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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 17, 2015

KEMPHARM, INC.
(Exact name of registrant as specified in its charter)

Delaware		
(State or other jurisdiction of incorporation)		
001-36913		**20-5894398**
(Commission File No.)		**(IRS Employer Identification No.)**

2656 Crosspark Road, Suite 100
Coralville, IA 52241
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (319) 665-2575

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 1.01 Entry into a Material Definitive Agreement.

On December 17, 2015, KemPharm, Inc., a Delaware corporation (the "Company"), entered into a Second Amendment (the "Second Amendment") to the Facility Agreement (as amended, the "Facility Agreement"), by and between the Company and Deerfield Private Design Fund III, L.P. ("Deerfield"). The Second Amendment, among other things, eliminates the Company's obligation to obtain a consent from Deerfield prior to effecting an underwritten public offering of the Company's common stock. Except as modified by the Second Amendment, all terms and conditions of the Facility Agreement remain in full force and effect. The foregoing summary of the Second Amendment is not complete and is qualified in its entirety by reference to the Second Amendment, which is filed as an exhibit to this Current Report on Form 8-K (the "Report") and incorporated herein by reference.

Item 8.01 Other Events.

Updated Company Disclosure

On December 18, 2015, the Company filed with the Securities and Exchange Commission (the "SEC") a registration statement on Form S-1 (the "Registration Statement"), in connection with a proposed public offering of shares of the Company's common stock. The Registration Statement contains updated Company risk factor disclosure, as well as an updated description of certain aspects of the Company's business. Accordingly, the Company is filing information with this Report for the purpose of supplementing and updating the risk factor disclosure contained in the Company's prior public filings, including those discussed under the heading "Item 1A. Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2015, filed with the SEC on November 13, 2015. The Company is also updating certain aspects of the description of its business from the disclosure contained in the Company's prior public filings. The updated disclosures are filed as Exhibit 99.1 to this Report and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
10.1	Second Amendment to Facility Agreement, by and between the Company and Deerfield Private Design Fund III, L.P., dated as of December 17, 2015.
99.1	Updated Company Disclosure.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

KEMPHARM, INC.

Date: December 18, 2015

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

EXHIBIT INDEX

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99.1	Updated Company Disclosure.

Exhibit 10.1

SECOND AMENDMENT TO FACILITY AGREEMENT

SECOND AMENDMENT TO FACILITY AGREEMENT (this "Amendment"), dated as of December 17, 2015, by and among KEMPHARM, INC., a Delaware corporation (the "Borrower") and, DEERFIELD PRIVATE DESIGN FUND III, L.P. (the "Lenders" and together with the Borrower, the "Parties").

RECITALS:

A. Borrower and Lenders have entered into that certain Facility Agreement dated as of June 2, 2014 (as the same may be amended, modified, restated or otherwise supplemented from time to time, the "Facility Agreement").

B. The Parties desire to amend the Facility Agreement on the terms set forth herein.

NOW, THEREFORE, in consideration of the mutual agreements contained herein, the Parties agree as follows:

1. Defined Terms. Capitalized terms used herein which are defined in the Facility Agreement, unless otherwise defined herein, shall have the meanings ascribed to them in the Facility Agreement. The Recitals to this Amendment are incorporated herein in their entirety by this reference thereto.

2. Amendments to Facility Agreement. Upon the satisfaction of the conditions set forth in Section 3 of this Amendment the Facility Agreement is hereby amended as follows:

a. Section 5.2(g) of the Facility Agreement is hereby deleted in its entirety and the following is inserted in substitution therefor:

"(g) Intentionally Deleted."

b. Section 1.1 of the Facility Agreement is hereby amended to add the following new defined term:

"Restricted Lender" means (i) the initial Lenders party to this Agreement and their Affiliates and (ii) any assignee of any interest in a Note that notifies the Borrower in writing that it wishes to be deemed a Restricted Lender.

c. Section 5.1 of the Facility Agreement is hereby amended by adding the following new provision to the end of such Section:

Notwithstanding anything set forth in this Agreement to the contrary, if any notice or information required to be furnished contains material non-public information (any

such notice or information, a "Public Notice"), the Borrower, instead of delivering such Public Notice to all the Lenders shall promptly deliver such Public Notice to each Lender that is not a Restricted Lender and promptly notify each Restricted Lender in writing or orally that Borrower desires to deliver to such Restricted Lender a Public Notice. Within five Business Days of receipt of such notification the Restricted Lender may either (i) refuse the delivery of such Public Notice, in which case Borrower's obligations with respect to such Public Notice and such Restricted Lender shall be deemed satisfied, or (ii) enter into good faith negotiations with the Parent to agree to the time period within which the Borrower will make the material non-public information contained in such Public Notice publicly available by including such information in a filing with the SEC. If Borrower and such Restricted Lender agree on such time period, the Borrower shall promptly deliver to such Restricted Lender such Public Notice and shall cause Parent to include the applicable material non-public information in a public filing with the SEC within such agreed to time period. The failure to agree on such time period will be deemed to satisfy Borrower's obligations with respect to such Public Notice and such Restricted Lender.

3. Conditions Precedent. The effectiveness of this Amendment is subject to the following conditions precedent:

a. Delivery of Documents. The Borrower and the Lenders shall each execute and deliver this Amendment.

b. Performance; No Default. The Borrower shall have performed and complied with all material agreements and conditions contained in the Facility Agreement and the other Loan Documents to be performed by or complied with by the Borrower prior to the date hereof.

4. Representations and Warranties. The Borrower hereby represents and warrants to Lenders that, except as set forth in the disclosure schedules attached to and made a part of this Amendment:

a. The execution, delivery and performance by the Borrower of this Amendment (i) are within the Borrower's corporate powers, (ii) have been duly authorized by all necessary action pursuant to its Organizational Documents, (iii) except for filings with the Securities Exchange Commission, require no further action by or in respect of, or filing with, any Government Authority, and (iv) do not violate, conflict with or cause a breach or a default under any provision of applicable law or regulation or of Borrower's Organizational Documents or of any agreement, judgment, injunction, order, decree or other instrument binding upon Borrower, except to the extent such violation, conflict, breach or default would not individually or in the aggregate reasonably be expected to have a Material Adverse Effect;

c. This Amendment constitutes the valid and binding obligation of the Borrower, enforceable against the Borrower in accordance with its terms, except as enforceability may be limited by applicable bankruptcy, insolvency, or similar laws relating to the enforcement of creditor's rights generally and by general equitable principles; and

d. No Event of Default exists.

5. No Further Amendments; Ratification of Liability. Except as amended hereby, the Facility Agreement and each of the other Loan Documents shall remain in full force and effect in accordance with their respective terms. The Lenders' agreement to the terms of this Amendment or any other amendment of the Facility Agreement or any other Loan Document shall not be deemed to establish or create a custom or course of dealing among Borrower, Lenders, Assignees, or any of them. This Amendment, together with the other Loan Documents, contains the entire agreement among Borrower and Lenders contemplated by this Amendment.

6. Legal fees and Expenses. The Borrower shall reimburse Lenders for all reasonable out-of-pocket costs, fees and expenses, including reasonable attorneys' fees and expenses, incurred by Lenders in connection with the negotiation, documentation and closing of this Amendment.

7. Incorporation by Reference. The provisions of Article 6 of the Facility Agreement are incorporated herein by reference *mutatis mutandis*.

[Remainder of Page Intentionally Left Blank, signature page follows]

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date set forth above.

BORROWER:

KEMPHARM, INC.

By: /s/ Travis C. Mickle
Name: Travis C. Mickle
Title: President

LENDERS:

DEERFIELD PRIVATE DESIGN FUND III, L.P.

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

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

Unless the context otherwise requires, we use the terms "KemPharm," the "Company," "we," "us" and "our" in this Current Report on Form 8-K, or this Report, to refer to KemPharm, Inc. We have proprietary rights to a number of trademarks used in this Report that are important to our business, including KemPharm® and the KemPharm logo. All other trademarks, trade names and service marks appearing in this Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Report 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Report contains forward-looking statements that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- our plans to develop and commercialize our product candidates;
- our planned clinical trials for our product candidates;
- the timing of the availability of data from our clinical trials;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates, including expectations about our ability to use the regulatory pathway under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act and expedited U.S. Food and Drug Administration review and the timing of U.S. Drug Enforcement Administration scheduling;
- the clinical utility of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional product candidates with significant commercial potential that are consistent with our commercial objectives; and
- our estimates regarding future revenue, expenses and needs for additional financing.

The "Risk Factors" section of this Report contains a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. We qualify all of our forward-looking statements by these cautionary statements.

RISK FACTORS

Risks Related to Our Financial Position and Capital Needs

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

We have incurred losses since our inception and, as of September 30, 2015, had an accumulated deficit of $95.6 million. Our net losses for the nine months ended September 30, 2014 and 2015, were $12.6 million and $45.5 million, respectively. We have financed our operations to date with $52.7 million raised in private placements of redeemable convertible preferred stock, convertible promissory notes and term debt and $59.9 million in aggregate net proceeds from our initial public offering.

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 not completed development of any of our product candidates. 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 KP201/APAP and for any other 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;
- potentially establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize any 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;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our prodrug development and potential future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

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 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. 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.

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.

We believe that the net proceeds from our proposed offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 21 months. However, we will need to obtain substantial additional funding in connection with our continuing operations. 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 scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the ability to obtain abuse-deterrent claims in the labels for our product candidates, including KP201/APAP;
- 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, we receive from commercial sales of our product candidates for which we obtain marketing approval, which may be affected by market conditions, including obtaining coverage and adequate reimbursement of our product candidates from third-party payors, including government programs and managed care organizations, and competition within the therapeutic class to which 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 never 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, our product candidates, if approved, may not achieve commercial success. Our commercial

revenue, if any, will be derived from sales of prodrug products that we do not expect to be commercially available for at least 15 months, if at all. 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 convertible debt securities, or exercise our right to borrow additional tranches under our credit facility, or the Deerfield facility, with Deerfield Private Design Fund III, L.P., or Deerfield, the terms of these securities or this debt may restrict our ability to operate. The Deerfield facility 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. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

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

We commenced active operations in 2006, and our operations to date have been largely focused on raising capital, identifying potential product candidates, broadening our expertise in the development of our prodrugs, undertaking preclinical studies and conducting clinical trials. We have not yet demonstrated an ability to obtain regulatory approvals, manufacture a prodrug on a commercial scale or arrange for a third party to do so, or conduct sales and marketing activities necessary for successful commercialization or enter into a collaboration for that purpose. 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.

Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements for the year ended December 31, 2014.

Our report from our independent registered public accounting firm for the year ended December 31, 2014 includes an explanatory paragraph stating that our recurring losses from operations and stockholders' deficit 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 that the proceeds from our initial public offering or our proposed offering will be able to resolve our liquidity issues or eliminate our operating losses. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to

liquidate our assets and may receive less than the value at which those assets are carried on our audited consolidated financial statements, and it is likely that investors will lose all or a part of their investment. Future reports from our independent registered public accounting firm may also contain statements expressing substantial doubt about our ability to continue as a going concern. 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.

Risks Related to the Development of Our Product Candidates

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

A key element of our strategy is to use our LAT platform technology to build a pipeline of prodrugs and progress product candidates based on these prodrugs through clinical development for the treatment of a variety of diseases and conditions. The scientific discoveries that form the basis for our efforts to discover and develop prodrugs are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Although our research and development efforts to date have resulted in a pipeline of prodrug product candidates, we may not be able to develop prodrugs that are bioequivalent, safe and effective and that have commercially significant improvements over already approved drugs. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of 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. If we do not successfully develop and commercialize product candidates based upon our LAT platform technology, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

If we are not able to obtain required regulatory approvals for KP201/APAP or any of our other 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.

In December 2015, we submitted to the FDA an NDA for KP201/APAP for an indication of the short-term management of acute pain. The timeline for the FDA to complete its review of an 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. For KP201/APAP, the FDA has also indicated that our NDA raises issues that will likely require advisory committee review. Accordingly, the FDA may not approve our NDA on a timely basis, or at all, and therefore we may never receive approval to market KP201/APAP in the United States.

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 KP201/APAP 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 nonclinical 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. Other than the submission of our NDA for KP201/APAP to the FDA, we have not yet submitted comparable applications to other regulatory authorities. If our development efforts for KP201/APAP, including regulatory approval, are not successful for its planned indications or are delayed, or if adequate demand for KP201/APAP is not generated, our business will be harmed.

The success of KP201/APAP 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 FDA may determine that our bridging analysis to Ultracet and Vicoprofen may not provide acceptable evidence of KP201/APAP's safety and efficacy;
- 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 of KP201/APAP 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 KP201/APAP;
- the data collected from clinical trials may not be sufficient to support the submission of an NDA or other submission 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.

In particular, we cannot guarantee that regulators will agree with our assessment of the results of the clinical trials we have conducted to date or that any future trials will be successful. For example, the FDA may not agree that the data from our completed clinical trials, our bridging analysis to Ultracet and Vicoprofen and other data and information in our NDA demonstrate sufficient efficacy or clinical benefit of KP201/APAP. We have no way of knowing whether the FDA will deem the data and literature review in our NDA sufficient to demonstrate KP201/APAP's safety and efficacy. The FDA and other regulators have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional clinical trials, or nonclinical or other studies.

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 nonclinical 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. KP201/APAP or any future product candidates we may 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, and our ability to generate revenue will be impaired.

The FDA may determine that our NDA for KP201/APAP for the short-term management of acute pain is not sufficiently complete to permit a substantive review.

In December 2015, we submitted to the FDA an NDA for KP201/APAP for the short-term management of acute pain. 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 FFDCA, or the FDA's regulations;
- the NDA does not contain a statement that each nonclinical laboratory study was conducted in compliance with the Good Laboratory Practices, or GLP, 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 abbreviated new drug application, or 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, also known as a 505(b)(2) NDA, the U.S. regulatory pathway we are pursuing with KP201/APAP, 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 a 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 our 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 our 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 our NDA, 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 our NDA. If the agency refuses to file our NDA, we will need to address the deficiencies cited by the FDA, which could substantially delay the review process.

Our NDA for KP201/APAP includes a Paragraph IV certification which, if accepted for filing by the FDA, will require us to provide notice of this certification to the holders of certain patents and NDAs. This notice may result in a delay in the approval of our NDA by the FDA and potential patent infringement lawsuit by the patent or NDA holder.

The NDA for KP201/APAP that we submitted to the FDA in December 2015 included a Paragraph IV certification. A Paragraph IV certification is a certification to the FDA that any patents referenced in an NDA and that are listed for an approved drug in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book, publication are invalid, unenforceable or will not be infringed by the manufacture, use or sale of our prodrug. This certification was required since the reference listed drug product, Vicoprofen, has two unexpired patents in the Orange Book. If the FDA accepts our 505(b)(2) NDA for KP201/APAP for filing, we will be required to notify the patent owner and NDA holder of our Paragraph IV certification and of the factual and legal bases therefore. Upon such notice, the patent owner or NDA holder may file a patent infringement suit on one or both of the patents included in the Paragraph IV certification. If the patent owner or NDA holder does not bring suit within 45 days of receiving such notice, the FDA may issue final approval of our NDA once its approval requirements have been satisfied. If an infringement suit is brought by the patent owner or NDA holder within this 45-day period, the FDA may not approve our NDA until the earlier of the end of 30 months, the patents expiration or the patents involved are deemed invalid or not infringed, or such shorter or longer period as determined by a court. Approval of our 505(b)(2) NDA could therefore be delayed for a significant period of time if the owner of the Vicoprofen patent or NDA decides to initiate patent litigation. We will also be subject to a similar risk of a patent infringement action, and any related delay of FDA approval, if we file any future 505(b)(2) NDAs that contain a Paragraph IV certification.

We are very early in our development efforts and have only two product candidates, KP201/APAP and KP201/IR (APAP-free), under clinical development. All of our other product candidates are still in preclinical development. If we are unable to commercialize our product candidates, including KP201/APAP and KP201/IR (APAP-free), or experience significant delays in doing so, our business will be harmed.

We are very early in our development efforts and have only two product candidates, KP201/APAP and KP201/IR (APAP-free), that are under clinical development. All of our other product candidates are still in preclinical development. We have not completed the development of any product candidates, we generate no revenue from the sale of any prodrugs and we may never be able to develop a marketable prodrug product. We have invested substantially all of our efforts and financial resources in the development of our LAT platform technology, the identification of potential product candidates and the development of our product candidates. Our ability to generate revenue from our product candidates, which we do not expect will occur for at least 15 months, if ever, will depend heavily on their successful development and eventual commercialization. The success of 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 our product candidates are outweighed by the benefits;
- successful development of our manufacturing processes for our product candidates, including entering into and maintaining arrangements with third-party manufacturers;
- successful completion of an FDA preapproval inspection of the facilities used to manufacture our product candidates, as well as select clinical trial sites;
- receipt of timely marketing approvals from applicable regulatory authorities, including the determination by the U.S. Drug Enforcement Agency, or DEA, of the controlled substance schedule for a product candidate, taking into account the recommendation of the FDA;
- obtaining abuse-deterrent claims in the labels for our product candidates, including KP201/APAP;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs;
- launching commercial sales of product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of 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.

It is possible that none of our existing product candidates or any of our future product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval.

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

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

The commercial success of KP201/APAP and most of our other product candidates will depend upon our ability to obtain FDA-approved labeling describing their abuse-deterrent features. Our failure to achieve FDA approval of product labeling containing such information will prevent our advertising

and promotion of the abuse-deterrent features of our product candidates in order to differentiate them from other similar products. This would make our products less competitive in the market.

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

- Category 1–in vitro data demonstrate the product has physical and chemical properties that are expected to deter intravenous abuse. However, abuse is still possible by the oral and nasal routes.
- Category 1 and 2–in vitro data demonstrate that the product has physical and chemical properties that are expected to deter oral, nasal and intravenous abuse. However, abuse of intact product is still possible by the oral route.
- Category 2 and 3–pharmacokinetic and clinical abuse potential studies indicate that the product has properties that are expected to deter abuse via the oral, intranasal and intravenous routes. However, abuse of product by these routes is still possible.
- Category 4–data demonstrated a reduction in the abuse of the product in the community setting compared to the levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available. This reduction in abuse appears to be attributable to the product's formulation, which deters abuse by injection or snorting of the manipulated product. However, such abuse of this product is still possible, and the product's abuse deterrence properties do not deter abuse associated with swallowing the intact formulation.

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

Although we conducted trials intended to support approval by the FDA of Category 1, 2 and potentially 3. labeling claims for KP201/APAP, there can be no assurance that KP201/APAP or any of our other product candidates will receive FDA-approved labeling that describes the abuse-deterrent features of such products. The FDA may find that our trials do not support abuse-deterrent labeling or that our product candidates do not provide substantial abuse deterrence because, for example, their deterrence mechanisms do not address the way they are most likely to be abused. For instance, during our May 2015 pre-NDA meeting, the FDA had questions about the relevance of the intranasal route of administration based on the agency's experience. The agency stated that it would likely address this issue in a future advisory committee meeting. The agency also observed that while there is epidemiological evidence that hydrocodone/APAP products are abused via intranasal and intravenous routes of administration, the most common abuse route of administration is oral. The agency further expressed concern that, if injected, KP201/APAP may precipitate in the blood posing a safety concern and requested that we characterize the solubility of the drug in the blood. The results of our KP201.T02 study, which was designed to evaluate the properties of KP201 that could reduce the likelihood of intravenous abuse of KP201/APAP, indicated that preparation of KP201/APAP for intravenous use resulted in a cloudy substance with excipient particles, which may have been APAP. Upon review of our NDA, the FDA will weigh a number of factors, including the most common route of abuse, information showing that hydrocodone/APAP is abused via the nasal and intravenous routes, information suggesting a risk for harm by intravenous abuse as compared to existing products, and results of testing concerning abuse deterrent characteristics.

As with all claims, we will be required to provide adequate substantiation. For example, we will need to demonstrate that KP201/APAP has abuse-deterrent properties sufficient to achieve Category 1, 2 and potentially 3 abuse-deterrent labeling. Further, the FDA is not required to follow its guidance and could change this guidance, which could require us to conduct additional trials. If the FDA does not approve abuse-deterrent labeling, we will not be able to promote such products based on their abuse-deterrent features and may not be able to differentiate such products from other similar products.

Even if we do receive FDA approval for abuse-deterrent claims, the claims may not be broad enough to demonstrate a substantial benefit to health care providers and patients. For instance, the claims may not encompass the more common forms of abuse for products like our product candidates. Moreover, continued investigation in Phase 4 studies following product approval, may not support the continued use of abuse-deterrent claims. We have proposed certain post-marketing studies and observations to the FDA in our NDA for KP201/APAP.

If 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, including KP201/APAP, through the 505(b)(2) NDA pathway. 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. 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. 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 a number of products by the FDA under 505(b)(2) over the last few years, pharmaceutical companies and others have objected to the FDA's interpretation of 505(b)(2). If the FDA's interpretation of 505(b)(2) is successfully challenged, the FDA may change its policies and practices with respect to 505(b)(2) regulatory approvals, which could delay or even prevent the FDA from approving any NDA that we submit under 505(b)(2).

Even if our product candidates are approved under 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed, including more limited subject populations than we request, may require that contraindications, warnings or precautions be

included in the product labeling, including a black box warning, may be subject to other conditions of approval, or may contain requirements for costly post-marketing clinical trials, testing and surveillance to monitor the safety or efficacy of the products, or other post-market requirements, such as a Risk Evaluation and Mitigation Strategy, or REMS. The FDA also may not approve a product candidate with a label that includes the labeling claims necessary or desirable for the successful commercialization of that product candidate. Based upon currently approved products, we anticipate that we will be required to conduct Phase 4 studies and to implement a REMS and will have a black box warning for at least some of our product candidates.

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 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.

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 institutional review boards 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 institutional review boards 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.

We anticipate that most of our product candidates, if approved by the FDA, may be subject to mandatory REMS programs, which could increase the cost, burden and liability associated with the commercialization of these product candidates.

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

We anticipate that most of our product candidates, including KP201/APAP, if approved by the FDA, may 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.

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 our product candidates, 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. Most of our product candidates, including KP201/APAP, KP201/IR (APAP-free), KP511/ER, KP415 and KP606/IR, if approved, will be regulated as “controlled substances” as defined in the Controlled Substances Act of 1970, or 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 product candidates may be listed by the DEA as Schedule II controlled substances under the CSA. Consequently, the manufacturing, shipping, storing, selling and using of the products will be subject to a high degree of regulation. However, we have requested in our NDA that KP201/APAP be listed as a Schedule III controlled substance based on its differential abuse potential when compared to other Schedule II controlled substances, such as IR hydrocodone combination products. None of the previously approved abuse deterrent formulations of opioids have received Schedule III designations and in 2014, the DEA reclassified hydrocodone combination products as Schedule II products 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 and IV, 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. Although, 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. 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 manufacturing and procurement quotas on an annual basis. If we or our contract manufacturers or suppliers do not obtain a sufficient quota from 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 effect 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 institutional review board 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.

Clinical trials of our most advanced product candidate KP201/APAP have thus far found adverse events, such as dizziness, euphoria, drug withdrawal syndrome and nausea and other adverse events consistent with other opioid products.

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 our product candidates.

Media stories regarding prescription drug abuse and the diversion of opioids, stimulants and other controlled substances are commonplace. Law enforcement and regulatory agencies may apply policies that seek to limit the availability of opioids and stimulants. Such efforts may inhibit our ability to commercialize our product candidates. Aggressive enforcement and unfavorable publicity regarding, for example, the use or misuse of hydrocodone or other opioid drugs, the limitations of abuse-deterrent formulations, public inquiries and investigations into prescription drug abuse, litigation or regulatory activity, sales, marketing, distribution or storage of our products could harm our reputation. Such negative publicity could reduce the potential size of the market for our product candidates and decrease the revenue we are able to generate from their sale, if approved. Similarly, to the extent prescription drug abuse becomes a less prevalent or less urgent public health issue, regulators and third-party payors may not be willing to pay a premium for abuse-deterrent formulations 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 our product candidates. For example, in April 2014, the FDA approved class-wide labeling changes to the indications for use of all approved ER and long-acting opioids so that ER and long-acting opioids will be indicated only for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. It is possible that such changes could reduce the number of prescriptions for opioids written by physicians and negatively impact the potential market for our product candidates. The FDA also held a public meeting in October 2014 on the development and

regulation of abuse-deterrent formulations of opioid medications. Further, the Centers for Disease Control and Prevention recently issued draft guidelines for the prescribing of opioids for chronic pain, providing recommendations for primary care providers prescribing opioids for chronic pain on when to initiate or continue opioids, opioid selection and discontinuation, and the assessment of the risk and addressing harms of opioid use, among other areas. It is possible that the 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 our product candidates.

We are party to non-competition restrictions that may prevent us from investigating, developing or commercializing specified amphetamine-based product candidates.

On March 21, 2012, we entered into an asset purchase agreement with Shire LLC, or Shire, pursuant to which we sold assets and intellectual property to Shire. As partial consideration for this sale, we and our chief executive officer, Travis C. Mickle, Ph.D., agreed not to compete with Shire in the development, commercialization, production or distribution of amphetamine amino acid conjugate products until March 21, 2017. As a result, we have not engaged in any development efforts for such product candidates and will not engage in any such development efforts until the expiration of this non-competition provision, if at all. Prior to such time, our competitors may make substantial development progress regarding similar product candidates and even obtain FDA or other regulatory approval for similar product candidates. This could result in our competitors establishing a strong market position before we are able to enter the market or begin our development process, which may prevent us from entering such market altogether.

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 a third party for the manufacture of KP201/APAP used in our clinical trials and with a sole source supplier for the manufacture of bulk quantities of KP201 used in KP201/APAP 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 KP201 or KP201/APAP 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 or personnel. We procure KP201 bulk drug substance from a sole source, third-party manufacturer and the KP201/APAP used in our clinical trials from another third party. 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 other product candidates, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of KP201, other bulk drug substances or our 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 our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing application to the FDA, and these facilities could fail to obtain FDA approval.

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

Further, if our product candidates are approved, our suppliers will be subject to regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to our product candidates, 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 KP201 bulk drug substance. If our current contract manufacturer for KP201 bulk drug substance cannot perform as agreed, we may be required to replace such manufacturer and we may incur added costs and delays in identifying and qualifying any such replacement.

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

We may seek third-party collaborators for the development and commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators include large and mid-size pharmaceutical companies, regional, national and international pharmaceutical companies and biotechnology companies. If we do enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

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

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

Our prodrug development programs and the potential commercialization of our product candidates 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.

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 or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. 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 them to market and generate product revenue.

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

Under our asset purchase agreement with Shire, we granted Shire a right of first refusal to acquire, license or commercialize KP415. 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.

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

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

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

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

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents, licensed to third parties by us. Further, we may also not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents, licensed from third parties to us. Therefore, any such patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors or licensees fail to maintain such patents, or lose rights to those patents, the rights we have in- or out-licensed may be reduced or eliminated.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much

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

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

- we may fail to seek patent protection for inventions that are important to our success;
- our pending patent applications may not result in issued patents;
- we cannot be certain that we are the first to invent the inventions covered by pending patent applications or that we are the first to file such applications and, if we are not, we may be subject to priority disputes or lose rights;
- we may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications;
- we may file patent applications but have claims restricted or we may not be able to supply sufficient data to support our claims and, as a result, may not obtain the original claims desired or we may receive restricted claims; alternatively, it is possible that we may not receive any patent protection from an application;
- even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, and may not be of sufficient scope or strength to provide us with any commercial advantage;
- our competitors may be able to design around our owned or licensed patents by developing similar or alternative technologies or drugs without infringing on our intellectual property rights;
- we could inadvertently abandon a patent or patent application, resulting in the loss of protection of intellectual property rights in a particular country, and we, our collaborators or our patent counsel may take action resulting in a patent or patent application becoming abandoned which may not be able to be reinstated or if reinstated, may suffer patent term adjustments;
- the claims of our issued patents or patent applications when issued may not cover our product candidates;
- no assurance can be given that our patents would be declared by a court to be valid or enforceable or that a competitor’s technology or product would be found by a court to infringe our patents and our patents or patent applications may be challenged by third parties in patent litigation or in proceedings before the United States Patent and Trademark Office, or USPTO, or its foreign counterparts, and may ultimately be declared invalid or unenforceable or narrowed in scope;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim and there may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim;
- third parties may develop products that have the same or similar effect as our products without infringing our patents;

- third parties may intentionally circumvent our patents by means of alternate designs or processes or file applications or be granted patents that would block or hurt our efforts;
- there may be dominating patents relevant to our product candidates of which we are not aware;
- obtaining regulatory approval for pharmaceutical products is a lengthy and complex process, and as a result, any patents covering our product candidates may expire before or shortly after such product candidates are approved and commercialized;
- the patent and patent enforcement laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions; and
- we may not develop additional proprietary technologies that are patentable.

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

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

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

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

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

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted in the United States, redefine prior art and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For instance, the Leahy-Smith Act established the

inter partes review and post grant review procedures that has lowered the burden of proof for invalidity challenges to issued patents and limited the ability to amend patent claims in response to such challenges. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our owned and licensed patents and/or patent applications.

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

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

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

Our commercial success depends upon our ability, and the ability of any collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. In particular, we are focused on developing product candidates based on widely used therapeutic agents or drugs, many of which may be protected by proprietary rights of third parties. Although we seek to develop proprietary prodrug formulations that do not infringe the intellectual property rights of others, we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our prodrugs or other aspects of our technology, including, for example, interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

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

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

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

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

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

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

A third party may hold intellectual property rights, including patent rights, that 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.

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

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

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

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

Many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees do not use the proprietary information, show-how or know-how of others in their work for us, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed intellectual property, including

trade secrets or other proprietary information, of any such employee's former employer. For example, in March 2012, we settled litigation regarding similar matters with Shire. We may also in the future be subject to claims that we have caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these potential claims.

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

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

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

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have not yet solicited trademarks for our product candidates and have not yet begun the process of applying to register trademarks for our product candidates. 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. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

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

In addition to seeking patent and trademark protection for our 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 United States 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 in order to save costs. We may be forced to abandon or return the rights to specific patents due to a lack of financial resources.

Risks Related to the Commercialization of Our Product Candidates

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, we may not be successful in commercializing those product candidates in the United States, if and when they are approved.

We do not have a sales or 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. We have not yet determined our commercialization strategy for KP201/APAP or any of our other product candidates. Should we decide to establish our own sales, marketing and distribution capabilities, we would encounter a number of risks. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of 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 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. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us, including as a result of restrictions in the Deerfield facility. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. Further, we may be liable for conduct of third parties acting on our behalf, including failure to comply with legal requirements applicable to sales and marketing of our products. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if any of our product candidates receives marketing approval, they 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.

If any of our product candidates receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of market acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of 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 abuse-deterrent claims in the labels for KP201/APAP and most of our other 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 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 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.

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

If approved, KP201/APAP 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, if approved, KP201/APAP will face potential competition from any abuse-deterrent IR or other hydrocodone/APAP combination products for the short-term management of acute pain that are currently in or may enter into clinical development.

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

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

If approved, KP606/IR will compete against currently marketed, branded and generic, abuse-deterrent and other IR and ER oxycodone products approved for the management of moderate to severe pain where the use of an opioid analgesic is appropriate or for use in opioid-tolerant patients for the treatment of acute pain and pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Some of these currently marketed products include Purdue Pharma L.P.'s OxyContin and Mallinckrodt plc's Roxicodone, in addition to multiple other branded and generic, abuse-deterrent and other, IR and ER oxycodone products marketed by companies including Allergan plc, Endo International plc, and Mallinckrodt plc. In addition, if approved, KP606/IR will face potential competition from any abuse-deterrent and other, IR and ER oxycodone products that are currently in or which may enter into clinical development.

We believe the key competitive factors that will affect the development and commercial success of our 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 abuse-deterrent or other products for 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 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 abuse deterrence sufficient weight in a comparative clinical-cost effectiveness analysis. For some of the indications that we are pursuing, drugs used off-label serve as cheaper alternatives to our product candidates. Their lower prices could result in significant pricing pressure, even if our product candidates are otherwise viewed as a preferable therapy. Additional drugs may become available on a generic basis over the coming years.

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

The FDA provides periods of regulatory exclusivity following their approval of an NDA, which provide the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug. Five-year exclusivity precludes approval of 505(b)(2) applications or ANDAs by delaying the submission or approval of the application, while three-year exclusivity precludes the approval of the application. We intend to seek new chemical entity, or NCE, status for KP415, and we may seek NCE status for other 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 KP415 or 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 abuse-deterrent mechanisms or may be able to obtain approval for similar products without an abuse-deterrent mechanism.

Even if we are able to commercialize any product candidates, they may be subject to unfavorable pricing regulations, third-party coverage and reimbursement policies or healthcare reform initiatives.

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for our product candidates will be available from government payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers, 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, 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 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 our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available, or that third-party payors' reimbursement policies will not adversely affect our ability to sell 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 the abuse-deterrent 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 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 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 if we commercialize any prodrug products that we may develop. This includes the risk that our products may be misused. For example, we anticipate that, if approved, our products may carry boxed warnings 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. Regardless of merit or eventual outcome, liability claims may result in:

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

commercialization of our product candidates. 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;
- 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 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 our product candidates internationally could affect our business.

We may seek regulatory approval for 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 Foreign Corrupt Practices Act of 1977 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.

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

Any product candidate for which we obtain marketing approval will 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. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, payment of substantial annual product and establishment fees, labeling requirements, promotional, marketing and advertising requirements, requirements related to further development, packaging, storage and distribution requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. If there are any modifications to the drug, including changes in indications, labeling, manufacturing processes or facilities, or new safety issues arise, a new or supplemental NDA, a post-implementation notification or other reporting may be required or requested depending on the change, which may require additional data or additional preclinical studies and clinical trials.

Even if marketing approval of a product candidate is granted, the approval 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. If any of our product candidates receives marketing approval, the accompanying label may

limit its approved uses, including more limited subject populations, than we request, and regulatory authorities may require that contraindications, warnings or precautions be included in the product labeling, including a black box warning, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, which could limit sales of the product.

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. 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 FFDCA 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 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 federal 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 federal False Claims Act, which impose criminal and civil penalties, including 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 civil False Claims Act, for violations of the Anti-Kickback Statute in conjunction 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 federal Health Insurance Portability and Accountability Act of 1996, 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 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, and its implementing regulations, which imposes new annual reporting requirements for certain 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.

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, 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 and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell 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 Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- establishment of a new and distinct methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% 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 beginning in 2014, 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.

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 will stay in effect through 2024 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. 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.

There have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. We continue to evaluate the effect that the ACA has on our business. Final regulations, guidance, amendments and judicial orders are anticipated in the near future and we will continue to assess the ACA's impact on us as final regulations, guidance, amendments and judicial orders are issued.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may, among other things, result in more rigorous coverage criteria, additional downward pressure on the price that we receive for any approved product and anti-inflation measures that restrict our ability to increase prices. 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 new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this 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 computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it 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, Tracy Woody, our chief commercial officer, R. LaDuane Clifton, our chief financial officer, Sven Guenther, Ph.D., our executive vice president research and development, Christal M.M. Mickle, our vice president operations and product development, and Christopher M. Lauderback, our vice president commercial operations, 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. Dr. Mickle also has consulting obligations to Shire Pharmaceuticals, LLC in addition to his duties as our president and chief executive officer, which may limit his availability to us.

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

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

As of November 30, 2015, we had 25 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The 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.

BUSINESS

Overview

We are a clinical-stage specialty pharmaceutical company engaged in the discovery and development of proprietary prodrugs that we believe will be improved versions of widely prescribed, approved drugs. We employ our Ligand Activated Therapy, or LAT, platform technology to create our prodrugs. Our most advanced product candidate, KP201/APAP, consists of KP201, our prodrug of hydrocodone, combined with acetaminophen, or APAP. We are developing KP201/APAP as an immediate release, or IR, product candidate for the short-term, or no longer than 14 days, management of acute pain. We designed KP201/APAP with abuse-deterrent properties to address the epidemic of opioid abuse in the United States. We submitted a new drug application, or NDA, under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, otherwise known as a 505(b)(2) NDA, for KP201/APAP to the U.S. Food and Drug Administration, or FDA, in December 2015. We are also building a pipeline of additional prodrug product candidates that target large market opportunities in pain and attention deficit hyperactivity disorder, or ADHD.

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 approval. New River Pharmaceuticals was acquired by Shire plc in 2007 and Vyvanse generated over $1.4 billion in sales in 2014.

We use our LAT platform technology to discover and develop prodrugs that improve one or more of the attributes of approved drugs, such as susceptibility to abuse, bioavailability and safety. A prodrug is a precursor chemical compound of a drug that is inactive or less than fully active, which is then converted in the body to its active form through a normal metabolic process. We primarily seek to develop prodrugs that will be eligible for approval under the 505(b)(2) NDA pathway, 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. Because our prodrugs are novel combinations of an FDA-approved drug, referred to as the parent drug, with one or more ligands, they may be new molecular entities, or NMEs, and thus may be eligible for composition-of-matter patent protection. An NME is a drug containing an active ingredient that has not been approved or marketed in the United States.

IMS Health Incorporated, or IMS, a healthcare information firm, estimates that IR hydrocodone bitartrate, or HB, formulated in combination with APAP, or hydrocodone/APAP, products accounted for 127 million prescriptions in the United States in 2013. We designed KP201/APAP to offer significant benefits over these widely prescribed hydrocodone/APAP products. We believe that KP201/APAP will provide abuse-deterrence while offering equivalent efficacy to these products.

According to the U.S. Department of Health and Human Services, or HHS, prescription drug overdose death rates in the United States have increased five-fold since 1980, and by 2009, drug overdose deaths outnumbered deaths due to motor vehicle crashes. HHS also estimates that, in 2010, opioid analgesics were involved in approximately 60% of U.S. drug overdose deaths where a drug was specified.

We designed KP201/APAP to deter tampering and abuse by selecting a molecular structure that prevents the release of the opioid upon crushing, physical manipulation and the application of other commonly employed extraction techniques. This approach to abuse-deterrence at the molecular level contrasts with other abuse-deterrent technologies, which are formulation-based, combining the opioid drug with another drug or use an abuse-deterrent capsule or physical matrix. We believe our molecular-based approach to abuse deterrence may be more effective than many formulation-based approaches. We believe the KP201 prodrug releases hydrocodone less effectively than hydrocodone bitartrate, the form of hydrocodone in Norco, upon intranasal administration. We also believe the KP201 prodrug has very poor solubility in blood, water and other solvents, thus rendering it unsuitable for intravenous, or IV, administration.

We believe the data from our clinical trials suggest comparable bioavailability between the hydrocodone released from KP201/APAP and the hydrocodone in Vicoprofen, and comparable bioavailability between the APAP in KP201/APAP and the APAP in Ultracet. In addition, the FDA has confirmed that the results of our bioavailability trial comparing KP201/APAP to Norco, an approved hydrocodone/APAP combination product, support a finding that KP201/APAP is bioequivalent to Norco for hydrocodone. Vicoprofen, Ultracet and Norco are listed drugs that we cited in our 505(b)(2) NDA. Two drugs are said to be bioequivalent if there is no clinically significant difference in their bioavailability. Based on communications with the FDA, we believe that we will not be required to conduct any additional efficacy trials for KP201/APAP. At our pre-NDA meeting with the FDA in May 2015, we received feedback on the bioequivalence findings to Norco, the potential sufficiency of our proposed preclinical and clinical data package to support our NDA and the design of our abuse liability studies.

We believe that KP201/APAP has the potential to be the first FDA-approved IR product for the short-term management of acute pain with the efficacy of hydrocodone/APAP combination products and abuse-deterrent labeling. We have conducted clinical trials designed with the goal of obtaining abuse-deterrent claims in our product label for KP201/APAP. We conducted these trials in accordance with guidance that the FDA finalized in 2015 specifying the necessary studies and data required for obtaining abuse-deterrent claims in a product label. We submitted our NDA to the FDA in December 2015 and we believe it will receive priority review like other abuse-deterrent opioids.

Additionally, we intend to advance our pipeline of other product candidates for the treatment of various pain indications and ADHD and we anticipate reporting human proof-of-concept, or POC, data for three product candidates in 2016 and 2017. We expect to file an Investigational New Drug application, or IND, for each of KP511, KP415 and KP201/IR (APAP-free) in 2016, followed with an NDA for KP201/IR (APAP-free) as early as 2017. We plan to employ our LAT platform technology and development expertise to develop additional product candidates that address unmet medical needs in large, established markets. We believe our product candidates will be eligible for composition-of-matter patent protection and we intend to use the 505(b)(2) NDA pathway when available, which we believe will reduce drug development time, risk and expense. We own worldwide commercial rights for all of our product candidates, including KP201/APAP, except that Shire has a right of first refusal to acquire, license or commercialize KP415.

As of November 30, 2015, our patent portfolio consisted of 47 granted patents and 75 pending patent applications worldwide, including a granted U.S. composition-of-matter patent covering KP201, a granted U.S. patent covering KP201-related compositions-of-matter, and granted U.S. composition-of-matter patents covering the prodrugs underlying two of our other product candidates.

Our Strategy

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

- ***Secure FDA approval for KP201/APAP as the first IR pain therapeutic product with the efficacy of hydrocodone/APAP combination products and an abuse-deterrent label.*** We are developing KP201/APAP for the short-term management of acute pain. We submitted a 505(b)(2) NDA to the FDA in December 2015 and we expect that the NDA will be subject to priority review, with potential approval as early as the third quarter of 2016. Prior to product launch, the U.S. Drug Enforcement Administration, or DEA, would then need to determine the controlled substance schedule of KP201/APAP, taking into account the recommendation of the FDA, which we expect could occur as early as 2017.
- ***Commercialize KP201/APAP.*** We intend to evaluate U.S. commercialization options for KP201/APAP, if it is approved by the FDA, including pursuing a commercial collaboration, building a proprietary sales force, utilizing a contract sales force or pursuing a strategic transaction. We may also license the international commercial rights to KP201/APAP to one or more collaborators.

- ***Advance the development of our other pipeline product candidates***. We plan to advance the development of KP201/IR (APAP-free), our APAP-free formulation of our prodrug of hydrocodone, for the short-term management of acute pain, KP415, our prodrug of methylphenidate, for the treatment of ADHD, KP511/ER, our extended release, or ER, formulation of our prodrug for hydromorphone, 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, and KP606/IR, our IR formulation of our prodrug of oxycodone, for the management of moderate to severe pain where the use of an opioid analgesic is appropriate. We plan to advance three of these product candidates through human proof-of-concept trials to evaluate their bioequivalence to appropriate FDA-approved drugs, and expect to report data from these trials in 2016 and 2017. We expect to file INDs for KP511, KP415 and KP201/IR (APAP-free) in 2016, following with an NDA for KP201/IR (APAP-free) in 2017.
- ***Leverage our LAT platform technology to develop additional product candidates***. We plan to employ our LAT platform technology to develop additional prodrugs that have improved properties over approved drugs and address unmet medical needs in large, established markets. We intend to develop prodrugs of FDA-approved drugs in multiple therapeutic areas.
- ***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. As of November 30, 2015, our patent portfolio consisted of 47 granted patents and 75 pending patent applications worldwide, including a granted U.S. composition-of-matter patent covering KP201, a granted U.S. patent covering KP201-related compositions-of-matter, and granted U.S. composition-of-matter patents covering KP511, the prodrug underlying our KP511/ER product candidate, and KP415, the prodrug underlying our KP415 product candidate.

Our LAT Prodrug Platform Technology

We use our LAT platform technology to create prodrugs 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 for food use by the FDA. Our prodrugs are chemical successors of the parent drugs, but may be considered to be NMEs and thus may be eligible for protection by composition-of-matter patents. When the prodrug is administered to a patient as intended, the targeted human metabolic processes, such as those in the GI tract, separate the ligand from the prodrug and release the parent drug, which can then exert its therapeutic effect. We select particular ligands that, when combined with the parent drug, create prodrugs designed to have improved drug attributes while maintaining efficacy equivalent to the parent drug.

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

- ***Improved drug properties.*** We seek to develop prodrugs with improved attributes over FDA-approved drugs, such as reduced susceptibility to abuse, enhanced bioavailability and increased safety. For example, the molecular structure of KP201/APAP is designed to resist tampering and deter abuse.
- ***Composition-of-matter patent protection.*** Our prodrugs combine an FDA-approved parent drug with one or more ligands to create NMEs and may be eligible for patent protection as novel compositions of matter, provided that all other applicable requirements are met. We seek patent protection not only for our prodrug product candidates, but also for related compounds with the intention of creating heightened barriers to market entry.
- ***Eligibility for 505(b)(2) NDA pathway.*** Our LAT platform technology allows us to develop prodrugs that may be eligible to use the 505(b)(2) NDA pathway. Under that regulatory pathway, if we are able to demonstrate the bioequivalence of our product candidates to appropriate approved drugs, we will then be able to reference the FDA's previous findings of

safety and effectiveness for 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 Epidemic of Prescription Drug Abuse in the United States

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

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

- ***FDA Guidance.*** In January 2013, the FDA published draft guidance with regard to the evaluation and labeling of abuse-deterrent opioids. The guidance was published in final form in April 2015. The FDA guidance provides direction as to the studies and data required for obtaining abuse-deterrent claims in a product label. The draft guidance describes four categories of label claims for abuse-deterrent products. Depending on product and study data, a combination of categories can be included in the label claims. The FDA guidance lists the following theoretical examples:
  - Category 1–in vitro data demonstrate the product has physical and chemical properties that are expected to deter intravenous abuse. However, abuse is still possible by the oral and nasal routes.
  - Category 1 and 2–in vitro data demonstrate that the product has physical and chemical properties that are expected to deter oral, nasal and intravenous abuse. However, abuse of intact product is still possible by the oral route.
  - Category 2 and 3–pharmacokinetic and clinical abuse potential studies indicate that the product has properties that are expected to deter abuse via the oral, intranasal and intravenous routes. However, abuse of product by these routes is still possible.
  - Category 4–data demonstrated a reduction in the abuse of the product in the community setting compared to the levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available. This reduction in abuse appears to be attributable to the product's formulation, which deters abuse by injection or snorting of the manipulated product. However, such abuse of this product is still possible, and the product's abuse deterrence properties do not deter abuse associated with swallowing the intact formulation.

  If a product is approved by the FDA to include such claims in its label, the applicant may use information about the abuse-deterrent features of the product in its marketing efforts to physicians.
- ***FDA Authority.*** In an April 2013 letter to the U.S. House of Representatives' Committee on Energy and Commerce, the FDA outlined its authority to address the issue of prescription opioid abuse in the United States. The FDA asserted that, if it determines that a formulation of an extended-release opioid drug product has abuse-deterrent properties, it has the authority to refrain from approving non-abuse-deterrent formulations of the drug and to initiate procedures to withdraw the non-abuse-deterrent formulations already on the market.
- ***FDA Action.*** The FDA has approved the inclusion of language regarding the ability to deter abuse in the product labels for five abuse-deterrent opioids, OxyContin, Targiniq ER, Embeda, Hysingla and MorphaBond. These actions reinforce the FDA's public statement that the development of abuse-deterrent opioid analgesics is a public health priority.

- ***STOPP Act.*** In July 2012, a bipartisan group of Congressional leaders introduced the STOPP (Stop the Tampering of Prescription Pills) Act. Reintroduced in May 2015, the STOPP Act would require that non-abuse-deterrent opioids be removed from the market if an abuse-deterrent formulation of the same opioid is approved for marketing by the FDA. The STOPP Act is currently assigned to the House Committee on Energy and Commerce's Subcommittee on Health.
- ***FDA Public Meeting.*** In October 2014, the FDA hosted a public meeting to discuss the development, assessment and regulation of abuse-deterrent formulations of opioid medications. In the announcement for the public meeting, the FDA anticipated that, after abuse-deterrent formulations become available for a number of different opioid medications and after it gains more experience with formulations with meaningful abuse-deterrent properties, the FDA may determine that the risks outweigh the benefits for all or most opioid products without abuse-deterrent properties.

Our Prodrug Product Candidates

We have employed our LAT platform technology to create a portfolio of product candidates that we believe will offer significant improvements over FDA-approved and widely prescribed drugs. Our pipeline of product candidates is summarized in the table below:

Selected KemPharm Prodrug Product Candidates

Indication / Parent Drug	Product Candidate	Development Status	Key Milestone
Pain			
Hydrocodone (IR)	KP201/APAP	NDA Submitted December 2015	Potential FDA Approval – As Early As Q3 2016 Potential DEA Scheduling – As Early As 2017
Hydrocodone (IR)	KP201/IR (APAP-free)	Clinical	NDA Submission – 2017
Hydromorphone (ER)	KP511/ER	Preclinical	Human POC Data – 2016 NDA Submission – 2018
Oxycodone (IR)	KP606/IR	Preclinical	Human POC Data – 2017 NDA Submission – 2019
ADHD			
Methylphenidate (controlled release)	KP415	Preclinical	Human POC Data – 2016 NDA Submission – 2019

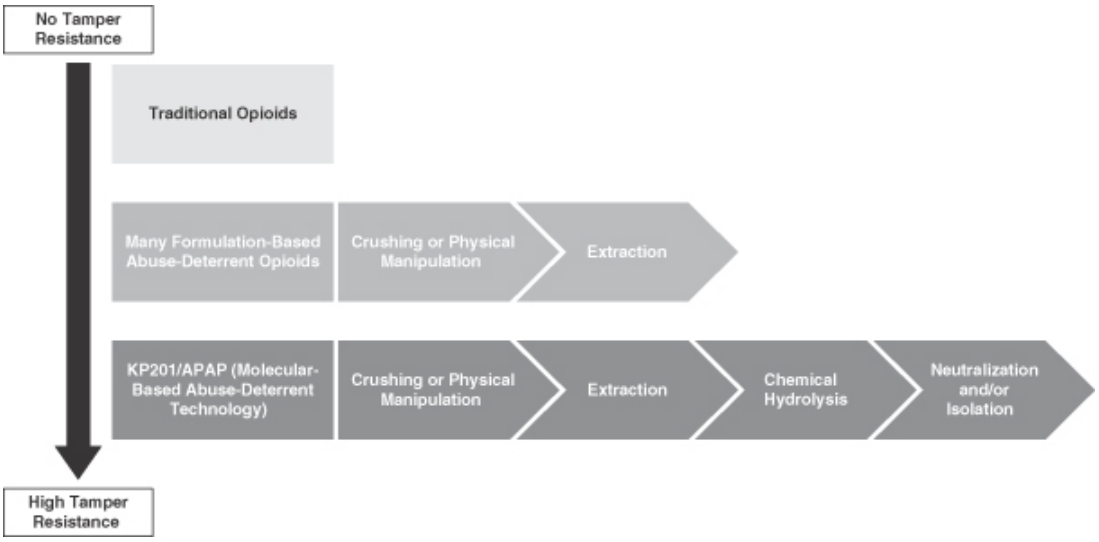
KP201/APAP

Overview

Our most advanced product candidate, KP201/APAP, is an IR combination of KP201, our prodrug of hydrocodone, and APAP. We are developing KP201/APAP for the short-term management of acute pain. KP201/APAP is designed to be an abuse-deterrent opioid product that offers equivalent efficacy to the existing standard-of-care, IR hydrocodone/APAP combination products, such as Vicodin, Norco and Lortab. KP201 combines hydrocodone with the ligand benzoic acid to form benzhydrocodone and can be formulated in both IR and ER dosage forms. KP201 is designed not to release its hydrocodone component until it is metabolized in the GI tract following oral administration. We believe KP201/APAP is highly tamper-resistant and is stable under conditions that can potentially defeat many other abuse-deterrent technologies.

The graphic below illustrates the steps required to extract abusable opioid from traditional opioid products that do not incorporate abuse-deterrent technology, from many formulation-based abuse-deterrent products and from KP201/APAP. We believe the molecular-based abuse-deterrent characteristics of KP201/APAP present a higher barrier to abuse than many formulation-based abuse-deterrent approaches.

Number and Complexity of Steps Required to Access Abusable Opioid



We are seeking approval of KP201/APAP under the 505(b)(2) NDA pathway, which permits companies to rely upon the FDA's previous findings of safety and effectiveness for an approved product or products and published medical and scientific literature. We submitted our 505(b)(2) NDA for KP201/APAP to the FDA in December 2015 and expect that KP201/APAP, like other abuse-deterrent opioids, will receive priority review, allowing for potential FDA approval as early as the third quarter of 2016. However, we are relying in our 505(b)(2) NDA in part on the FDA's prior findings of safety and effectiveness of Vicoprofen, a product that has two listed patents in the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book. Both listed patents expire in June 2017. As a result, FDA approval of our 505(b)(2) NDA may be delayed until June 10, 2017 or later if the patent or NDA holder files a patent infringement claim against us. In addition, and prior to product launch, the DEA would also need to determine the controlled substance schedule of KP201/APAP, taking into account the recommendation of the FDA. Subject to potential delay as a result of any delay in approval of our 505(b)(2) NDA, we expect the DEA could make a scheduling determination as early as 2017.

Market Opportunity

IMS estimates that in 2013, IR hydrocodone/APAP combination products represented the most frequently prescribed opioid products in the United States, accounting for 127 million U.S. prescriptions. Typically, patients are instructed to take four pills per day and prescriptions provide approximately 14 days of therapy. Hydrocodone is associated with more drug abuse and diversion than any other opioid and IR hydrocodone abuse results in more emergency department visits than any other prescription opioid. Currently, there are no IR hydrocodone/APAP combination products approved in the United States with an abuse-deterrent label.

Key Product Features of KP201/APAP

We believe KP201/APAP, if approved by the FDA, may have 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:

- ***Molecular-based abuse-deterrent technology.*** Unlike formulation-based opioid abuse-deterrent approaches, KP201/APAP incorporates our LAT platform technology to create its abuse-deterrent properties at the molecular level. This may provide a higher barrier against attempted abuse than many existing formulation-based approaches. Physical manipulation, common solvent extraction, smoking and other conventional extraction methods applied to KP201/APAP do not release significant amounts of hydrocodone when compared to hydrocodone/APAP. We believe the KP201 prodrug releases hydrocodone less effectively than hydrocodone bitartrate upon intranasal administration and has very poor solubility in blood, water and other solvents, thus rendering it unsuitable for IV administration.
- ***Composition-of-matter patent protection.*** KP201/APAP is protected by a U.S. composition-of-matter patent on KP201 that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2031. Our patent strategy is focused primarily on key geographic market opportunities, and, as of November 30, 2015, KP201 had received granted, issued or allowed patent status in 14 foreign jurisdictions and patent applications covering KP201 were pending in an additional 16 foreign jurisdictions.
- ***No generic equivalent product.*** KP201 is a prodrug with a new chemical name, benzhydrocodone. We expect KP201/APAP, if approved, will have a lower prescribed milligram strength of KP201 than the therapeutic equivalent amount of hydrocodone bitartrate used in existing IR hydrocodone/APAP combination products. The difference in chemical name and prescription strength will mean that there will be no generic equivalent product for KP201/APAP in most states, making substitution difficult at the pharmacy.
- ***Convenient dosing.*** Based on data from our food-effect clinical trial, we believe that KP201/APAP can be administered under both fed and fasting conditions and, accordingly, we believe that KP201/APAP will be as convenient as existing IR hydrocodone/APAP combination products.

KP201/APAP Clinical Development Program

We submitted our 505(b)(2) NDA for KP201/APAP to the FDA in December 2015 and we expect that KP201/APAP, like other abuse-deterrent opioids, will receive priority review. We are seeking approval of KP201/APAP under the 505(b)(2) NDA pathway, which permits companies to rely upon the FDA's previous findings of safety and effectiveness for one or more approved products and published medical and scientific literature. We completed a bioavailability trial comparing KP201/APAP to Norco, an approved hydrocodone/APAP combination product, and the FDA confirmed at our May 2015 pre-NDA meeting that the results of the trial support a finding that KP201/APAP is bioequivalent to Norco for hydrocodone. For APAP, the FDA found that KP201/APAP was close to meeting the agency's metrics for bioequivalence but that we may be able to justify the difference. In order to rely on the FDA's previous findings of safety and effectiveness for an approved product in a 505(b)(2) NDA, the approved product must be an NDA product. Because there are no approved NDAs for hydrocodone/APAP combination products, including for Norco, we are required to establish the safety and effectiveness of hydrocodone and the safety and effectiveness of APAP separately through other methods. We completed a bridging bioavailability trial of KP201/APAP and Vicoprofen, an FDA-approved hydrocodone/ibuprofen combination NDA product. The data from this trial suggests comparable bioavailability between the hydrocodone released from KP201/APAP and the hydrocodone in Vicoprofen. We also completed a bridging bioavailability trial of KP201/APAP and Ultracet, an FDA-approved tramadol/APAP combination NDA product. The data from this trial suggests comparable bioavailability between the APAP in KP201/APAP and the APAP in Ultracet. We referenced the FDA's prior findings of safety and effectiveness for the hydrocodone component of Vicoprofen and the APAP component of Ultracet in our 505(b)(2) NDA. Based on communications with the FDA, we believe that no additional efficacy trials will be required for KP201/APAP.

We also conducted two human abuse liability trials and one intranasal bioavailability study, each of which generated data that we included in our 505(b)(2) NDA submission. We designed these trials and this study with the goal of obtaining abuse-deterrent claims in our product label for KP201/APAP in accordance with FDA guidance.

Clinical Trials and Bioavailability Studies.

Abuse Quotient and Relative Abuse Potential. Clinical observations suggest that euphoric effects are enhanced both by increasing the peak plasma concentration, or C_{max}, of an active opioid and by reducing the time to peak plasma concentration, or T_{max}. The higher the opioid concentrations are in the blood and brain, and the faster they rise, the greater the reward to the abuser. It has also become apparent, however, that neither T_{max} nor C_{max} considered alone are sufficient to predict euphoria. Both parameters are important and need to be evaluated together.

As a result, the abuse quotient, or AQ, calculated as C_{max}/T_{max}, has been introduced to allow numerical assessment of peak drug exposure relative to the rate of rise in plasma concentration. AQ increases both as C_{max} is increased and as T_{max} is shortened. Thus higher AQ scores suggest greater abuse potential.

The AQ values for all treatments we assessed in studies KP201.A01, KP201.A02 and KP201.A03, our abuse deterrence clinical trials and intranasal bioavailability study, have been calculated to allow comparison of their relative abuse potentials based on pharmacokinetics and hydrocodone exposure, and are shown in the table below:

Abuse Quotient Values (Cmax/Tmax) for All Treatments Administered in Studies KP201.A01, KP201.A02, and KP201.A03

Rank[1]	Treatment	ROA[2]	Dose Units (mg)	AQ (SD)[3] (ng/mL/ hours)
1	KP201 API	IN	2 (13.34)	17.0 (11.6)
2	KP201/APAP	IN	2 (13.34/650)	31.9 (18.4)
3	HB/APAP	PO	2 (15/650)	34.5 (23.3)
4	KP201/APAP	PO	2 (13.34/650)	38.6 (21.8)
5	HB/APAP	IN	2 (15/650)	56.5 (43.8)
6	HB API	IN	2 (15)	87.3 (69.0)
7	KP201/APAP	PO	4 (26.68/1300)	99.6 (58.9)
8	HB/APAP	PO	4 (30/1300)	99.7 (57.1)
9	KP201/APAP	PO	8 (53.36/2600)	204.8 (125.2)
10	HB/APAP	PO	8 (60/2600)	222.7 (125.1)
11	KP201/APAP	PO	12 (80.04/3900)	287.58 (189.8)
12	HB/APAP	PO	12 (90/3900)	329.7 (201.9)

1 All treatments from studies KP201.A01, KP201.A02 and KP201.A03 are ranked from smallest to largest AQ
2 ROA = Route of Administration, IN = intranasal, PO = oral
3 SD = Standard Deviation

Of all the treatments we evaluated, intranasal KP201, either with or without APAP, had the lowest AQ when administered at an equimolar dose. This was the case when compared to oral KP201/APAP and when compared to all other hydrocodone treatments included in the trials, whether with or without APAP, oral or intranasal.

KP201 Pilot Pharmacokinetics and Comparative Bioavailability Trials. We submitted our IND application for KP201 to the FDA in January 2011, and conducted our first human clinical trial of KP201 from February through March 2011. This trial was intended to provide proof of concept of KP201's bioavailability compared to Norco. This trial assessed the pharmacokinetics of KP201, hydrocodone and hydromorphone, an opioid resulting from the metabolism of hydrocodone, over a 24-hour period after oral administration of KP201 at doses of 5 mg and 10 mg and the commercially available tablet version of Norco (10 mg of hydrocodone bitartrate / 325 mg of APAP) under fasted conditions. The 10 mg dose of KP201 and the tablet version of Norco are equimolar, meaning the number of KP201 molecules in the KP201 dose is the same as the number of molecules of hydrocodone in the Norco dose. Pharmacokinetics refers to the process by which a drug is distributed and metabolized in the body, including information on drug levels in the systemic circulation and how these levels change over time. A total of 24 healthy adult volunteers were enrolled in the trial and 21 of the subjects completed it.

The results of the trial were that the plasma concentrations for both hydrocodone and hydromorphone after administration of 10 mg of KP201 were comparable to the levels following an equimolar dose of Norco and the results were within the statistical parameters established for bioequivalence by the FDA. In addition, we observed dose proportionality of 5 mg of KP201 as compared to 10 mg of KP201. The systemic exposure to intact KP201 was below the measurement threshold in each subject at all of the measurement points.

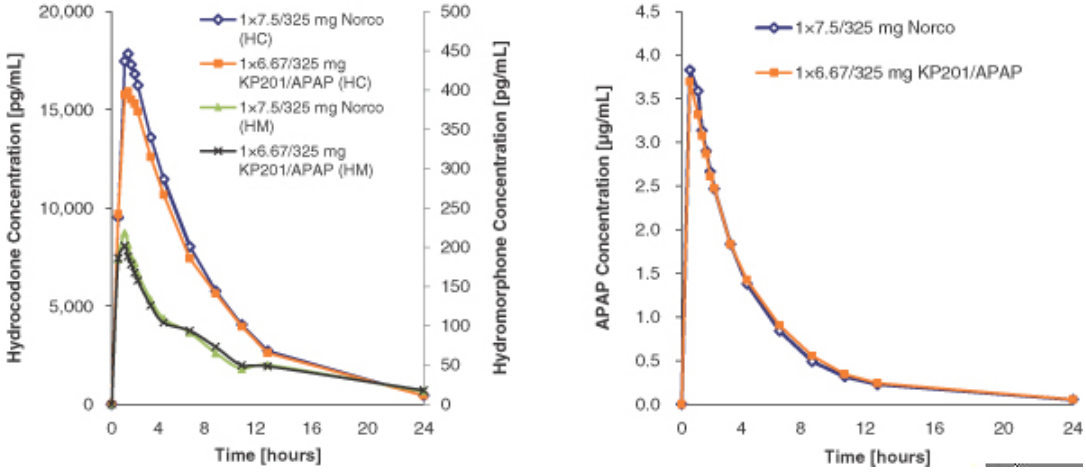
A total of 58 adverse events following dose administration were reported over the course of the trial. Of these, 35 were mild and 23 were moderate. We do not believe any of the adverse events were occurring in the trial unusual or unexpected following the administration of opioid medication.

KP201/APAP Bioequivalence Trial. In August 2013, we conducted our second human clinical trial of KP201, an open-label, bioequivalence trial comparing KP201/APAP to Norco. The primary objective of this trial was to compare the pharmacokinetic profile and exposure of hydrocodone, hydromorphone and APAP over a 24-hour period after a single dose of KP201/APAP (6.67 mg / 325 mg) relative to a single dose of Norco (7.5 mg / 325 mg) when administered orally under fasted conditions. These doses of KP201/APAP and Norco are equimolar even though the milligram dose of each drug per tablet is slightly different. Randomized subjects received two single-dose treatments, each separated by a seven-day washout period. A total of 30 healthy volunteers participated in the trial and 23 of the subjects completed it.

The results of the trial were that the plasma concentration levels for hydrocodone, hydromorphone and APAP after administration of KP201/APAP were comparable to the levels following an equimolar dose of Norco, and the results for hydrocodone and hydromorphone were within the statistical parameters established for bioequivalence by the FDA. The bioavailability data for APAP was slightly outside of the statistical range for bioequivalence.

The following charts summarize the bioequivalence data from this trial.

KP201/APAP Bioequivalence Trial



Note: HC refers to hydrocodone and HM refers to hydromorphone.

In addition, systemic exposure to intact KP201 was below the measurement threshold in each subject at all of the measurement points. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

KP201/APAP Multi-Dose/Steady State Trial. This trial, which we conducted in July and August 2013, was intended to assess the pharmacokinetics of KP201 after single and multiple doses of KP201/APAP in healthy volunteers. The primary objectives of this trial were to assess the pharmacokinetics of KP201, hydrocodone, hydromorphone and APAP following a single dose of two KP201/APAP tablets (6.67 mg / 325 mg) and to assess the steady-state pharmacokinetics of KP201, hydrocodone, hydromorphone and APAP following 13 doses of two KP201/APAP tablets administered every four hours under fasted conditions. A total of 26 healthy adult volunteers were enrolled in the trial and 24 of the subjects completed it.

The results of the trial were that all plasma concentrations of KP201 were below the measurement threshold at all time points for all subjects, indicating that there was no systemic exposure to the prodrug even after administration of two tablets every four hours for 13 doses. Naltrexone, a narcotic antagonist, was administered to minimize the occurrence of adverse effects often associated with administration of opioids. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

KP201/APAP Food-Effect Trial. This trial, which we conducted in December 2013 and January 2014, was intended to assess the effect of food on the bioavailability and pharmacokinetics of hydrocodone and APAP from KP201/APAP tablets, as well as to assess the relative bioavailability of hydrocodone and APAP from KP201/APAP tablets as compared to equimolar doses of Norco, each under fed conditions. Randomized subjects received a single dose of KP201/APAP (6.67 mg / 325 mg) administered orally under fed conditions in one period, a single dose of KP201/APAP (6.67 mg / 325 mg) under fasted conditions in one period, and a single dose of Norco (7.5 mg / 325 mg) under fed conditions in one period. Fed conditions reflected an FDA-standard high-fat, high-calorie breakfast. A total of 42 healthy adult volunteers enrolled in the trial and 38 of the subjects completed it.

The results of the trial were that there were no overall changes in exposure to hydrocodone or to APAP when KP201/APAP tablets were administered under fed conditions that would be of clinical significance compared to KP201/APAP administered under fasted conditions or compared to Norco administered under fed conditions. We believe the data from this trial suggest there is no food effect with regard to the administration of KP201/APAP and that the labeling for KP201 could indicate that it can be administered without regard to meals.

In addition, systemic exposure to intact KP201 was below the measurement threshold in each subject at all of the measurement points. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

Comparative Bioavailability of KP201/APAP and Vicoprofen Trial. This trial, which was conducted in June and July 2014, was intended to assess the relative bioavailability of KP201/APAP compared to Vicoprofen in order to allow us to reference the FDA's prior findings of safety and effectiveness of Vicoprofen in our 505(b)(2) NDA. Vicoprofen, like KP201/APAP, is a product containing hydrocodone. The primary objective of this trial was to compare the rate and extent of absorption of hydrocodone and hydromorphone from KP201/APAP relative to Vicoprofen when administered orally to healthy subjects under fasted conditions. Randomized subjects received a single dose of KP201/APAP (6.67 mg / 325 mg) and a single dose of Vicoprofen (7.5 mg of hydrocodone / 200 mg of ibuprofen) with the two administrations separated by a seven-day washout period. A total of 30 healthy adult volunteers enrolled in the trial and 28 of the 30 subjects completed it.

The results of the trial were that there were no overall differences in exposure to hydrocodone and active metabolite hydromorphone from KP201/APAP as compared to Vicoprofen. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

Comparative Bioavailability of KP201/APAP and Ultracet Trial. This trial, which was conducted in July and August 2014, was intended to assess the relative bioavailability of KP201/APAP compared to Ultracet in order to allow us to reference the FDA's prior findings of safety and effectiveness of Ultracet in our 505(b)(2) NDA. Ultracet, like KP201/APAP, is a combination product containing an opioid, in this case tramadol, and APAP. The primary objective of this trial was to compare the rate and extent of absorption of APAP from KP201/APAP relative to Ultracet when administered orally to healthy subjects under fasted conditions. Randomized subjects received a single dose of KP201/APAP (6.67 mg / 325 mg) and a single dose of Ultracet (37.5 mg of tramadol / 325 mg of APAP) with the two administrations separated by a seven-day washout period. A total of 30 healthy adult volunteers enrolled in the trial and 27 of the 30 subjects completed it.

The results of the trial were that there were no overall differences in exposure to APAP from KP201/APAP as compared to Ultracet. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

Abuse Deterrence Clinical Trials and Intranasal Bioavailability Study

In 2015, we completed two human abuse liability trials and one intranasal bioavailability study, each of which generated data that we included in our 505(b)(2) NDA submission. We believe the data from these trials and study, together with the data from the tamper-resistant extraction studies we have completed, may allow us to obtain the FDA's Category 1, Category 2 and potentially Category 3 abuse-deterrent language in the KP201/APAP product label, if it is approved.

KP201.A01 Oral Human Abuse Liability Trial. This trial, which was conducted from August 2014 through January 2015, was intended to compare the pharmacodynamic, or drug likability, effects, exposure levels and safety of KP201/APAP compared to Norco after oral administration at four, eight and twelve tablet dosages. Pharmacodynamics refers to the biochemical and physiological effects of a

drug on the human body and the purpose of a drug likeability analysis is to assess how probable it is that the drug will be attractive to abusers. Randomized subjects received tablets of Norco (7.5 mg hydrocodone bitartrate/325 mg APAP), and an equivalent amount of KP201/APAP. This was a single-center, double-blind, active- and placebo-controlled, crossover trial. A total of 71 opioid-experienced nondependent volunteers enrolled in the trial and 62 of the 71 subjects completed it.

The results of the trial were that KP201/APAP released less hydrocodone as compared to Norco at the two highest doses administered (eight and twelve tablets). At the lowest doses administered, there was no statistical difference in hydrocodone exposure between KP201/APAP and Norco. In addition, there was a numerically lower incidence of adverse events related to hypoxia for KP201/APAP at both the eight and twelve tablet doses as compared to Norco. Drug liking, as measured by peak maximum effect on the Visual Analogue Scale, was similar for KP201/APAP and Norco at each equivalent dose level. The Visual Analogue Scale is a psychometric response scale used to measure the subjective effect of a dose level based on responses from the subject and is commonly used to evaluate drug likability.

KP201.A02 Intranasal Human Abuse Liability Trial. This trial, which was conducted from September 2014 through July 2015, was intended to assess the relative drug likability effects, exposure levels and safety of KP201/APAP compared to Norco after crushing and intranasal administration. Randomized subjects received an intranasal or oral dose of Norco (7.5 mg hydrocodone bitartrate/325 mg APAP) and an intranasal or oral dose of KP201/APAP (6.67 mg / 325 mg). This was a single-center, double-blind, double-dummy, placebo-controlled, single-dose, two-part, five-way crossover trial. A total of 46 opioid-experienced nondependent volunteers enrolled in the trial and 42 of the 46 subjects completed it.

The results of the trial were that, overall, administration of intranasal crushed or oral intact KP201/APAP resulted in statistically similar results for drug liking relative to intranasal crushed or oral intact Norco. We believe this was potentially due to the effects of APAP. An important component of the APAP mechanism involves indirect activation of cannabinoid CB_1 receptors, which likely contribute to the analgesia of APAP and some of its other behavioral effects, such as euphoria. While the role of APAP associated with potential drug liking effects has not yet been determined, it appears plausible that APAP may “mask” negative drug effects or reduce differences in pharmacodynamic parameters, such as drug liking, between opioid combination products that contain large volumes of APAP. However, intranasal crushed KP201/APAP demonstrated, as compared to intranasal crushed Norco, a lower peak hydrocodone exposure and a decrease in exposure to hydrocodone in the early time points typically associated with an increased safety risk. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

KP201.A03 Intranasal Bioavailability Study. This study, which was conducted from May 2015 through July 2015, was intended to measure the amount of hydrocodone released from KP201, when insufflated without APAP, as compared directly to hydrocodone bitartrate. Randomized subjects received an intranasal dose of hydrocodone bitartrate (15 mg) and an intranasal dose of KP201 (13.34 mg). This was a single-center, cross-over pharmacokinetic study. A total of 66 opioid-experienced nondependent volunteers enrolled in the study and 51 of the 66 subjects completed it.

The results of the study were that KP201 demonstrated a statistically significant lowering in peak hydrocodone exposure, a delay in the time to achieve peak exposure and a decrease in total exposure to hydrocodone, especially in the early time points typically associated with increased drug liking and abuse. We do not believe any of the adverse events occurring in the trial were unusual or unexpected following the administration of opioid medication.

Tamper-Resistant Extraction Studies

In 2015, we completed three tamper-resistant extraction studies, each of which generated data that we included in our 505(b)(2) NDA submission. We believe the data from these three studies,

together with the data from our two human abuse liability trials and one intranasal bioavailability study described above, may allow us to obtain the FDA's Category 1, Category 2 and potentially Category 3 abuse-deterrent language in the KP201/APAP product label, if it is approved.

KP201.T01 Study. Our KP201.T01 study was designed to evaluate KP201/APAP for the possibility and potential for individuals to extract KP201 from its tablet formulation and convert the extracted KP201 active pharmaceutical ingredient, or API, into active hydrocodone, following a protocol that we developed with input from the FDA. The study evaluated how the abuse-deterrent properties of KP201 could be defeated or compromised, as compared to hydrocodone bitartrate/APAP tablets. The results of the study were that efforts to extract and hydrolyze KP201/APAP were less efficient compared to hydrocodone bitartrate/APAP tablets. Under the more than 1,000 conditions tested, KP201/APAP released less hydrocodone compared to the hydrocodone released from the hydrocodone bitartrate/APAP tablets in every case, and in many cases KP201/APAP released only the inactive prodrug, KP201.

KP201.T02 Study. Our KP201.T02 study was designed to evaluate the properties of KP201 that could reduce the likelihood of IV abuse of KP201/APAP as compared to hydrocodone bitartrate/APAP, based on a protocol developed by us with input from the FDA. The study evaluated the amount of KP201, APAP and hydrocodone detected in an extract derived from KP201/APAP tablets that would be suitable for IV abuse. The results of the study were that the traditional means used to prepare a drug for injection were likely not suitable for KP201/APAP. In each condition employed, only inactive KP201 was extracted, if anything at all, while up to 100% of the hydrocodone from hydrocodone bitartrate/APAP tablets could be extracted for injection. Cold water extraction methods typically used by abusers to "enrich" or "purify" the hydrocodone from hydrocodone bitartrate/APAP also yielded only inactive KP201 with no release of hydrocodone from the prodrug. Hydrocodone was readily extracted from hydrocodone bitartrate/APAP tablets by this method.

KP201.T03 Study. Our KP201.T03 study was designed to evaluate the potential to abuse KP201/APAP by smoking. The results of the study were that KP201/APAP could not be smoked in either tablet or KP201 form. The results also showed that freebasing KP201/APAP was not possible. By contrast, hydrocodone bitartrate/APAP can be prepared as a freebase and also smoked in the API form.

KP201/IR (APAP-free)

Overview

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

Based on our current development timelines, we anticipate submitting a 505(b)(2) NDA for KP201/IR (APAP-free) in 2017. We expect that KP201/IR (APAP-free), like other abuse-deterrent opioids, would receive priority review.

Market Opportunity

Currently, there are no IR hydrocodone products approved in the United States that are formulated without APAP, with or without an abuse-deterrent label. We believe KP201/IR (APAP-free) will provide physicians with a highly differentiated abuse-deterrent hydrocodone product to help them with the short-term management of acute pain.

Key Product Features of KP201/IR (APAP-free)

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

- ***Molecular-based abuse-deterrent technology.*** Similar to KP201/APAP, KP201/IR (APAP-free) uses our KP201 prodrug which incorporates our LAT platform technology to create its abuse-deterrent properties at the molecular level and thus may provide a higher barrier against attempted abuse than many existing formulation-based approaches.
- ***No added APAP.*** KP201/IR (APAP-free) contains no acetaminophen. According to the FDA, overdoses of APAP are the most common cause of drug-related liver injury. In 2011, the FDA limited the amount of APAP in prescription combination products and required warnings be added to all APAP prescription products.
- ***Composition-of-matter patent protection.*** KP201/IR (APAP-free) is protected by a U.S. composition-of-matter patent on KP201 that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2031.
- ***No generic equivalent product.*** Similar to KP201/APAP, the difference in chemical name, prescription strength and lack of APAP in the formulation will mean that there will be no generic equivalent product for KP201/IR (APAP-free) in most states.
- ***Convenient dosing.*** Based on data from our food-effect clinical trial of KP201/APAP, we believe that KP201/IR (APAP-free) will also be able to be administered under both fed and fasting conditions and, accordingly, we believe that KP201/IR (APAP-free) will be as convenient as existing IR hydrocodone/APAP combination products.

KP511/ER

Overview

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

We plan to seek approval of KP511/ER under the 505(b)(2) NDA pathway. Based on our preclinical data, we believe that KP511 may release hydromorphone after oral administration in humans in a manner that is comparable to the appropriate approved hydromorphone drug. We anticipate reporting human proof-of-concept data for KP511/ER in 2016 and submitting a 505(b)(2) NDA for KP511/ER in 2018.

Market Opportunity

Oral hydromorphone products are typically used 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. IMS estimates that in 2013 there were 3.5 million dispensed prescriptions of hydromorphone in the United States. Currently, there are no hydromorphone products approved in the United States with an abuse-deterrent label.

Key Product Features of KP511/ER

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

- ***Molecular-based abuse-deterrent technology.*** In order to evaluate the abuse-deterrent qualities of KP511, we conducted preclinical studies in rats to compare the exposure to hydromorphone following intranasal and IV administration of KP511 as compared to intranasal and IV administration of hydromorphone hydrochloride. We observed significantly lower concentrations of hydromorphone following intranasal and IV administration of KP511 compared to intranasal and IV administered hydromorphone hydrochloride. KP511/ER incorporates our LAT platform technology to create its abuse-deterrent properties at the molecular level and, based on our preclinical studies, we believe it may have abuse-deterrent characteristics similar to KP201/APAP.
- ***Oral overdose protection.*** In our preclinical studies, we observed that hydromorphone blood levels in rats increased more slowly and to a lesser extent after oral administration of increasing excessively large doses of KP511, as compared to increasing equimolar oral doses of hydromorphone hydrochloride. We also observed that the study animals began dying from the increasing excessively large oral doses of hydromorphone hydrochloride, but never died from an equimolar oral dose of KP511. Based on the molecular structure of KP511, we believe it is possible that the metabolic processes of releasing hydromorphone from the prodrug become saturated at excessively large oral doses. If confirmed by further studies, this could potentially mean that KP511 and KP511/ER may reduce the risk of oral overdosing by a mechanism that is inherent in the prodrug molecule itself.
- ***Composition-of-matter patent protection.*** KP511/ER is protected by a U.S. composition-of-matter patent on KP511 that will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2032. Our patent strategy is focused primarily on key geographic market opportunities, and, as of November 30, 2015, a composition-of-matter patent on KP511 was granted in Australia, Japan, Philippines, New Zealand, South Africa, and Singapore, and applications covering KP511 were pending in the United States and an additional 20 foreign jurisdictions.
- ***No generic equivalent product.*** KP511 is a prodrug that we believe will be given a new chemical name, which would mean that there would be no generic equivalent product for KP511/ER in most states, making substitution difficult at the pharmacy.

KP415

Overview

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

We plan to seek approval of KP415 under the 505(b)(2) NDA pathway. We anticipate reporting human proof-of-concept data for KP415 in 2016 and submitting a 505(b)(2) NDA for KP415 in 2019.

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 abuse-deterrent features and a more consistent controlled release drug delivery mechanism may provide a preferred treatment option in this large market segment. While methylphenidate is available as a generic product, the branded formulations, Concerta, Focalin and Ritalin, accounted for sales of $1.1 billion in 2014.

Key Product Features of KP415

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

- ***Molecular-based abuse-deterrent technology.*** In order to evaluate the abuse-deterrent qualities of KP415, we conducted preclinical studies in rats to compare the exposure to methylphenidate following intranasal and IV administration of KP415 as compared to intranasal and IV administration of methylphenidate hydrochloride. We observed significantly lower concentrations of methylphenidate following intranasal and IV administration of KP415 compared to intranasal and IV administered methylphenidate hydrochloride. KP415 incorporates our LAT platform technology to create its abuse-deterrent properties at the molecular level and, based on our preclinical studies, we believe it will have abuse-deterrent characteristics similar to KP201/APAP.
- ***Once-daily dosing.*** Pharmacokinetic data from our preclinical studies suggest that the time to maximum plasma concentration of methylphenidate after oral administration of KP415 is approximately three times longer than that after oral administration of currently marketed IR methylphenidate. We believe this inherent CR attribute of KP415's molecular structure may allow for convenient, once-daily dosing.
- ***Amenable to patient-friendly formulations.*** Although we believe our prodrug, KP415, possesses abuse-deterrent properties at the molecular level similar to KP201, our preclinical data shows that KP415 is highly water soluble and we believe it could ultimately be used in a variety of patient-friendly dosage forms such as oral thin film, orally dissolving tablets, chewable tablets and liquids as a means of increasing patient convenience and compliance.
- ***Composition-of-matter patent protection.*** KP415 is 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 market opportunities, and, as of November 30, 2015, a composition-of-matter patent on KP415 was granted in New Zealand and South Africa, and additional KP415 patent filings were pending in the United States and an additional 23 foreign jurisdictions. In addition, subject to further discussions with the FDA, KP415 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 is a prodrug that we believe will be given a new chemical name, which would mean that there would be no generic equivalent product for KP415 in most states, making substitution difficult at the pharmacy.

Other Product Candidates

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

We anticipate reporting human proof-of-concept data for KP606/IR in 2017 and submitting a 505(b)(2) NDA for KP606/IR in 2019.

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 as trade secrets our LAT platform technology, the process by which we identify, screen, evaluate and select ligands to be conjugated with parent drugs to create our prodrugs. Our current prodrugs all

consist of an approved parent drug and one or more ligands that we have selected using our LAT platform technology. The parent drug and ligand or ligands together may potentially constitute an NME and thus may be eligible for composition-of-matter patent protection, among other patent protections, in the United States and abroad.

To date, we have internally developed all of our intellectual property, including our LAT platform technology, and have not in-licensed or otherwise acquired our technology, patents, show-how or know-how from an outside source. As of November 30, 2015, we owned twelve issued patents within the United States, and an additional 35 foreign patents covering our prodrugs or product candidates. The terms of the twelve issued U.S. patents extend to various dates between 2030 and 2032. The term of our overall domestic and foreign patent portfolio related to our prodrugs and product candidates, including patent term adjustments but excluding possible patent term extensions, extend to various dates between 2030 and 2032, if pending patent applications in each of our patent families issue as patents. As of November 30, 2015, we owned seven pending patent applications under active prosecution in the United States, and an additional 68 pending foreign patent applications covering our prodrugs and product candidates. Our issued and granted patents provide protection in jurisdictions that include the United States, Australia, Canada, China, Colombia, Israel, Japan, Kazakhstan, Malaysia, Mexico, New Zealand, Russia, Ukraine, Singapore, Indonesia and South Africa.

In 2013, the United States Patent and Trademark Office, or the USPTO, issued a composition-of-matter patent covering KP201, which will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2031. Further, there are granted or recently allowed compositions-of-matter patents covering KP201 in Australia, Canada, China, Colombia, Israel, Japan, Kazakhstan, Malaysia, Mexico, New Zealand, Russia, Ukraine, Indonesia and South Africa. In addition, one U.S. patent application covering KP201-related compositions-of-matter is pending and patent applications covering KP201 are currently pending in the United Arab Emirates, Brazil, Belarus, Chile, Costa Rica, Cuba, Egypt, Europe, Hong Kong, India, South Korea, Oman, Philippines, Singapore, Thailand and Vietnam.

In August 2014, the USPTO issued a composition-of-matter patent covering KP511, which will expire, after utilizing all appropriate patent term adjustments but excluding possible patent term extensions, in 2032. In July 2015, the USPTO issued a composition-of-matter patent covering KP415, which will expire, after utilizing all appropriate patent term adjustments but excluding patent term extensions, in 2032. We have also filed composition-of-matter patent applications for KP415 and KP511 in the United States and in Argentina, Australia, Brazil, Canada, Chile, China, Egypt, Hong Kong, Europe, India, Israel, Indonesia, Japan, South Korea, Kazakhstan, Mexico, Malaysia, New Zealand, Philippines, Russia, Singapore, Thailand, Ukraine, Vietnam and South Africa. We anticipate filing additional patent applications for our prodrug product candidates.

We also depend upon the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our LAT platform technology as well as any proprietary know-how and show-how that is not 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 and inventions important to our business.

Commercialization

We have begun initial pre-approval commercialization activities for KP201/APAP although currently we do not have any internal sales or distribution infrastructure. These initial pre-approval commercialization activities include developing the marketing strategy, designing the product distribution infrastructure, coordinating managed care access and identifying the promotional sales force size and structure. These activities are aligned to support a planned promotional launch of KP201/APAP as early as the first quarter of 2017, subject to FDA approval and DEA scheduling.

Because many of our product candidates, including KP201/APAP, 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 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.

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

If approved, KP201/APAP 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, if approved, KP201/APAP will face potential competition from any abuse-deterrent IR or other hydrocodone/APAP combination products for the short-term management of acute pain that are currently in or may enter into clinical development.

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

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

If approved, KP606/IR will compete against currently marketed, branded and generic, abuse-deterrent and other IR and ER oxycodone products approved for the management of moderate to severe pain where the use of an opioid analgesic is appropriate or for use in opioid-tolerant patients for the treatment of acute pain and pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Some of these currently marketed products include Purdue Pharma L.P.'s OxyContin and Mallinckrodt plc's Roxicodone, in addition to multiple other branded and generic, abuse-deterrent and other, IR and ER oxycodone products marketed by companies including Allergan plc, Endo International plc, and Mallinckrodt plc. In addition, if approved, KP606/IR will face potential competition from any abuse-deterrent and other, IR and ER oxycodone products that are currently in or which may enter into clinical development.

Manufacturing

Our manufacturing strategy is to rely on contract manufacturers to produce our prodrug product candidates for clinical trials and, if approved, drug product for commercial sale. We currently have no manufacturing facilities and limited personnel with manufacturing experience. We rely on a third-party manufacturer to produce KP201/APAP for our clinical trials and we expect to continue to rely on third-party manufacturers to manufacture commercial quantities of KP201/APAP if and when we receive approval for marketing from the FDA. We also rely on Johnson Matthey Inc., or JMI, a third-party manufacturer, to produce the bulk quantities of KP201 required for the manufacture of the KP201/APAP used in our clinical trials under a supply agreement. We plan to continue to rely on JMI to manufacture commercial quantities of KP201 used in production of KP201/APAP for sale in the United States if and when we receive approval for marketing by the FDA. We expect to contract with third-party manufacturers for the manufacture of KP201 and KP201/APAP outside the United States if and when we receive approval for marketing 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, corporate integrity agreements, 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 imprisonments.

Supply Agreement with Johnson Matthey

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

Under the supply agreement, we retain sole ownership of KP201 and are required to use commercially reasonable efforts to develop and to pursue FDA marketing approval of KP201/APAP. We are responsible for product development, including formulation, preclinical studies and clinical trials, and for regulatory approval, quality assurance and commercialization. If KP201 is subject to a DEA scheduling quota, then each quarter, both we and JMI are responsible for using commercially reasonable efforts to obtain a quota from the DEA for the production of the KP201 API and for KP201.

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

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

The term of the supply agreement extends as long as we hold a valid and enforceable patent for KP201 or until the tenth anniversary of KP201's commercial launch, 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 LLC

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 LLC, or Shire, pursuant to which we sold assets and intellectual property to Shire for proceeds of $5.1 million. As partial consideration for this sale, we and Dr. Mickle agreed not to compete with Shire in the development, commercialization, production or distribution of amphetamine amino acid conjugate products until March 21, 2017. Pursuant to this agreement, we also granted Shire a right of first refusal to acquire, license or commercialize KP415.

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, managed care organizations and private insurers. Decisions regarding the extent of coverage and amount of reimbursement to be provided for each of our 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, KP201/APAP, KP201/IR (APAP-free), KP415, KP511/ER and KP606/IR 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 2020. To help achieve this reduction, pharmaceutical manufacturers are required to provide quarterly discounts of 50% 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:

- nonclinical laboratory and animal tests that must be conducted in accordance with good laboratory practices, or GLPs;
- submission of an IND, which must become effective before 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 to the FDA of an NDA;
- 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 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. Some preclinical studies may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the conduct of the clinical trial by imposing a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each study site proposing to conduct the clinical trial must review and approve the plan for any clinical trial, its informed consent form and other communications to study subjects before the clinical trial commences at that site. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans. Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, if the drug has been associated with unexpected serious harm to subjects, or based on evolving business objectives or competitive climate. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise us to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

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

- *Phase 1*—Studies are initially conducted to test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 trials may also be used to gain an initial indication of product effectiveness.
- *Phase 2*—Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

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

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

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 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 Federal Food, Drug and Cosmetic Act, or the FFDCA. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events occur.

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

505(b)(2) Approval Process

Section 505(b)(2) of the FFDCA, or 505(b)(2), provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, 505(b)(2) permits the filing of an NDA where at least some of the information required for

approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. The applicant may rely upon the FDA's prior findings of safety and effectiveness for an approved product that acts as the reference listed drug for purposes of a 505(b)(2) NDA. The FDA may also require 505(b)(2) applicants to perform additional studies or measurements to support any changes from the reference listed drug. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

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

Orange Book Listing

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

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

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

If the competitor has provided a Paragraph IV certification to the FDA, the competitor 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.

We have made a Paragraph IV certification in our 505(b)(2) NDA for KP201/APAP based on our reliance in part on the FDA's prior findings of safety and effectiveness of Vicoprofen, a product that remains under patent until June 2017. FDA approval of our 505(b)(2) NDA may be delayed until June 10, 2017 or later if the patent or application holder files a patent infringement claim against us. See "Risk Factors—Risks Related to the Development of Our Product Candidates—Our NDA for KP201/APAP includes a Paragraph IV certification which, if accepted for filing by the FDA, will require us to provide notice of this certification to the holders of certain patents and NDAs. This notice may result in a delay in the approval of our NDA by the FDA and potential patent infringement lawsuit by the patent or NDA holder" and "Risk Factors— Risks Related to the Development of Our Product Candidates—The FDA may determine that our NDA for KP201/APAP for the short-term management of acute pain is not sufficiently complete to permit a substantive review" for additional information regarding the risk associated with the 505(b)(2) NDA pathway and associated patent infringement lawsuits that may delay FDA approval of 505(b)(2) NDAs.

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, nonclinical 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 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. We have agreed with the FDA on a Pediatric Study Plan which outlines the adult, pediatric and nonclinical studies, as well as formulation work, that we plan to conduct and the associated schedule, which is subject to post-approval amendment of the NDA. We have requested a deferral of these efforts.

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 typically a panel that 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 has also previously indicated that our NDA for KP201/APAP raises issues that will likely require advisory committee review.

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 an 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 an 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. Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

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

FDA approval of any NDA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings or precautions in the product labeling, including a black box warning. For instance, we expect that at least some of our product candidates would likely be required to carry black box warnings, including warnings regarding tampering, lethality if our oral tablets are prepared for injection and hepatotoxicity. For example, Norco carries a black box warning related to the APAP component and the risk of liver failure or injury. If the FDA requires a black box 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 user fee requirements for any approved products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and to list their drug products, and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP regulations and other FDA regulatory requirements.

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

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

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

In addition, the distribution of prescription pharmaceutical products, including samples, is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. The Drug Supply Chain Security Act also imposes obligations on manufacturers of pharmaceutical products related to product tracking and tracing.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment,

injunctions, fines, consent decrees, corporate integrity agreements, 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 imprisonment. Any of these sanctions could result in adverse publicity, among other adverse consequences.

Risk Evaluation and Mitigation Strategy (REMS)

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 an NME. If the FDA determines a REMS is necessary, the drug sponsor must develop the REMS program, which the FDA reviews and approves. A REMS may be required for a single drug or an entire class of drugs.

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

Based upon currently approved product REMS programs and class-wide REMS programs, including the class-wide REMS programs for extended-release and long-acting opioid analgesics, we believe that most of our product candidates, if approved, may be subject to a REMS. Accordingly, we expect to have to take prescribed measures to ensure the safe use of our products, if they are approved.

DEA Regulation

Most of our 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 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 product candidates may be listed by the DEA as Schedule II controlled substances under the CSA. However, we have requested in our NDA that KP201/APAP be listed as a Schedule III controlled substance based on its differential abuse potential when compared to other Schedule II controlled substances, such as IR hydrocodone combination products. None of the previously approved abuse deterrent formulations of opioids have received Schedule III designation. In 2014, the DEA also rescheduled hydrocodone combination products into Schedule II from Schedule III. If our product candidates are ultimately listed as Schedule II controlled substances, then the importation of APIs for our product candidates, as well as the manufacture, shipping, storage, sales and use of the products, will be subject to a high degree of regulation. In addition to maintaining an importer and/or exporter registration, importers and exporters of controlled substances must obtain a permit for every import of a Schedule I or II substance and a narcotic substance in Schedule III, IV and V, as well as every export of a Schedule I or II substance and a narcotic substance in Schedule III and IV. For all other drugs in Schedule III, IV and V, importers and exporters must submit an import or export declaration. Schedule II drugs are subject to the strictest requirements for registration, security, recordkeeping and reporting. Also, distribution and dispensing of these drugs are highly regulated. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Electronic prescriptions may also be permissible depending on the state, so long as the prescription complies with the DEA's requirements for electronic prescriptions.

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

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

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

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance or Schedule III narcotic must also be accompanied by special order forms, with copies provided to the DEA. Because most of our product candidates may be regulated as Schedule II controlled substances, they may be subject to the DEA's production and procurement quota scheme. The DEA establishes annually an

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

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

Other Healthcare Regulations

Our business activities, including but not limited to, research, sales, promotion, distribution, medical education and other activities following product approval will be 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, 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 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 Anti-Kickback Statute, or the specific intent to violate it, to have violated the statute. 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, 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.

We, and our business activities, are subject to 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.

As a condition of Medicaid payment for prescription drugs, the Medicaid Drug Rebate statute requires manufacturers to calculate and report to CMS their Average Manufacturer Price, which is used to determine rebate payments shared between the states and the federal government and, for some multiple source drugs, Medicaid payment rates for the drug, and for drugs paid under Medicare Part B, to also calculate and report their average sales price, which is used to determine the Medicare Part B payment rate for the drug. Drugs that are approved under a biologics license application, or BLA, or an NDA, including a 505(b)(2) NDA, are subject to an additional requirement to calculate and report the manufacturer's best price for the drug and inflation penalties which can substantially increase rebate payments. For BLA and NDA drugs, the Veterans Health Care Act requires manufacturers to calculate and report to the Department of Veterans Affairs a different price called the Non-Federal Average Manufacturing Price, offer the drugs for sale on the Federal Supply Schedule, and charge the government no more than a statutory price referred to as the Federal Ceiling Price, which includes an inflation penalty. A separate law requires manufacturers to pay rebates on these drugs when paid by the Department of Defense under its TRICARE Retail Pharmacy Program. Knowingly submitting false pricing information to the government creates potential False Claims Act liability.

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 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 civil monetary penalties of up to an aggregate of $150,000 per year and up to an aggregate of $1.0 million per year for "knowing failures." Manufacturers must submit reports by the 90th day of each calendar year. CMS released the data for the first reporting period on a public website on September 30, 2014.

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 on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also 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 the federal HIPAA laws 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.

Enforcement actions can be brought by federal or state governments or as "qui tam" actions brought by individual whistleblowers in the name of the government. Depending on the circumstances, failure to comply with these laws can result in penalties, including criminal, civil and/or administrative criminal penalties, damages, fines, disgorgement, debarment from government contracts, exclusion of products from reimbursement under 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. We expect that the ACA will continue to create significant changes in the healthcare 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, and we expect there will be additional challenges and amendments to the ACA in the future. 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 will remain in effect through 2024 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.

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.

Facilities

We occupy 7,800 square feet of headquarters office and laboratory space in Coralville, Iowa under a lease that expires in 2016 and we have the right to extend the term of the lease for an additional three years. We also maintain additional leased spaces in several locations, including Celebration, Florida; Durham, North Carolina and Blacksburg, Virginia. We believe that our facilities are adequate for our current needs.

Employees

As of November 30, 2015, we employed 25 full-time employees. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective bargaining arrangements. We consider our employee relations to be good.

Legal Proceedings

We are currently party to a lawsuit against DeWaay Financial Network, L.L.C., or DFN, a financial advisor. We instituted the lawsuit by filing a declaratory judgment action against DFN on September 13, 2013, in the Iowa District Court for Johnson County, Iowa. The lawsuit was subsequently transferred to the Iowa District Court for Polk County, Iowa.

On June 6, 2011, we entered into an agreement with DFN, or the DFN agreement, pursuant to which we granted to DFN a purported right of first refusal to serve as our exclusive financial advisor for specified strategic transactions, including a sale of our company, private and public capital raising

transactions, and joint ventures, licenses or similar transactions with respect to our product candidates. Pursuant to the DFN agreement we also granted a purported right to receive, subject to specified conditions including non-exercise of such right of first refusal, a cash fee equal to the greater of $250,000 and 1.5% of the total consideration received by us, our affiliates and our equity owners and related to any such strategic transaction, in each case, irrespective of whether any such strategic transaction occurred during or after the term of the DFN agreement.

In the lawsuit, we are seeking a declaratory judgment finding invalid and unenforceable such purported right of first refusal or right to receive a cash fee related to any such strategic transaction. DFN filed an answer requesting that the court declare that such rights are valid and survive termination of the DFN agreement and counterclaims requesting that the court award damages to DFN, including a fee based upon the total consideration that we have received and in the future will receive under the Deerfield facility. Two former members of our board of directors joined the lawsuit as intervenors based on DFN's purported assignment of its rights, or a portion thereof, under the DFN agreement to the intervenors. In September 2015, the court granted summary judgment in our favor with respect to our declaratory judgment action and DFN's counterclaims and we separately entered into settlement agreements with each of the intervenors. DFN subsequently filed a notice of appeal of the court's ruling with the Supreme Court of Iowa and the appeal is pending. We cannot predict the timing or ultimate outcome of this litigation. However, if it is determined that such purported right of first refusal and right to receive a cash fee related to any such strategic transaction are valid, then we could be required to pay DFN a portion of the consideration or proceeds received in any such strategic transaction, including potentially the Deerfield facility, our initial public offering, the sale of our Series D-1 convertible redeemable preferred stock and future capital raising and other strategic transactions.

From time to time we are involved in legal proceedings arising in the ordinary course of business. We believe there is no other litigation pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.