as to the amount of such indemnification submitted to the Company by Investor shall be conclusive evidence, absent manifest error, of the amount due from the Company to Investor; provided that the Indemnitee shall undertake to repay any amount paid to it hereunder if it is ultimately determined, by a final and non-appealable order of a court of competent jurisdiction, that the Indemnitee is not entitled to be indemnified against such Indemnified Liabilities by the Company pursuant to this Agreement. If any action shall be brought against any Indemnitee in respect of which indemnity may be sought pursuant to this Agreement, such Indemnitee shall promptly notify the Company in writing, and the Company shall have the right to assume the defense thereof with counsel of its own choosing reasonably acceptable to the Indemnitee. Any Indemnitee shall have the right to employ separate counsel in any such action and participate in the defense thereof, but the fees and expenses of such counsel shall be at the expense of such Indemnitee, except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is, in the reasonable opinion of such separate counsel, a material conflict on any material issue between the position of the Company and the position of such Indemnitee, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel.

10. EVENTS OF DEFAULT.

An "Event of Default" shall be deemed to have occurred at any time as any of the following events occurs:

(a) the effectiveness of the Registration Statement registering the Securities lapses for any reason (including, without limitation, the issuance of a stop order or similar order), the Registration Statement is unavailable for the sale by the Company to the Investor (or the resale by the Investor) of any or all of the Securities to be issued to the Investor under the Transaction Documents, and any such lapse or unavailability continues for a period of ten (10) consecutive Business Days or for more than an aggregate of thirty (30) Business Days in any 365-day period, but excluding a lapse or unavailability where (i) the Company terminates a registration statement after the Investor has confirmed in writing that all of the Securities covered thereby have been resold or (ii) the Company supersedes one registration statement with another registration statement, including (without limitation) by terminating a prior registration statement when it is effectively replaced with a new registration statement covering Securities (provided in the case of this clause (ii) that all of the Securities covered by the superseded (or terminated) registration statement that have not theretofore been resold are included in the superseding (or new) registration statement);

(b) the suspension of the Common Stock from trading or the failure of the Common Stock to be listed on the Principal Market for a period of one (1) Business Day, provided that the Company may not direct the Investor to purchase any Common Stock during any such suspension;

(c) the delisting of the Common Stock from the Nasdaq Global Market provided, however, that the Common Stock are not immediately thereafter trading on the New York Stock Exchange, the Nasdsaq Global Select Market, The Nasdaq Capital Market, the NYSE Arca, the OTC Bulletin Board or OTC Markets (or nationally recognized successor to any of the foregoing);

(d) the failure for any reason by the Transfer Agent to issue Purchase Shares to the Investor within three (3) Business Days after Purchase Date, Accelerated Purchase Date or Additional Accelerated Purchase Date, as applicable, on which the Investor is entitled to receive such Purchase Shares;

(e) the Company breaches any representation, warranty, covenant or other term or condition under any Transaction Document if such breach could have a Material Adverse Effect and except, in the case of a breach of a covenant which is reasonably curable, only if such breach continues for a period of at least five (5) Business Days;

(f) if any Person commences a proceeding against the Company pursuant to or within the meaning of any Bankruptcy Law;

(g) if the Company is at any time insolvent, or pursuant to or within the meaning of any Bankruptcy Law, (i) commences a voluntary case, (ii) consents to the entry of an order for relief against it in an involuntary case, (iii) consents to the appointment of a Custodian of it or for all or substantially all of its property, or (iv) makes a general assignment for the benefit of its creditors or is generally unable to pay its debts as the same become due;

(h) a court of competent jurisdiction enters an order or decree under any Bankruptcy Law that (i) is for relief against the Company in an involuntary case, (ii) appoints a Custodian of the Company or for all or substantially all of its property, or (iii) orders the liquidation of the Company or any Subsidiary;

(i) if at any time the Company is not eligible to transfer its Common Stock electronically as DWAC Shares; or

(j) if at any time after the Commencement Date, the Exchange Cap is reached (to the extent the Exchange Cap is applicable pursuant to Section 2(d) hereof) and the Company's stockholders have not approved the transactions contemplated by this Agreement in accordance with the applicable rules and regulations of the Nasdaq Global Market, any other Principal Market on which the Common Stock may be listed or quoted after the date of this Agreement, the Certificate of Incorporation and the Bylaws.

In addition to any other rights and remedies under applicable law and this Agreement, so long as an Event of Default has occurred and is continuing, or if any event which, after notice and/or lapse of time, would become an Event of Default, has occurred and is continuing, or so long as the Closing Sale Price is below the Floor Price, the Company shall not deliver to the Investor any Regular Purchase Notice or Accelerated Purchase Notice, and the Investor shall not purchase any Common Stock under this Agreement.

11. TERMINATION

This Agreement may be terminated only as follows:

(a) If pursuant to or within the meaning of any Bankruptcy Law, the Company commences a voluntary case or any Person commences a proceeding against the Company, a Custodian is appointed for the Company or for all or substantially all of its property, or the Company makes a general assignment for the benefit of its creditors (any of which would be an Event of Default as described in Sections 10(f), 10(g) and 10(h) hereof), this Agreement shall automatically terminate without any liability or payment to the Company (except as set forth below) without further action or notice by any Person.

(b) In the event that the Commencement shall not have occurred on or before April 30, 2019, due to the failure to satisfy the conditions set forth in Sections 7 and 8 above with respect to the Commencement, either the Company or the Investor shall have the option to terminate this Agreement at the close of business on such date or thereafter without liability of any party to any other party (except as set forth below); provided, however, that the right to terminate this Agreement under this Section 11(b) shall not be available to any party if such party is then in breach of any covenant or agreement contained in this Agreement or any representation or warranty of such party contained in this Agreement fails to be true and correct such that the conditions set forth in Section 7(c) or Section 8(d), as applicable, could not then be satisfied.

(c) At any time after the Commencement Date, the Company shall have the option to terminate this Agreement for any reason or for no reason by delivering notice (a "Company Termination Notice") to the Investor electing to terminate this Agreement without any liability whatsoever of any party to any other party under this Agreement (except as set forth below in this Section 11). The Company Termination Notice shall not be effective until one (1) Business Day after it has been received by the Investor.

(d) This Agreement shall automatically terminate on the date that the Company sells and the Investor purchases the full Available Amount as provided herein, without any action or notice on the part of any party and without any liability whatsoever of any party to any other party under this Agreement (except as set forth below).

(e) If for any reason or for no reason the full Available Amount has not been purchased in accordance with Section 2 of this Agreement by the Maturity Date, this Agreement shall automatically terminate on the Maturity Date, without any action or notice on the part of any party and without any liability whatsoever of any party to any other party under this Agreement (except as set forth below).

Except as set forth in Sections 11(a) (in respect of an Event of Default under Sections 10(f), 10(g), 10(h), 11(d) and 11(e)), any termination of this Agreement pursuant to this Section 11 shall be effected by written notice from the Company to the Investor, or the Investor to the Company, as the case may be, setting forth the basis for the termination hereof. The representations and warranties and covenants of the Company and the Investor contained in Sections 3, 4, 5, and 6 hereof, the indemnification provisions set forth in Section 9 hereof and the agreements and covenants set forth in Sections 10, 11 and 12 shall survive the Commencement and any termination of this Agreement. No termination of this Agreement shall (i) affect the Company's or the Investor's rights or obligations under this Agreement with respect to pending Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases and the Company and the Investor shall complete their respective obligations with respect to any pending Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases under this Agreement or (ii) be deemed to release the Company or the Investor from any liability for intentional misrepresentation or willful breach of any of the Transaction Documents.

12. MISCELLANEOUS.

(a) Governing Law; Jurisdiction; Jury Trial. The corporate laws of the State of Delaware shall govern all issues concerning the relative rights of the Company and its stockholders. All other questions concerning the construction, validity, enforcement and interpretation of this Agreement and the other Transaction Documents shall be governed by the internal laws of the State of New York, without giving effect to any choice of law or conflict of law provision or rule (whether of the State of New York or any other jurisdictions) that would cause the application of the laws of any jurisdictions other than the State of New York. Each party hereby irrevocably submits to the exclusive jurisdiction of and venue in the U.S. District Court for the Southern District of New York or, if that court does not have subject matter jurisdiction, in any state court located in The City and County of New York, for the adjudication of any dispute hereunder or under the other Transaction Documents or in connection herewith or therewith, or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof to such party at the address for such notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law. **EACH PARTY HEREBY IRREVOCABLY WAIVES ANY RIGHT IT MAY HAVE, AND AGREES NOT TO REQUEST, A JURY TRIAL FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HEREWITH OR ARISING OUT OF THIS AGREEMENT OR ANY TRANSACTION CONTEMPLATED HEREBY.**

(b) Counterparts. This Agreement may be executed in two or more identical counterparts, all of which shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to the other party; provided that a facsimile signature or signature delivered by e-mail in a ".pdf" format data file shall be considered due execution and shall be binding upon the signatory thereto with the same force and effect as if the signature were an original signature.

(c) Headings. The headings of this Agreement are for convenience of reference and shall not form part of, or affect the interpretation of, this Agreement.

(d) Severability. If any provision of this Agreement shall be invalid or unenforceable in any jurisdiction, such invalidity or unenforceability shall not affect the validity or enforceability of the remainder of this Agreement in that jurisdiction or the validity or enforceability of any provision of this Agreement in any other jurisdiction.

(e) Entire Agreement; Amendment. This Agreement supersedes all other prior oral or written agreements between the Investor, the Company, their affiliates and Persons acting on their behalf with respect to the subject matter hereof, and this Agreement, the other Transaction Documents and the instruments referenced herein contain the entire understanding of the parties with respect to the matters covered herein and therein and, except as specifically set forth herein or therein, neither the Company nor the Investor makes any representation, warranty, covenant or undertaking with respect to such matters. The Company acknowledges and agrees that it has not relied on, in any manner whatsoever, any representations or statements, written or oral, other than as expressly set forth in the Transaction Documents. The Investor acknowledges and agrees that it has not relied on, in any manner whatsoever, any representations or statements, written or oral, other than as expressly set forth in the Transaction Documents. No provision of this Agreement may be amended other than by a written instrument signed by both parties hereto.

(f) Notices. Any notices, consents or other communications required or permitted to be given under the terms of this Agreement must be in writing and will be deemed to have been delivered: (i) upon receipt when delivered personally; (ii) upon receipt when sent by facsimile or email (provided confirmation of transmission is mechanically or electronically generated and kept on file by the sending party); or (iii) one Business Day after deposit with a nationally recognized overnight delivery service, in each case properly addressed to the party to receive the same. The addresses for such communications shall be:

If to the Company:

KemPharm, Inc.
1180 Celebration Boulevard
Suite 103
Celebration, FL 34747
Telephone: (321) 939-3416
E-mail: lclifton@kempharm.com
Attention: R. LaDuane Clifton

With a copy to (which shall not constitute notice or service of process):

Cooley LLP
1299 Pennsylvania Avenue, NW, Suite 700
Washington, DC 2004
E-mail: bsiler@cooley.com
Attention: Brent Siler

If to the Investor:

Lincoln Park Capital Fund, LLC
440 North Wells, Suite 410
Chicago, IL 60654
Telephone: 312.822.9300
Facsimile: 312.822.9301
E-mail: jscheinfeld@lpcfunds.com/jcope@lpcfunds.com
Attention: Josh Scheinfeld/Jonathan Cope

With a copy to (which shall not constitute notice or service of process):

K&L Gates, LLP
200 South Biscayne Boulevard
Suite 3900
Miami, Florida 33131
Telephone: 305.539.3300
Facsimile: 305.358.7095
E-mail: clayton.parker@klgates.com/matthew.ogurick@klgates.com
Attention: Clayton E. Parker, Esq./Matthew Ogurick, Esq.

or at such other address and/or facsimile number and/or to the attention of such other Person as the recipient party has specified by written notice given to each other party three (3) Business Days prior to the effectiveness of such change. Written confirmation of receipt (A) given by the recipient of such notice, consent or other communication, (B) mechanically or electronically generated by the sender's facsimile machine or email account containing the time, date, and recipient facsimile number or email address, as applicable, and an image of the first page of such transmission or (C) provided by a nationally recognized overnight delivery service, shall be rebuttable evidence of personal service, receipt by facsimile or receipt from a nationally recognized overnight delivery service in accordance with clause (i), (ii) or (iii) above, respectively.

(g) Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties and their respective successors and assigns. The Company shall not assign this Agreement or any rights or obligations hereunder without the prior written consent of the Investor, including by merger or consolidation. The Investor may not assign its rights or obligations under this Agreement.

(h) No Third Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto and their respective permitted successors and assigns and, except as set forth in Section 9, is not for the benefit of, nor may any provision hereof be enforced by, any other Person.

(i) Publicity. The Company shall afford the Investor and its counsel with the opportunity to review and comment upon, shall consult with the Investor and its counsel on the form and substance of, and shall give due consideration to all such comments from the Investor or its counsel on, any press release, SEC filing or any other public disclosure by or on behalf of the Company relating to the Investor, its purchases hereunder or any aspect of the Transaction Documents or the transactions contemplated thereby, not less than 24 hours prior to the issuance, filing or public disclosure thereof. The Investor must be provided with a final version of any information related to Lincoln Park contained within such press release, SEC filing or other public disclosure at least 24 hours prior to any release, filing or use by the Company thereof, or such shorter time as is reasonably necessary. The Company agrees and acknowledges that its failure to fully comply with this provision constitutes a Material Adverse Effect.

(j) Further Assurances. Each party shall do and perform, or cause to be done and performed, all such further acts and things, and shall execute and deliver all such other agreements, certificates, instruments and documents, as the other party may reasonably request in order to carry out the intent and accomplish the purposes of this Agreement and the consummation of the transactions contemplated hereby.

(k) No Financial Advisor, Placement Agent, Broker or Finder. The Company represents and warrants to the Investor that, except as disclosed in Schedule 4(x), it has not engaged any financial advisor, placement agent, broker or finder in connection with the transactions contemplated hereby. The Investor represents and warrants to the Company that it has not engaged any financial advisor, placement agent, broker or finder in connection with the transactions contemplated hereby. The Company shall be responsible for the payment of any fees or commissions, if any, of any financial advisor, placement agent, broker or finder relating to or arising out of the transactions contemplated hereby. The Company shall pay, and hold the Investor harmless against, any liability, loss or expense (including, without limitation, reasonable attorneys' fees and out of pocket expenses) arising in connection with any such claim.

(l) No Strict Construction. The language used in this Agreement will be deemed to be the language chosen by the parties to express their mutual intent, and no rules of strict construction will be applied against any party.

(m) Remedies, Other Obligations, Breaches and Injunctive Relief. The Investor's remedies provided in this Agreement, including, without limitation, the Investor's remedies provided in Section 9, shall be cumulative and in addition to all other remedies available to the Investor under this Agreement, at law or in equity (including a decree of specific performance and/or other injunctive relief), no remedy of the investor contained herein shall be deemed a waiver of compliance with the provisions giving rise to such remedy and nothing herein shall limit the Investor's right to pursue actual damages for any failure by the other party to comply with the terms of this Agreement. The parties acknowledge that a breach by any party of its obligations hereunder will cause irreparable harm to the non-breaching party and that the remedy at law for any such breach may be inadequate. The parties therefore agree that, in the event of any such breach or threatened breach, the non-breaching party shall be entitled, in addition to all other available remedies, to an injunction restraining any breach, without the necessity of showing economic loss and without any bond or other security being required.

(n) Enforcement Costs. If: (i) this Agreement is placed by the Investor or the Company in the hands of an attorney for enforcement or is enforced by the Investor or the Company through any legal proceeding; (ii) an attorney is retained to represent the Investor or the Company in any bankruptcy, reorganization, receivership or other proceedings affecting creditors' rights and involving a claim under this Agreement; or (iii) an attorney is retained to represent the Investor or the Company in any other proceedings whatsoever in connection with this Agreement, then the party against which redress is sought under this section shall pay all reasonable costs and expenses including attorneys' fees incurred in connection therewith to the party incurring such costs and expenses, as incurred, in addition to all other amounts due hereunder.

(o) Waivers. No provision of this Agreement may be waived other than in a written instrument signed by the party against whom enforcement of such waiver is sought. No failure or delay in the exercise of any power, right or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise of any such power, right or privilege preclude other or further exercise thereof or of any other right, power or privilege.

(p) Adjustments for Share Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement shall be adjusted to take into account any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction effected with respect to the Common Stock except as specifically stated herein.

*** * * * ***

IN WITNESS WHEREOF, the Investor and the Company have caused this Agreement to be duly executed as of the Execution Date.

THE COMPANY:

KEMPHARM, INC.

By: /s/ R. LaDuane Clifton
Name: R. LaDuane Clifton
Title: Chief Financial Officer

INVESTOR:

LINCOLN PARK CAPITAL FUND, LLC
BY: LINCOLN PARK CAPITAL, LLC
BY: ALEX NOAH INVESTORS, INC.

By: /s/ Jonathan Cope
Name: Jonathan Cope
Title: President

SCHEDULES

Schedule 4(c) Capitalization
Schedule 4(x) Agent Fees

EXHIBITS

Exhibit A	Form of Officer's Certificate
Exhibit B	Form of Secretary's Certificate
Exhibit C	Information About Investor Furnished to the Company

DISCLOSURE SCHEDULES

Schedule 4(c) Capitalization

Schedule 4(x) – Agent Fees

EXHIBIT A

FORM OF OFFICER'S CERTIFICATE

This Officer's Certificate ("Certificate") is being delivered pursuant to Section 8(d) of that certain Purchase Agreement dated as of February 28, 2019, ("Purchase Agreement"), by and between **KEMPHARM, INC.**, a Delaware corporation (the "Company"), and **LINCOLN PARK CAPITAL FUND, LLC** (the "Investor"). Terms used herein and not otherwise defined shall have the meanings ascribed to them in the Purchase Agreement.

The undersigned, _____, _____ of the Company, hereby certifies as follows:

1. I am the _____ of the Company and make the statements contained in this Certificate;

2. The representations and warranties of the Company contained in the Purchase Agreement are true and correct in all material respects (except to the extent that any of such representations and warranties are qualified as to materiality in the Purchase Agreement, in which case, such representations and warranties are true and correct in all material respects as so qualified) as of the date of the Purchase Agreement and as of the Commencement Date as though made at that time (except for representations and warranties that speak as of a specific date, in which case such representations and warranties are true and correct in all material respects as of such date);

3. The Company has performed, satisfied and complied in all material respects with covenants, agreements and conditions required by the Transaction Documents to be performed, satisfied or complied with by the Company at or prior to the Commencement Date, to the extent not otherwise waived.

4. The Company has not taken any steps, and does not currently expect to take any steps, to seek protection pursuant to any Bankruptcy Law nor does the Company or any of its Subsidiaries have any knowledge or reason to believe that its creditors intend to initiate involuntary bankruptcy or insolvency proceedings. The Company is financially solvent and is generally able to pay its debts as they become due.

IN WITNESS WHEREOF, I have hereunder signed my name on this ___ day of _____.

_____

Name:
Title:

EXHIBIT B

FORM OF SECRETARY'S CERTIFICATE

This Secretary's Certificate ("Certificate") is being delivered pursuant to Section 8(j) of that certain Purchase Agreement dated as of February 28, 2019 (the "Purchase Agreement"), by and between **KEMPHARM, INC.**, a Delaware corporation (the "Company") and **LINCOLN PARK CAPITAL FUND, LLC** (the "Investor"). Terms used herein and not otherwise defined shall have the meanings ascribed to them in the Purchase Agreement.

The undersigned, _____, Secretary of the Company, hereby certifies as follows:

1. I am the Secretary of the Company and make the statements contained in this Secretary's Certificate.

2. Attached hereto as Exhibit A are true, correct and complete copies of the Company's Certificate of Incorporation and Bylaws, as amended through the date hereof, and no action has been taken by the Company, its directors, officers or stockholders, in contemplation of the filing of any further amendment relating to or affecting such documents.

3. Attached hereto as Exhibit B are true, correct and complete copies of the resolutions either duly adopted by the Board of Directors on _____, at which a quorum was present and acting throughout, or executed by all directors in accordance with Delaware General Corporations Law. Such resolutions have not been amended, modified or rescinded and remain in full force and effect and such resolutions are the only resolutions adopted by the Board of Directors or the stockholders of the Company relating to or affecting (i) the entering into and performance of the Purchase Agreement, or the issuance, offering and sale of the Purchase Shares and the Commitment Shares and (ii) and the performance of the Company of its obligation under the Transaction Documents as contemplated therein.

4. As of the date hereof, the authorized, issued and reserved capital stock of the Company is as set forth on Exhibit C hereto.

IN WITNESS WHEREOF, I have hereunder signed my name on this ___ day of _____ 2019.

_____
Secretary

EXHIBIT C

Information About The Investor Furnished To The Company By The Investor
Expressly For Use In Connection With Prospectuses

Information With Respect to Lincoln Park Capital

Immediately prior to the date of the Agreement, Lincoln Park Capital Fund, LLC, beneficially owned 300,000 shares of Common Stock. Josh Scheinfeld and Jonathan Cope, the Managing Members of Lincoln Park Capital, LLC, the manager of Lincoln Park Capital Fund, LLC, are deemed to be beneficial owners of all of the Common Stock owned by Lincoln Park Capital Fund, LLC. Messrs. Cope and Scheinfeld have shared voting and investment power over the shares being offered under the prospectus supplement filed with the SEC in connection with the transactions contemplated under the Agreement. Lincoln Park Capital, LLC is not a licensed broker dealer or an affiliate of a licensed broker dealer.

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, No. 333-216858 and No. 333-224062) on Form S-8 of KemPharm, Inc. of our report dated March 1, 2019, 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, 2018.

/s/ RSM US LLP

Orlando, Florida
March 1, 2019

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 1, 2019

/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 1, 2019

/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, 2018, 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 1, 2019

/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, 2018, 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 1, 2019

/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.