Flexion Therapeutics Inc
Form 424B4
December 12, 2014
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Filed Pursuant to Rule 424(b)(4)
Registration Statement Nos. 333-200668 and 333-200875

Prospectus

5,040,000 Shares

Common Stock

Flexion Therapeutics, Inc.

We are offering 5,040,000 shares of our common stock.

Our common stock is listed on the Nasdaq Global Market under the symbol FLXN . The closing price of our common stock on the Nasdaq Global Market on December 11, 2014, was $17.31 per share.

We have granted the underwriters an option to purchase up to 756,000 additional shares of our common stock.

Investing in our common stock involves risks. See Risk Factors beginning on page 10.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, we have elected to take advantage of certain reduced reporting requirements for this prospectus and may elect to comply with certain reduced public company reporting requirements for future filings.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total

Public Offering Price	$	17.00	$ 85,680,000
Underwriting Discount(1)	$	1.02	$ 5,140,800
Proceeds to Flexion (before expenses)	$	15.98	$ 80,539,200

(1) We refer you to Underwriting beginning on page 109 for additional information regarding underwriting compensation.

The underwriters expect to deliver the shares to purchasers on or about December 17, 2014 through the book-entry facilities of The Depository Trust Company.

BMO Capital Markets RBC Capital Markets

Needham & Company

Janney Montgomery Scott Summer Street Research Partners

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We are responsible for the information contained in or incorporated by reference into this prospectus and in any free-writing prospectus we prepare or authorize. We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in or incorporated by reference into this prospectus is accurate as of any date other than the date of this prospectus or the date of the document incorporated by reference, as applicable.

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SUMMARY

This summary highlights information contained in other parts of or incorporated by reference into this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere or incorporated by reference into this prospectus. You should read the entire prospectus and the information incorporated herein carefully, especially Risk Factors and our consolidated financial statements and the related notes incorporated by reference into this prospectus, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to Flexion Therapeutics, we, us and our refer to Flexion Therapeutics, Inc.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of novel, injectable pain therapies. We are targeting anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, or OA, a type of degenerative arthritis. Our broad and diversified portfolio of product candidates addresses the OA pain treatment spectrum, from moderate to severe pain, and provides us with multiple opportunities to achieve our goal of commercializing novel, targeted pain therapies.

Our lead product candidate, FX006, is a first-in-class injectable, sustained-release, intra-articular, or IA, meaning in the joint, steroid treatment for patients with moderate to severe OA pain. FX006 combines a commonly administered steroid, triamcinolone acetonide, or TCA, with poly lactic-co-glycolic acid, referred to as PLGA, to provide sustained therapeutic concentrations in the joint and persistent analgesic effect. We specifically designed FX006 to address the limitations of current IA therapies by providing long-lasting, local analgesia while avoiding systemic side effects, which are effects that occur throughout the body as a result of drug that is released from the site of injection into circulating blood. In a completed Phase 2b dose-ranging clinical trial, FX006 has demonstrated clinically meaningful and significantly better pain relief compared to the current injectable standard of care.

In April 2014, we initiated a pivotal Phase 2b clinical trial of FX006 to further identify a safe and well-tolerated dose of FX006 that demonstrates superior pain relief to placebo. On September 16, 2014, the U.S. Food and Drug Administration, or FDA, notified us that it had placed a clinical hold on the FX006 investigational new drug application IND due to a single occurrence of what was then reported as septic arthritis, an infection of the injected knee joint, in a patient in the clinical trial. We subsequently performed testing and investigation requested by the FDA, which demonstrated that the FX006 drug product was not contaminated. This is consistent with the fact that no production batch of FX006 has ever failed sterility testing. On October 28, 2014, we received notification that based on the highly atypical nature of the patient s clinical presentation as it relates to knee joint infection and the patient s subsequent clinical course which was most consistent with rheumatoid arthritis, the principal investigator had changed the initial serious adverse event diagnosis from septic arthritis, possibly related to study drug treatment, to inflammatory arthritis, unrelated to study drug treatment. This information was promptly shared with the FDA. It is assumed that the original, and only, positive synovial fluid culture obtained from this patient was a false positive, which occurs in approximately 5% of such cases. Thus there have been no confirmed diagnoses of septic arthritis and no serious adverse events related to drug treatment among the more than 300 patients treated with FX006 in all clinical trials to date. After reviewing the information we provided in response to the FDA s requests, on December 1, 2014, the FDA notified us that it had lifted the clinical hold on FX006. As a result we immediately resumed recruitment and dosing in the pivotal Phase 2b trial of FX006, and we expect to report top-line data from the trial in the second half of 2015.

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In 2014, the FDA informed us that it will consider our on-going pivotal Phase 2b trial as one of two pivotal efficacy trials required for registration of a single-dose administration of FX006. In addition, the FDA informed us that a second placebo-controlled pivotal trial would be sufficient to support the filing of a new drug application, or NDA, for single-dose administration of FX006 and that data from a repeat-dose safety trial would not be required. As a result, we plan to initiate a placebo-controlled Phase 3 trial of FX006 in early 2015 and expect to develop and file repeat-dose safety data in a supplemental NDA after an approval and launch of FX006 for single-dose administration.

We believe that FX006 has the potential to be a superior front line injectable treatment for OA pain management compared to existing therapies by providing safe, more effective and sustained pain relief to patients. We believe the following attributes make FX006 an attractive development candidate:

A first-in-class injectable, IA, sustained-release treatment for patients with moderate to severe OA pain that has demonstrated in clinical trials to date:

- clinically meaningful and significantly better pain relief compared to the current injectable standard of care,
- persistent therapeutic concentrations of drug in the joint and durable efficacy, and
- an attractive safety profile with limited systemic exposures and the potential for fewer side effects.

Among the largest analgesic effects seen in OA clinical trials.

Strong proprietary position through a combination of patents, trade secrets and proprietary know-how, as well as eligibility for marketing exclusivity.

Well-defined Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, regulatory pathway seeking approval for a novel formulation of the same dose of the already approved immediate-release steroid used by orthopedists and rheumatologists.

Familiarity of orthopedists and rheumatologists with IA injections utilizing the same steroid in the same dose.

Potential for pharmacoeconomic benefits due to superior efficacy and durability and the potential to delay costly and invasive total joint replacement, also referred to as total joint arthroplasty, or TJA.

Our other product candidates include FX007 for post-operative pain and FX005 for the treatment of end-stage OA patients. FX007 is a locally administered TrkA receptor antagonist that is designed to provide persistent relief of post-operative pain, including in patients who have undergone TJA. We are conducting preclinical local toxicology experiments and plan to initiate a proof of concept, or PoC, clinical trial for FX007 following the generation of the preclinical data. FX005 is a sustained-release p38 MAP, or mitogen-activated protein, kinase inhibitor which has both analgesic and anti-inflammatory effects. FX005 successfully completed a Phase 2a PoC clinical trial demonstrating significant pain relief and function improvement. We will continue to evaluate further development of FX005 taking into consideration, among other factors, our available capital resources.

We have worldwide commercialization rights to all of our product candidates. We also have an exclusive worldwide license agreement with Southwest Research Institute, or SwRI, with respect to the use of SwRI s proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including FX006. We intend to market our products in the United States through our own sales force targeting specialty physicians, including orthopedists and rheumatologists. Outside of the United States, we are exploring selective partnerships with third parties for the development and commercialization of our product candidates. Each of our product candidates and our PLGA formulation technology is protected through a combination of patents, trade secrets and proprietary know-how, and we intend to seek marketing exclusivity for any approved products.

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OA is a type of degenerative arthritis that is caused by the progressive breakdown and eventual loss of cartilage in one or more joints. Arthritis is the most common cause of disability in the United States and OA is the most common joint disease, affecting 27 million Americans, with numbers expected to grow as a result of aging, obesity and sports injuries. Recent data suggest that OA accounts for over $185 billion of annual healthcare expenditures in the United States, which does not include loss of productivity costs. We estimate that by 2030, 45 million people will have OA. OA commonly affects large weight-bearing joints like the knees and hips, but also occurs in the shoulders, hands, feet and spine. Patients with OA suffer from joint pain, tenderness, stiffness and limited movement. As the disease progresses, it becomes increasingly painful and debilitating, culminating, in many cases, in the need for TJA.

Current therapies for OA are suboptimal and, because there is no cure for the disease, controlling pain and delaying surgery are the primary goals for treatment regimens. Oral drugs, such as non-steroidal anti-inflammatory drugs, or NSAIDs, including COX II inhibitors, and Cymbalta, as well as topical NSAIDs, are used to treat early-stage OA pain but have limited effect on pain and, given the amount and frequency of use in OA patients, are associated with serious side effects. For example, NSAIDs have shown increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction and stroke. Furthermore, this class of drugs can cause serious gastrointestinal (GI) adverse events including bleeding, ulceration and perforation of the stomach or intestines. These serious side effects are particularly worrisome because OA patients often have co-existing medical conditions, including diabetes and hypertension. For patients with moderate to severe OA pain, IA medicines, such as immediate-release steroids and hyaluronic acid, or HA, injected into the joint, are generally considered safe, but leave the joint rapidly and fail to produce or maintain meaningful pain relief. For patients who progress to end-stage OA, physicians prescribe opioids, which in addition to the risk of addiction, have numerous systemic side effects, such as respiratory depression, hypotension and constipation, and cause a higher incidence of falls and fractures in older OA patients. As a result of these suboptimal therapies, many OA patients experience persistent and worsening pain, which often culminates in the decision for TJA, a painful and expensive procedure. Further, because the initial joint replacement wears out over time, the younger the patient is at the time of the joint replacement, the more likely it is that he or she will require repeat surgery in their lifetime.

Our projections indicate that by 2030 approximately 23.5 million of the 45 million OA patients will have knee OA. According to IMS Health, each year over four million OA patients in the United States receive IA steroid injection treatments in the knee, hip, shoulder, hand and foot, with over three million of these being knee injections. In 2012, the number of patients that received knee injections of IA steroids increased approximately 12%. We estimate that an additional 1.3 million patients received knee injections of IA HA, which the FDA has approved for use only in the knee. Sales of HA in the United States were approximately $700 million in 2013, the vast majority of which we believe were related to knee therapy. Our clinical trials to date have treated patients with knee OA, which represents the most common joint treated with IA therapies.

While worldwide sales of HA injections are approaching $2 billion, recent negative guidance from specialty societies (e.g. the American Academy of Orthopedic Surgeons (AAOS) and the Osteoarthritis Research Society International (OARSI)) may begin to put downward pressure on HA sales. For example, Sanofi Biosurgery, which sells the market leading HA treatment, Synvisc, reported a 7% drop in U.S. net sales during the first-nine months of 2014 when compared to the first nine months of 2013. This could be in part due to the fact that select payer groups have limited reimbursement for the entire class of HA products.

Given the limitations of current therapies, we believe FX006, if successfully commercialized, would provide an attractive therapeutic alternative. Clinical trials to date for FX006 have demonstrated clinically meaningful and significantly better pain relief compared to the current injectable standard of care, persistent therapeutic concentrations of drug in the joint and durable efficacy, and an attractive safety profile with limited systemic exposures and the potential for fewer side effects.

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Our Strategy

Our goal is to cost-effectively develop and commercialize novel therapies that will provide safe and substantial analgesia, or pain relief. Initially, we intend to develop a diverse portfolio of product candidates for the treatment of OA and post-operative pain where we believe there are significant unmet needs. The principal elements of our strategy to accomplish this goal are the following:

Focus on novel product candidates that provide long-lasting analgesia locally while avoiding systemic side effects. We intend to develop anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with OA and post-operative pain. Many OA patients will eventually require IA injection therapies to control their pain as the disease progresses. Currently available IA steroids, none of which are formulated for sustained release, leave the joint rapidly and confer pain relief that typically wanes after two to four weeks. Since, by medical practice, steroids are not typically injected more frequently than every three months, patients can experience months of pain during that time. While the benefits of HA injections generally last for a longer period of time than steroid injections, they are only marginally more effective than placebo. As a result, we believe there is a significant unmet medical need for persistent, effective and safe OA pain relief that can be addressed by IA sustained-release injection therapies. We have therefore formulated our IA product candidates, FX006 and FX005, with the goal of achieving effective drug concentrations in the joint for months, while avoiding significant plasma concentrations of drug that have been linked to systemic side effects. FX007 is being developed to treat post-operative pain and is being formulated to remain in the tissues for a sufficient period of time to effectively treat patients experiencing post-operative pain.

Mitigate development risk and expedite regulatory timeline to product approval. We seek to mitigate development risk by selecting product candidates with validated mechanisms of action. Each of our product candidates also utilizes a unique mechanism of action for achieving analgesia and/or anti-inflammatory effects, which diversifies development risk across multiple targets. In addition, for FX006 and FX005, our sustained-release technology employs PLGA delivery systems, which are already used in approved sustained-release drug products outside of OA and in approved surgical devices. Because FX006 incorporates an already approved steroid in PLGA, we believe it qualifies for the Section 505(b)(2) NDA pathway under the FDCA which can be an expeditious, cost-effective means to seek product approval, as well as potentially to expand indications for this product candidate. Section 505(b)(2) of the FDCA enables the applicant to rely, in part, on published literature or the FDA s findings of safety and efficacy for an existing product in support of its application.

Target multiple points in the OA pain treatment spectrum. To maximize the likelihood of bringing products to market successfully, our product candidates target different elements of the OA treatment continuum. FX006 is targeted for front line IA therapy in patients with moderate to severe OA pain with the potential to replace IA steroids and HA, FX005 is targeted for patients who progress to end-stage disease as an alternative to opioids and FX007 is targeted for patients with post-operative pain, including those undergoing TJAs.

Retain commercial rights in the United States and selectively partner outside of the United States. Because IA therapies in the United States are administered by a relatively small number of specialists, particularly orthopedists and rheumatologists, we believe that we can cost-effectively commercialize our product candidates, if approved, with our own specialty sales and marketing organization in the United States, and thereby retain more of the commercial value of these product candidates. In prior years, Genzyme Corp., which has been acquired by Sanofi, supported sales of Synvisc utilizing a sales force of approximately 100 representatives. We believe we can establish an effective U.S. commercial organization with our own specialty sales force of approximately 60 to 100 representatives that target orthopedists and rheumatologists. Outside of the United States, we are exploring selective partnerships with third parties for the development and commercialization of our product candidates.

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Risk Factors

Our business is subject to many risks and uncertainties of which you should be aware before you decide to invest in our common stock. These risks are discussed more fully under Risk Factors in this prospectus and in the documents incorporated herein by reference. Some of these risks include:

- we have incurred significant losses since our inception resulting in an accumulated deficit of $85.7 million as of September 30, 2014, and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability;
- we have not generated any revenue from, or received regulatory approval for, any of our product candidates;
- we are a development stage company and may require additional capital beyond this offering, including prior to approval and commercialization of FX006 or any of our other product candidates;
- we have not completed a pivotal clinical trial for FX006 or any of our other product candidates and may be unable to successfully complete the development of, obtain regulatory approval for, or commercialize any of our product candidates;
- we rely on third parties to manufacture and conduct the clinical trials of our product candidates, which could delay or limit their future development or regulatory approval;
- we currently do not have the infrastructure to commercialize any of our product candidates if such products receive regulatory approval; and
- we may be unable to adequately maintain and protect our proprietary intellectual property assets, which could impair our commercial opportunities.

Implications of Being an Emerging Growth Company

We qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- reduced disclosure about our executive compensation arrangements;
- no requirement that we solicit non-binding advisory votes on executive compensation or golden parachute arrangements; and

an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We will cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.0 billion or more; (ii) December 31, 2019; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Also, we have irrevocably elected to opt out of the exemption for the delayed adoption of certain accounting standards and, therefore, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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Corporate and Other Information

We were incorporated in Delaware in November 2007. Our principal executive offices are located at 10 Mall Road, Suite 301, Burlington, Massachusetts 01803, and our telephone number is (781) 305-7777. Our corporate website address is www.flexiontherapeutics.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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The Offering

Common stock offered by us	5,040,000 shares
Common stock to be outstanding after this offering	20,667,288 shares
Option to purchase additional common stock	756,000 shares
Use of proceeds	We intend to use the net proceeds from this offering to complete our planned Phase 3 clinical trial and the submission of an NDA for FX006, for preparatory activities for commercial launch of FX006, for development of FX007 and for general development expenses, working capital and other general corporate purposes. See Use of Proceeds for more information.
Risk factors	You should read the Risk Factors section of this prospectus for a discussion of certain of the factors to consider carefully before deciding to purchase any shares of our common stock.
Nasdaq Global Market symbol	FLXN

The number of shares of our common stock to be outstanding after this offering is based on 15,627,288 shares of common stock outstanding as of September 30, 2014 and excludes:

- 420,974 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014, at a weighted average exercise price of $3.20 per share;
- 967,502 shares of common stock reserved for future issuance under our 2013 equity incentive plan, or the 2013 plan, as of September 30, 2014; and
- 209,102 shares of common stock reserved for future issuance under our 2013 employee stock purchase plan, or the 2013 purchase plan, as of September 30, 2014.

Unless otherwise indicated, all information contained in this prospectus assumes:

- no exercise of the outstanding options described above; and

no exercise by the underwriters of their option to purchase up to an additional 756,000 shares of our common stock.

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Summary Financial Data

The following table summarizes certain of our financial data. We derived the summary statement of operations data for the years ended December 31, 2012 and 2013 from our audited consolidated financial statements incorporated by reference into this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2013. The summary statement of operations data for the nine months ended September 30, 2013 and 2014, and the summary balance sheet data as of September 30, 2014 were derived from our unaudited financial statements incorporated by reference into this prospectus from our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014. The unaudited financial statements, in management s opinion, have been prepared on the same basis as the audited consolidated financial statements and related notes incorporated herein by reference, and include all adjustments, consisting only of normal recurring adjustments, that management considers necessary for a fair presentation of the financial information as of and for the periods presented. Our historical results are not necessarily indicative of the results that may be expected in the future, and results of interim periods are not necessarily indicative of the results for the entire year. The summary financial data should be read together with our consolidated financial statements and related notes, Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus or incorporated by reference herein.

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2012	2014	2013
			(unaudited)	
	(in thousands, except per share data)			
Statement of Operations Data:				
Revenue	$	$	$	$
Operating expenses:				
Research and development	11,061	11,065	12,424	8,825
General and administrative	6,704	3,947	6,822	5,363
Total operating expenses	17,765	15,012	19,246	14,188
Loss from operations	(17,765)	(15,012)	(19,246)	(14,188)
Other income (expense):				
Interest income	234	194	319	219
Interest expense	(449)		(315)	(335)
Other income (expense), net	(207)	(164)	(266)	(192)
Total other income (expense)	(422)	30	(262)	(308)
Net loss	$ (18,187)	$ (14,982)	$ (19,508)	$ (14,496)
Net loss attributable to common stockholders	$ (18,187)	$ (14,982)	$ (19,508)	$ (14,496)
Net loss per share attributable to common stockholders, basic and diluted[(1)]	$ (23.02)	$ (27.58)	$ (1.50)	$ (18.37)
Weighted average common shares outstanding, basic and diluted[(1)]	790	543	13,008	789

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	As of September 30, 2014	
	Actual	Pro Forma[2]
	(unaudited)	
	(in thousands)	
Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 66,589	$ 146,628
Working capital[3]	61,104	141,143
Total assets .	68,125	148,164
Total debt[4]	4,082	4,082
Total stockholders equity	59,791	139,831

(1) For further details on the calculation of basic and diluted net loss per share attributable to common stockholders, see Note 3 to our consolidated financial statements incorporated by reference in this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2013.

(2) The unaudited pro forma balance sheet data give effect to our issuance and sale of 5,040,000 shares of our common stock in this offering at the public offering price of $17.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities.

(4) Total debt includes the current and long-term portion of our debt.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with all of the other information included or incorporated by reference in this prospectus, including the risks and uncertainties discussed under Risk Factors in the documents incorporated by reference herein, before deciding whether to invest in our common stock. The occurrence of any of the risks described below or incorporated by reference in this prospectus could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We have limited operating history. To date, we have focused primarily on developing our lead product candidate, FX006. We have two additional product candidates, FX007 and FX005. All of our product candidates will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We have incurred significant net losses in each year since our inception, including net losses of $19.5 million for the nine months ended September 30, 2014 and $18.2 million, and $15.0 million for fiscal years 2013, and 2012, respectively. As of September 30, 2014, we had an accumulated deficit of $85.7 million.

We have devoted most of our financial resources to product development, including our non-clinical development activities and clinical trials. To date, we have financed our operations exclusively through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenue. To date, none of our product candidates have been commercialized, and if our product candidates are not successfully developed or commercialized, or if revenue is insufficient following marketing approval, we will not achieve profitability and our business may fail. Even if we successfully obtain regulatory approval to market our product candidates in the United States, our revenue is also dependent upon the size of the markets outside of the United States, as well as our ability to obtain market approval and achieve commercial success.

We expect to continue to incur substantial and increased expenses as we expand our development activities and advance our clinical programs, particularly with respect to FX006. We also expect a continued increase in our expenses associated with our operations as a publicly-traded company. As a result of the foregoing, we expect to continue to incur significant and increasing losses and negative cash flows for the foreseeable future.

We have never generated any revenue and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize our product candidates. We do not anticipate generating revenue from sales of our product candidates for the foreseeable future, if ever. Our ability to generate future revenue from product sales depends heavily on our success in:

completing clinical development of FX006, as well as advancing clinical development of our other product candidates;

obtaining regulatory approval for FX006 as well as our other product candidates; and

launching and commercializing any product candidates for which we receive regulatory approval, either by building our own targeted sales force or by collaborating with third parties.

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Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses, when, or if, we will begin to generate revenue from product sales, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are required by the FDA to perform studies in addition to those that we currently anticipate.

Even if one or more of our product candidates is approved for commercial sale, to the extent we do not engage a third party collaborator, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

If we fail to obtain additional financing, we would be forced to delay, reduce or eliminate our product development programs.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our clinical programs, including our on-going and planned clinical trials for FX006.

We estimate that the net proceeds from this offering will be approximately $80.0 million, based on the public offering price of $17.00 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. As of September 30, 2014, we had cash, cash equivalents and marketable securities of $66.6 million and working capital of $61.1 million. Based upon our current operating plan, we believe that the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, will enable us to fund our operating expenses and capital requirements at least into mid-2017, including through completion of our pivotal Phase 2b and Phase 3 clinical trials for FX006 and the submission of an NDA for FX006. Regardless of our expectations as to how long the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, will fund our operations, changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. For example, our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expect or the FDA could impose additional or different clinical development requirements on us prior to our submission of an NDA for FX006. In any event, we may require additional capital prior to commercializing FX006 or any of our other product candidates.

Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of our product candidates;
- seek corporate partners for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;
- relinquish or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves; or
- significantly curtail, or cease, operations.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects.

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We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, which could adversely impact our existing stockholders and new investors participating in this offering, as well as our business. The sale of additional equity or convertible debt securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

Our credit and security agreement with MidCap Financial SBIC, LP, or MidCap, contains restrictions that limit our flexibility in operating our business. We may be required to make a prepayment or repay the outstanding indebtedness earlier than we expect under our credit and security agreement if a prepayment event or an event of default occurs, including a material adverse change with respect to us, which could have a materially adverse effect on our business.

In January 2013, we entered into a credit and security agreement with MidCap and drew down the full $5.0 million under the facility. The agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- incur or assume certain debt;
- merge or consolidate or acquire all or substantially all of the capital stock or property of another entity;
- enter into any transaction or series of related transactions that would be deemed to result in a change in control of us under the terms of the agreement;
- change the nature of our business;
- change our organizational structure or type;
- amend, modify or waive any of our organizational documents;
- license, transfer or dispose of certain assets;
- grant certain types of liens on our assets;
- make certain investments;

pay cash dividends;

enter into material transactions with affiliates; and

amend or waive provisions of material agreements in certain manners.

The restrictive covenants of the agreement could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial.

A breach of any of these covenants could result in an event of default under the agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations or condition occurs, which could potentially include negative results in our planned clinical trials, or a material impairment of the prospect of our repayment of any portion of the amounts we owe under the agreement occurs. In the case of a continuing event of default under the agreement, MidCap could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted MidCap a security interest under the agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the agreement are secured by all of our existing and future assets, excluding intellectual property, which is subject to a negative pledge arrangement.

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We may not have enough available cash or be able to raise additional funds on satisfactory terms, if at all, through equity or debt financings to repay our indebtedness at the time any such repayment is required. In such an event, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result.

Risks Related to Clinical Development and Regulatory Approval

We are heavily dependent on the success of our lead product candidate FX006, which is in a later stage of development than our other product candidates. We cannot give any assurance that FX006 will successfully complete clinical development or receive regulatory approval, which is necessary before it can be commercialized.

Our business and future success is substantially dependent on our ability to successfully develop, obtain regulatory approval for, and successfully commercialize our lead product candidate FX006, for which we are conducting a pivotal Phase 2b clinical trial and plan to initiate a Phase 3 clinical trial in early 2015. Any delay or setback in the development of any of our product candidates, but particularly FX006, could adversely affect our business and cause our stock price to decline. Should our planned FX006 clinical development fail to be completed in a timely manner or at all, we may rely on our other product candidates, FX007 and FX005, which are at an earlier development stage and will require additional time and resources to obtain regulatory approval and proceed with commercialization. We cannot assure you that our planned clinical development for FX006 will be completed in a timely manner, or at all, or that we will be able to obtain approval for FX006 from the FDA or any foreign regulatory authority.

Clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Clinical failure can occur at any stage of clinical development. We have never completed a pivotal clinical trial or submitted an NDA.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of subsequent clinical trials. In particular, the positive results generated in the completed FX006 Phase 2b dose-ranging clinical trial do not ensure that our pivotal Phase 2b clinical trial or planned Phase 3 clinical trial will demonstrate similar results.

In our completed Phase 2b dose-ranging clinical trial, the 60 mg dose of FX006 unexpectedly showed inferior efficacy compared to the 40 mg dose. While we have investigated potential causes of this clinical outcome and believe we understand the basis for the performance of the 60 mg dose, we may not be correct. Therefore, we cannot guarantee that the underlying cause is unique to the 60 mg dose and will not impact the doses we are studying in our pivotal Phase 2b clinical trial, or will not otherwise result in regulatory delays or the need for additional studies prior to seeking or obtaining regulatory approval.

We have conducted preclinical toxicology studies in healthy dogs with single and repeat doses of FX006, blank microspheres and immediate-release TCA. The findings from the studies related to the administration of TCA were similar between the immediate-release TCA and FX006 groups and known effects of immediate-release TCA. In the single dose study, local cartilage findings of reduced extracellular matrix had completely reversed by the end of the nine-month recovery period in both the FX006 and TCA study arms. In the repeat-dose toxicity study, three doses were administered either one month or three months apart. A larger reduction in extracellular matrix in cartilage was noted which partially recovered by six months following the last dose, however, structural changes in cartilage were observed with repeat

administrations of both FX006 and immediate-release TCA. All of our clinical trials to date have been, and our planned Phase 3 clinical trial will be, conducted with single doses of FX006. However, we intend to study FX006 in a separate repeat dose safety clinical trial and to submit repeat dose data in a supplemental NDA after an approval and launch of FX006 for

single-dose administration. Immediate-release TCA has a long history of safe clinical use in patients and in a randomized, double-blind clinical trial conducted in 2003 by Raynauld et al administering immediate-release TCA or saline every three months for up to two years in 68 OA patients, it was well-tolerated and demonstrated no deleterious effects in the knee joint when assessed by clinical exam and X-ray evaluation. Nonetheless, it is possible that we could observe similar outcomes to those observed in our preclinical studies with repeated doses of FX006 that would harm our ability to maintain regulatory approval or would limit the commercial potential of FX006.

Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. In addition to the safety and efficacy traits of any product candidate, clinical trial failures may result from a multitude of factors including flaws in trial design, dose selection, placebo effect and patient enrollment criteria. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Our future clinical trial results may not be successful.

If FX006 or any other product candidate is found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for it and our business would be materially harmed. For example, if the results of our on-going pivotal Phase 2b, planned Phase 3 or other clinical trials for FX006 demonstrate unexpected safety findings or do not achieve the primary efficacy endpoints, the prospects for approval of FX006 as well our stock price and our ability to create stockholder value would be materially and adversely affected.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in composition of the patient populations, adherence to the dosing regimen and other trial elements and the rate of dropout among clinical trial participants. We do not know whether any future clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates. If we are unable to bring any of our current or future product candidates to market, our ability to create long-term stockholder value will be limited.

If the FDA does not conclude that FX006 satisfies the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for FX006 under Section 505(b)(2) are not as we expect, the approval pathway for FX006 will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We intend to seek FDA approval through the Section 505(b)(2) regulatory pathway for FX006. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we may still need to conduct additional trials and we cannot guarantee that FX006 will receive the requisite approvals for commercialization. If this were to occur, the time and financial resources required to obtain FDA approval for FX006, and complications and risks associated with FX006, would likely substantially increase. We may also need to obtain additional funding, which could result in significant dilution to the ownership interests of our then existing stockholders to the extent we issue equity securities or convertible debt. We cannot assure you that we would be able to obtain such additional financing on terms acceptable to us, if at all. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market faster than FX006, which could materially adversely impact our competitive position and prospects.

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

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

We may experience delays in clinical trials of our product candidates. We are conducting a pivotal Phase 2b clinical trial of FX006, for which we expect to report topline data in the second half of 2015, and we plan to initiate a Phase 3 clinical trial of FX006 in early 2015. We are conducting preclinical local toxicology experiments and plan to initiate a PoC clinical trial for FX007 following the generation of the additional preclinical data. Our clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients, or be completed on schedule, if at all. Our clinical trials can be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold for safety reasons or following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required institutional review board approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

For example, our completed Phase 2b dose-ranging clinical trial for FX006 was subject to a clinical hold imposed by the FDA due to the observation of effects of PLGA microspheres on synovial tissue from FX006 injections. While we were able to begin enrollment initially at non-U.S. sites and later at U.S. sites after the clinical hold was lifted without restriction by the FDA, the hold delayed our completion of the trial and resulted in additional expense. Also on September 16, 2014, the FDA notified us that it had placed a clinical hold on the FX006 IND due to a single occurrence of what was then reported to be septic arthritis, an infection of the injected knee joint, of a patient in the clinical trial. While the clinical hold was lifted on December 1, 2014 following our successful completion of testing and investigation requested by the FDA, the hold has delayed our completion of our pivotal Phase 2b clinical trial and the initiation of our planned Phase 3 clinical trial.

If initiation or completion of our clinical trials are delayed for any of the above reasons or other reasons, our development costs may increase, our approval process could be delayed and our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

Our product candidates may cause adverse events or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events, or AEs, caused by our product candidates or other potentially harmful characteristics of our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to

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interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. For example, in rat toxicology studies with repeat doses of FX005, an abnormal decrease of cartilage cells and components of cartilage matrix was observed. Based on these findings, we conducted additional non-clinical studies involving different doses and/or dose frequencies for FX005 to guide further clinical development. While we have identified a lower dose of FX005 that avoids these toxicology issues, we will need to demonstrate that doses lower than those used in the Phase 2a clinical trial will be effective, or we may need to pursue further development of FX005 as a single-dose treatment, which could limit its overall market potential.

While no serious adverse events, or SAEs, related to study drug have been observed in any of our clinical trials to date, there have been some AEs at least possibly related to the study drug. For example, although 17.6% of patients treated with immediate-release TCA experienced AEs, 10.7% of FX006 patients were judged by their physicians to have an AE at least possibly related to study drug. The most commonly observed FX006 AEs were arthralgia (joint pain) and joint stiffness and were generally mild to moderate in severity. If drug-related SAEs are observed in any of our clinical trials, our ability to obtain regulatory approval for our product candidates may be adversely impacted.

Further, if any of our approved products cause serious or unexpected side effects after receiving market approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified Risk Evaluation and Mitigation Strategy;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical studies;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate s clinical development and may vary among jurisdictions. For example, we cannot guarantee that the FDA will not require additional or different clinical trials in support of our submission of an NDA for FX006 despite the most recent guidance we have received from the FDA. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or

any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, scope or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;

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- we may be unable to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates 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; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change significantly in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market FX006 or our other product candidates, which would harm our business, results of operations and prospects significantly.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, 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. Any of the foregoing scenarios could harm the commercial prospects for our product candidates. For example, we believe that, to the extent our clinical development of FX006 continues to focus on knee OA, any initial indication of FX006 would be limited to the treatment of knee OA, as opposed to the treatment of OA generally. If an initial indication is limited to knee OA, we would likely need to conduct additional clinical trials in order to market FX006 for other indications and expand its market potential. In addition, we are choosing to pursue an initial approval of FX006 for single-dose administration. While we intend to develop and submit clinical data for repeated dosing of FX006 in a supplemental NDA, if we were unable to expand the label for FX006 to include repeat dosing, our ability to fully market FX006 would be limited.

We have not previously submitted an NDA or any similar drug approval filing to the FDA or any comparable foreign authority for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approval for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market one or more of our product candidates, our revenue will be dependent, to a significant extent, upon the size of the markets in the territories for which we gain regulatory approval. If the markets for patients or indications that we are targeting are not as significant as we estimate, we may not generate significant revenue from sales of such products, if approved.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product s approved labeling. For example, if we receive marketing approval for FX006 as a single-dose therapy for knee OA, physicians may nevertheless use FX006 for their patients in a manner that is inconsistent with the

approved label, potentially including repeat dosing or as an

injection in other joints. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Even if we obtain regulatory approval for FX006 or other product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. FX006 and our other product candidates, if approved, will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we or a regulatory agency discovers previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of a product candidate, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or

refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

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Any relationships with potential customers and third party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, marketing expenditure tracking and disclosure (or sunshine) laws, government price reporting, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Our operations may be directly, or indirectly, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance are also likely to increase. These laws may impact, among other things, our current activities with investigators and research subjects, as well as proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The laws that may affect our ability to operate include, but are not limited to:

the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third party payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology and Clinical Health Act of 2009, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform services involving the use or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;

the federal Open Payments program, created under Section 6002 of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, PPACA, and its implementing regulations requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, or HHS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to HHS ownership and investment interests held by physicians (as defined above) and their immediate family members;

state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third party payor, including commercial insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy

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and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals); and

federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

In addition, the FDA approval and commercialization of any of our product candidates in the United States will also likely subject us to the following types of laws, among others:

state and federal government price reporting laws that require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts); and

state and federal marketing expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported (compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities).

Efforts to ensure that our 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 interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil, criminal, and administrative penalties, damages, fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other government healthcare programs, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Even if we obtain FDA approval for FX006 or any other product candidate in the United States, we may never obtain approval for or commercialize our product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approval in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

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If we fail to develop, acquire or in-license other product candidates or products, our business and prospects will be limited.

Our long-term growth strategy is to develop, acquire or in-license and commercialize a portfolio of product candidates in addition to FX006 and our other existing product candidates. We do not have internal new drug discovery capabilities. As a result, our primary means of expanding our pipeline of product candidates is to develop improved formulations and delivery methods for existing FDA-approved products and/or select and acquire or in-license product candidates for the treatment of therapeutic indications that complement or augment our current targets, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Developing new formulations of existing products or identifying, selecting and acquiring or licensing promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual development, acquisition or license of a particular product candidate, potentially resulting in a diversion of our management s time and the expenditure of our resources with no resulting benefit. If we are unable to add additional product candidates to our pipeline, our long-term business and prospects will be limited.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We rely upon and plan to continue to rely upon third party CROs to monitor and manage data for our preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with FDA laws and regulations regarding current good clinical practice, or GCP, which are also required by the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for all of our products in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. While we have agreements governing activities of our CROs, we have limited influence over their actual performance. In addition, portions of the clinical trials for our product candidates are being conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCP. Failure to comply with applicable regulations in the conduct of the clinical trials for our product candidates may require us to repeat clinical trials, which would delay the regulatory approval process.

Some of our CROs have an ability to terminate their respective agreements with us if, among other reasons, it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. If any of our relationships with these third party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the

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quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of any approved product candidate.

If we were to experience an unexpected loss of supply of our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, clinical trials. We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our preclinical and clinical drug supplies and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers or other third party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. While we work closely with our third party manufacturers on the manufacturing process for our product candidates, including quality audits, we generally do not control the implementation of the manufacturing process of, and are completely dependent on, our contract manufacturers or other third party manufacturers for compliance with cGMP regulatory requirements and for manufacture of both active drug substances and finished drug products. If our contract manufacturers or other third party manufacturers cannot successfully manufacture material that conforms to applicable specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers or other third party 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 regulatory approval for or market our product candidates, if approved.

We rely on our manufacturers to purchase from third party suppliers the materials necessary to produce our product candidates for our clinical trials. There are a limited number of suppliers for raw materials that we use to manufacture our drugs and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and if approved, for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our product candidates.

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We expect to continue to depend on contract manufacturers or other third party manufacturers for the foreseeable future. We have not entered into long-term commercial supply agreements with our current contract manufacturers or with any alternate fill/finish suppliers. Although we intend to do so prior to any commercial launch in order to ensure that we maintain adequate supplies of finished drug product, we may be unable to enter into such an agreement or do so on commercially reasonable terms, which could have a material adverse impact upon our business.

We rely on limited sources of supply for our product candidates and any disruption in the chain of supply may cause delay in developing and commercializing our product candidates.

Currently, for FX006, we use Farmabios SpA as our sole source of TCA, and for both FX006 and FX005, Evonik Corporation as our sole source of finished microspheres drug product. Because of the unique equipment and process for loading TCA onto PLGA microspheres, transferring manufacturing activities for FX006 to an alternate supplier would be a time-consuming and costly endeavor, and there are only a limited number of manufacturers that we believe are capable of performing this function for us. Switching FX006 finished drug suppliers may involve substantial cost and could result in a delay in our desired clinical and commercial timelines. For FX006, we expect that initially only one supplier will be qualified as a vendor with the FDA. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. Any alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new FX006 supplier is relied upon for commercial production.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.

As we scale up manufacturing of our product candidates and conduct required stability testing, we may encounter product, packaging, equipment and process-related issues that may require refinement or resolution in order to proceed with our planned clinical trials and obtain regulatory approval for commercial marketing. In the future, we may identify impurities, which could result in increased scrutiny by regulatory authorities, delays in our clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our product candidates.

We may not be successful in establishing development and commercialization collaborations which could adversely affect, and potentially prohibit, our ability to develop our product candidates.

Because developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, establishing manufacturing capabilities and marketing approved products are expensive, we are exploring collaborations with third parties outside of the United States that have more resources and experience. For example, we are exploring selective partnerships with third parties for FX006 development and commercialization outside of the United States. If we are unable to obtain a partner for FX006, we may be unable to advance the development of FX006 in territories outside of the United States, which may limit the market potential for this product candidate. In situations where we enter into a development and commercial collaboration arrangement for a product candidate, we may also seek to establish additional collaborations for development and commercialization in territories outside of those addressed by the first collaboration arrangement for such product candidate. If

any of our product candidates receives marketing approval, we may enter into sales and marketing arrangements with third parties with respect to otherwise unlicensed or

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unaddressed territories outside of the United States. There are a limited number of potential partners, and we expect to face competition in seeking appropriate partners. If we are unable to enter into any development and commercial collaborations and/or sales and marketing arrangements on acceptable terms, if at all, we may be unable to successfully develop and seek regulatory approval for our product candidates and/or effectively market and sell future approved products, if any, in all of the territories outside of the United States where it may otherwise be valuable to do so.

In addition, under the terms of our license agreement with AstraZeneca AB, or AstraZeneca, for FX007, we may not, without the consent of AstraZeneca, grant sublicenses to FX007 except in the territory of Japan prior to the achievement of a specified development milestone. Further, the agreement provides that in the event we desire to offer rights to FX007 to a third party prior to the achievement of a specified development milestone, we must make certain diligence materials available to AstraZeneca, and AstraZeneca will have the right to make an offer to re-acquire rights to FX007. In such circumstances, we are not required to accept AstraZeneca s offer, but we may not enter into an agreement with a third party containing financial terms and conditions that on the whole are more favorable to the third party than the terms and conditions last offered by AstraZeneca. These provisions may limit our ability to partner with a third party during the early development stages of FX007.

We may not be successful in maintaining development and commercialization collaborations, and our partners may not devote sufficient resources to the development or commercialization of our product candidates or may otherwise fail in development or commercialization efforts, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results.

Even if we are able to establish collaboration arrangements, any such collaboration may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. If we partner with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. It is possible that a partner may not devote sufficient resources to the development or commercialization of our product candidate or may otherwise fail in development or commercialization efforts, in which event the development and commercialization of such product candidate could be delayed or terminated and our business could be substantially harmed. In addition, the terms of any collaboration or other arrangement that we establish may not prove to be favorable to us or may not be perceived as favorable, which may negatively impact the trading price of our common stock. In some cases, we may be responsible for continuing development of a product candidate or research program under a collaboration, and the payment we receive from our partner may be insufficient to cover the cost of this development. Moreover, collaborations and sales and marketing arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain.

We are subject to a number of additional risks associated with our dependence on collaborations with third parties, the occurrence of which could cause our collaboration arrangements to fail. Conflicts may arise between us and partners, such as conflicts concerning the interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. If any such conflicts arise, a partner could act in its own self-interest, which may be adverse to our best interests. Any such disagreement between us and a partner could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating sufficient revenue to achieve or maintain profitability:

- reductions in the payment of royalties or other payments we believe are due pursuant to the applicable collaboration arrangement;
- actions taken by a partner inside or outside our collaboration which could negatively impact our rights or benefits under our collaboration; or

unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities.

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Risks Related to Commercialization of Our Product Candidates

Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, healthcare payors, patients and the medical community.

Even if we obtain regulatory approval for FX006 or any of our other product candidates, the product may not gain market acceptance among physicians, healthcare payors, patients and the medical community, which is critical to commercial success. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- acceptance by physicians, the medical community and patients of the product candidate as a safe and effective treatment;
- the convenience of prescribing and initiating patients on the product candidate;
- the potential and perceived advantages of such product candidate over alternative treatments;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- the availability of coverage and adequate reimbursement and pricing by third party payors and government authorities;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of sales and marketing efforts.

If our product candidates, including FX006, are approved but fail to achieve an adequate level of acceptance by physicians, healthcare payors, patients and the medical community, we will not be able to generate significant revenue, and we may not become or remain profitable.

Guidelines and recommendations published by various organizations can reduce the use of our product candidates.

Government agencies promulgate regulations and guidelines directly applicable to us and to our product candidates. In addition, professional societies, such as the American Academy of Orthopedic Surgeons, practice management groups, private health and science foundations and organizations involved in various diseases from time to time may also publish guidelines or recommendations to the healthcare and patient communities. Recommendations of government agencies or these other groups or organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Recommendations or guidelines suggesting the reduced use of our product candidates or the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use of our product candidates.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

Although we intend to establish a targeted sales and marketing organization to promote any approved products in the United States, we currently have no such organization or capabilities, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, we must build sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We may enter into strategic partnerships with third parties to commercialize our product candidates outside of the United States.

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To date, we have not entered into any strategic partnerships for any of our product candidates. We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document. We may not be able to negotiate strategic partnerships for territories outside of the United States on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic partnerships outside of the United States because of the numerous risks and uncertainties associated with establishing strategic partnerships. To the extent that we enter into collaboration arrangements, our future collaboration partners may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our product candidates in territories outside of the United States, or if our potential future collaboration partners do not successfully commercialize our product candidates in these territories, our ability to generate revenue from product sales will be adversely affected.

If we are unable to negotiate a strategic partnership or obtain additional financial resources for a product candidate, we may be forced to curtail the development of such product candidate, delay potential commercialization, reduce the scope of our sales or marketing activities or undertake development or commercialization activities at our own expense. In addition, without a partnership, we will bear all the risk related to the development of the product candidate, including in territories outside of the United States. If we elect to increase our expenditures to fund development or commercialization activities ourselves, we will 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 will not be able to bring FX006 or any other product candidates to market or generate product revenue.

We and any collaboration partners that we may engage will be competing with many companies that currently have extensive and well-funded marketing and sales operations. If we, alone or with commercialization partners, are unable to compete successfully against these established companies, the commercial success of any approved products will be limited.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If FX006 or other product candidates are approved for commercialization, we may enter into agreements with third parties to market these products outside of the United States. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- 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 taxes, including withholding of payroll taxes;

foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;

workforce uncertainty in countries where labor unrest is more common than in the United States;

production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters, including earthquakes, typhoons, floods and fires.

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If we are unable to differentiate our lead product candidate, FX006, from existing generic therapies for the treatment of OA, or if the FDA or other applicable regulatory authorities approve generic products that compete with any of our product candidates, the ability to successfully commercialize those product candidates would be adversely affected.

Immediate-release TCA and other injectable immediate-release steroids, which are the current standard of care, are available in generic form and are therefore relatively inexpensive compared to the price we would expect to receive for FX006. These generic steroids also have well-established market positions and familiarity with physicians, healthcare payors and patients. Although we believe FX006 has the potential for clinically meaningful differentiation in sustained pain relief as compared to immediate-release TCA, as clinical development of FX006 advances and we receive data from additional clinical trials, it is possible that the data will not support such differentiation. If we are unable to achieve significant differentiation for FX006 from immediate-release TCA and other injectable immediate-release steroids, our opportunity for FX006 to achieve premium pricing and be commercialized successfully, if approved, would be adversely affected.

In addition to existing generic steroids, such as immediate-release TCA, the FDA or other applicable regulatory authorities may approve generic products that could compete with our product candidates. Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a listed drug which can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. The FDCA, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration, conditions of use, or labeling as our product candidate and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent as our product candidate. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our product candidates would materially adversely impact our ability to successfully commercialize our product candidates.

We face significant competition from other biopharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industries are intensely competitive and subject to rapid and significant technological change. In addition, the competition in the pain and OA market is intense. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. For example, the injectable OA treatment market today includes many injectable immediate-release steroids, including TCA, the active ingredient in FX006, as well as HA injections. In addition, we expect that injectable therapies such as FX006 will continue to be used primarily after oral medications no longer provide adequate pain relief. To the extent that new or improved oral pain medications are introduced that demonstrate better long-term efficacy and safety, patients and physicians may further delay the introduction of injectable therapies such as FX006 in the OA treatment continuum. FX006 could also face competition from other formulations or devices that deliver pain medication on a sustained basis, such as transdermal delivery systems or implantable devices.

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staffs and experienced commercial and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with

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large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis drug products or drug delivery technologies that are more effective or less costly than FX006 or any other drug candidate that we are currently developing or that we may develop.

We believe that our ability to successfully compete will depend on, among other things:

- the efficacy and safety of our product candidates, including as relative to marketed products and product candidates in development by third parties;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- the ability to maintain a good relationship with regulatory authorities;
- the ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect intellectual property rights related to our product candidates;
- the ability to manufacture on a cost-effective basis and sell commercial quantities of any of our product candidates that receive regulatory approval; and
- acceptance of any of our product candidates that receive regulatory approval by physicians and other healthcare providers.

If our competitors market products that are more effective, safer or less expensive than our future products, if any, or that reach the market sooner than our future products, if any, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because we have limited research and development capabilities, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

If we are unable to achieve and maintain adequate levels of third party payor coverage and reimbursement for FX006 or any other product candidates, if approved, on reasonable pricing terms, their commercial success may be severely hindered.

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

In addition, the market for FX006 and any of our other product candidates will depend significantly on access to third party payors drug formularies, or lists of medications for which third party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to

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downward pricing pressures on pharmaceutical companies. Also, third party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third party payors. Therefore, coverage and reimbursement for drug products 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 obtained.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third party coverage and reimbursement for FX006 or any of our other product candidates for which we may receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Recently enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and may affect the prices we may obtain.

The United States and some foreign jurisdictions are considering, or have enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, once they are approved for sale. 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, PPACA was enacted, which includes measures that have or will significantly change the way healthcare is financed by both governmental and private insurers. Among the PPACA provisions of importance to the pharmaceutical industry are the following:

- an annual, non-deductible 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, that began in 2011;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50.0% point-of-sale discounts to negotiated prices 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;

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 133.0% of the Federal Poverty Level, thereby potentially increasing manufacturers Medicaid rebate liability;

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

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new requirements under the federal Open Payments program, created under Section 6002 of PPACA, and its implementing regulations that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program (with certain exceptions) report annually to HHS information related to payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and that applicable manufacturers and applicable group purchasing organizations report annually to HHS ownership and investment interests held by physicians (as defined above) and their immediate family members, with data collection currently required and reporting to the Centers for Medicare & Medicaid Services required by the 90th day of each calendar year;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

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;

a licensure framework for follow-on biologic products;

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

creation of the Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending that began on January 1, 2011.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. In August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation s automatic reductions to several government programs. These reductions, which began in 2013, include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, 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 have a material adverse effect on our customers and accordingly, our financial operations.

Risks Related to Our Business Operations and Industry

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 principal members of our executive team listed under Management located elsewhere in this prospectus, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are at will employees.

Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive or key employee might impede the progress of our development and commercialization objectives.

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We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of September 30, 2014, we had 21 full-time employees. As our company matures, we expect to expand our employee base to increase our managerial, scientific and engineering, operational, sales, marketing, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our existing or future product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize FX006 and our other product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management s attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We currently carry product liability insurance with limits of $10 million in the aggregate and $10 million per occurrence. Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for our product candidates, we intend to expand

our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

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We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data 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 were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our development programs and the development of our product candidates could be delayed.

Business interruptions could delay us in the process of developing our product candidates and could disrupt our sales.

Our headquarters are located in Burlington, Massachusetts. We are vulnerable to natural disasters such as hurricanes, tornadoes and severe storms, as well as other events that could disrupt our operations. We do not carry insurance for natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection, confidentiality agreements and proprietary know how, and intend to seek marketing exclusivity for any approved product, in order to protect the intellectual property related to product candidates, and to date we have only one issued patent covering FX006. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. If this were to occur, early generic competition could be expected against FX006 and potentially our other product candidates in development. Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Also, a third party may challenge our ownership of patents and patent applications assigned to us, or may challenge our exclusive rights to patents and patent applications that we license from third parties. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the additional patent applications we hold with respect to FX006 or our other product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop them and threaten our ability to commercialize any resulting products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will not be found invalid and unenforceable or will go unthreatened by third parties. Further, if we encounter delays in regulatory approvals, the period of time during which we could market FX006 or any other product candidate under patent protection could be reduced. Furthermore, patent applications by third parties can result in an interference proceeding in the United States being provoked by a third party or instituted by us to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. See Business Patents and Patent Applications for additional information regarding our material patents and patent applications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to

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enforce and any other elements of our drug development process that involve proprietary know-how, information or technology that is not covered by patents. For example, we maintain trade secrets with respect to certain of the formulation and manufacturing techniques related to the TCA-formulated PLGA microspheres in FX006, including those that relate to precise pharmaceutical release. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the U.S. Patent and Trademark Office, or U.S. PTO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of FX006 and/or our other product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any drug substance formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtain a license under the applicable patents, or until such patents expire. Similarly, if any third party patent were held by a court of competent jurisdiction to cover aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtain a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may request and/or obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products or manufacturing processes, which may be impossible or require substantial time and monetary expenditure. We

cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research, manufacture clinical trial supplies or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

If we fail to comply with our obligations in the agreements under which we license rights to technology from third parties, or if the license agreements are terminated for other reasons, we could lose license rights that are important to our business.

We are a party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, our rights to FX007 and FX005 are the subject of separate exclusive license agreements with AstraZeneca. If we fail to comply with our obligations under our agreements with AstraZeneca (including, among other things, if we fail to use commercially reasonable efforts to develop, commercialize and sell products based on FX007 and FX005 in major markets) or our other license agreements, or we are subject to a bankruptcy or insolvency, the licensor may have the right to terminate the license. In addition, under our agreement with AstraZeneca for FX007, AstraZeneca has a right to terminate the agreement in the event of a change of control of us prior to the achievement of a specified development milestone, unless we pay a fee to AstraZeneca. In the event that any of our important technology licenses were to be terminated by the licensor, we would likely cease further development of the related program or be required to spend significant time and resources to modify the program to not use the rights under the terminated license.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also 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 have a material adverse effect on the price of our common stock.

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

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Risks Related to this Offering and Ownership of Our Common Stock

The market price of our common stock may be highly volatile, you may not be able to resell your shares at or above the public offering price and you could lose all or part of your investment.

The trading price of our common stock after this offering may be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in clinical trials;
- inability to obtain additional funding;
- any delay in filing an NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA s review of that NDA;

failure to successfully develop and commercialize our product candidates;

changes in laws or regulations applicable to our product candidates;

inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;

adverse regulatory decisions;

introduction of new products or technologies by our competitors;

failure to meet or exceed product development or financial projections we provide to the public;

failure to meet or exceed the estimates and projections of the investment community;

the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

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announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

sales of our common stock by us or our stockholders in the future; and

trading volume of our common stock.

In addition, the stock market in general, and the Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of October 31, 2014, our executive officers, directors and stockholders affiliated with our officers and directors beneficially owned approximately 45% of our voting stock. Based upon the number of shares to be sold in this offering as set forth on the cover page of this prospectus, upon the closing of this offering, that same group will beneficially own approximately 34% of our outstanding voting stock (assuming no exercise of the underwriters option to purchase additional shares). These ownership percentages do not reflect purchases of shares in this offering by existing investors affiliated with certain of our directors. See Underwriting. Therefore, even after this offering, these stockholders may have the ability to influence us through this ownership position. These stockholders may be able to determine or significantly influence all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control or significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and

proxy statements, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenue of at least $1 billion, (b) December 31, 2019, (c) the date on which we are deemed to be a large accelerated filer, which would occur at the beginning of a year if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (d) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company which would allow us to take advantage of many of the same exemptions from disclosure requirements including exemption from compliance with the auditor attestation requirements of Section 404 of

the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

We will continue to incur significant increased costs as a result of operating as a new public company, and our management is required to devote substantial time to new compliance initiatives.

We completed our initial public offering on February 18, 2014. As a new public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. For example, we are now subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. We have incurred and will continue to incur costs associated with the preparation and filing of these reports. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC, and the Nasdaq Global Market have imposed various other requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact (in ways we cannot currently anticipate) the manner in which we operate our business. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the pro forma book value per share of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock in this offering will incur immediate dilution of $10.23 per share, based on the public

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offering price of $17.00 per share and our pro forma net tangible book value as of September 30, 2014. For more information on the dilution you may suffer as a result of investing in this offering, see Dilution.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2014, options to purchase 1,238,973 shares of our common stock at a weighted average exercise price of $9.78 per share were outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

Our directors, executive officers and the entities affiliated with our directors are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders ability to transfer shares of our common stock for at least 90 days from the date of this prospectus, other than with respect to 16,000 shares held by one of our executive officers which shares will not be subject to such restrictions. The lock-up agreements limit the number of shares of common stock that may be sold immediately following this offering. Subject to certain limitations, all of our outstanding shares held by our directors, executive officers and entities affiliated with our directors prior to this offering will become eligible for sale upon expiration of the lock-up period. In addition, shares issued or issuable upon exercise of options held by these stockholders and vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the 90-day lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to the 2013 plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2013 plan will automatically increase each year by 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for

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issuance under the 2013 plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management s attention and resources, which could harm our business.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in Use of Proceeds, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, contains rules that limit the ability of a company that undergoes an ownership change to utilize its net operating losses, NOLs, and tax credits existing as of the date of such ownership change. Under the rules, such an ownership change is generally any change in ownership of more than 50% of a company s stock within a rolling three-year period. The rules generally operate by focusing on changes in ownership among stockholders considered by the rules as owning, directly or indirectly, 5% or more of the stock of a company and any change in ownership arising from new issuances of stock by the company. During the quarter ended June 30, 2014, we completed a Section 382 study through February 11, 2014. The results of this study showed that as of February 11, 2014, one historical ownership change within the meaning of Section 382 had occurred in 2009. As a result of this Section 382 limitation, approximately $0.3 million of NOLs will expire unutilized. Subsequent ownership changes as defined by Section 382 may further limit the amount of NOL carryforwards that could be utilized annually to offset future taxable income.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Additionally, our credit and security agreement with MidCap contains covenants that restrict our ability to pay dividends. Any return to stockholders will therefore be limited to the appreciation of their stock.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

authorizing the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;

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limiting the removal of directors by the stockholders;

creating a staggered board of directors;

prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;

eliminating the ability of stockholders to call a special meeting of stockholders; and

establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder of such corporation for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated herein by reference contain forward-looking statements. The forward-looking statements are contained principally in the sections entitled Summary, Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business in this prospectus or in the documents incorporated herein by reference. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations beyond this offering, including funding necessary to obtain regulatory approval for FX006 and continue research and development of our other product candidates;
- our plans to develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;
- the performance of our third party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;

our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;

our use of the proceeds from this offering;

the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and

our expectations regarding our ability to obtain and adequately maintain sufficient intellectual property protection for our product candidates.

In some cases, you can identify these statements by terms such as anticipate, believe, could, estimate, expects, intend, may, plan, predict, project, should, will, would or the negative of those terms, and similar expressions. These forward-looking statements reflect our management s beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus and are subject to risks and uncertainties. We discuss many of these risks in greater detail under the heading Risk Factors and in the risk factors incorporated herein by reference. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our

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management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act do not protect any forward-looking statements that we make in connection with this offering.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

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USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately $80.0 million (or approximately $92.1 million if the underwriters over-allotment option is exercised in full) from the sale of the shares of common stock offered by us in this offering, based upon the public offering price of $17.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations. We anticipate that we will use the net proceeds of this offering as follows:

- approximately $34.4 million to fund the continued clinical development of FX006, including a planned Phase 3 clinical trial and pre-launch commercial activities;
- approximately $13.0 million to fund the continued research and development of FX007; and
- the remainder for working capital and other general corporate purposes.

We may also use a portion of the net proceeds from this offering to in-license, acquire or invest in complementary businesses, technologies, products or assets. However we have no current plan, commitments or obligations to do so.

We believe that the net proceeds from this offering and our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations into mid-2017, including through completion of our planned Phase 3 clinical trial for FX006 and the submission of an NDA for FX006.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to obtain additional financing, the progress, cost and results of our preclinical and clinical development programs, including our pivotal Phase 2b and Phase 3 clinical trials for FX006, and whether we are able to enter into future collaboration arrangements. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from this offering.

Pending their use, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

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PRICE RANGE OF OUR COMMON STOCK

Our common stock has been listed on the Nasdaq Global Market since February 12, 2014 under the symbol FLXN. Prior to that date, there was no public market for our common stock. Shares sold in our initial public offering were priced on February 11, 2014 at $13.00 per share.

On December 11, 2014, the closing price for our common stock as reported on the Nasdaq Global Market was $17.31 per share. The following table sets forth the ranges of high and low sales prices per share of our common stock as reported on the Nasdaq Global Market for the periods indicated. Such quotations represent inter-dealer prices without retail markup, markdown or commission and may not necessarily represent actual transactions.

Year Ending December 31, 2014	High	Low
First Quarter (from February 12, 2014)	$ 20.85	$ 14.05
Second Quarter	$ 18.23	$ 11.06
Third Quarter	$ 20.35	$ 12.00
Fourth Quarter (from October 1, 2014 through December 11, 2014)	$ 20.50	$ 14.50

As of September 30, 2014, there were 27 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. In addition, pursuant to our credit and security agreement with MidCap, we are prohibited from paying cash dividends without the prior consent of MidCap. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities, and our capitalization as of September 30, 2014:

- on an actual basis;
- on a pro forma basis, giving effect to the sale by us of 5,040,000 shares of our common stock in this offering at the public offering price of $17.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the sections entitled Selected Financial Data in this prospectus and Management s Discussion and Analysis of Financial Condition and Results of Operations in our quarterly report on Form 10-Q for the quarter ended September 2014, and with our financial statements and related notes appearing elsewhere in this prospectus or incorporated herein by reference.

	As of September 30, 2014 (unaudited)	
	Actual	Pro Forma
	(in thousands, except share and per share amounts)	
Cash, cash equivalents and marketable securities	$ 66,589	$ 146,628
Long-term debt, including current maturities	$ 4,082	$ 4,082
Stockholders equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, no shares issued or outstanding, actual; 10,000,000 shares authorized, no shares issued or outstanding, pro forma		
Common stock, $0.001 par value; 100,000,000 shares authorized, 15,627,288 shares issued and outstanding, actual; 100,000,000 shares authorized, 20,667,288 shares issued and outstanding, pro forma	16	21
Additional paid-in-capital	145,447	225,482
Accumulated other comprehensive income		
Accumulated deficit	(85,672)	(85,672)
Total stockholders equity	59,791	139,831
Total capitalization	$ 63,873	$ 143,913

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The number of common shares shown as issued and outstanding on a pro forma basis in the table is based on the number of shares of our common stock outstanding as of September 30, 2014 and excludes:

- 420,974 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014 at a weighted average exercise price of $3.20 per share;
- 967,502 shares of common stock reserved for future issuance under the 2013 plan, as of September 30, 2014; and
- 209,102 shares of common stock reserved for future issuance under the 2013 purchase plan, as of September 30, 2014.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the pro forma net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of September 30, 2014 was $59.8 million, or $3.83 per share of common stock. Our historical net tangible book value is the amount of our total tangible assets less our liabilities. Historical net tangible book value per share is our historical net tangible book value divided by the number of shares of common stock outstanding as of September 30, 2014.

After giving pro forma effect to the sale of 5,040,000 shares of our common stock in this offering at the public offering price of $17.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2014 would have been approximately $139.8 million, or $6.77 per share of common stock. This represents an immediate increase in pro forma net tangible book value of $2.94 per share to our existing stockholders and an immediate dilution of $10.23 per share to new investors purchasing shares of common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 17.00
Historical net tangible book value per share as of September 30, 2014	$ 3.83	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	2.94	
Pro forma net tangible book value per share after this offering		6.77
Dilution per share to new investors participating in this offering		$ 10.23

If the underwriters exercise their option in full to purchase an additional 756,000 shares of our common stock in this offering, the pro forma net tangible book value will increase to $7.09 per share, representing an immediate increase to existing stockholders of $3.26 per share and an immediate dilution of $9.91 per share to new investors participating in this offering.

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The foregoing discussion is based on 15,627,288 shares of common stock outstanding as of September 30, 2014 and excludes:

- 420,974 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014 at a weighted average exercise price of $3.20 per share;
- 967,502 shares of common stock reserved for future issuance under the 2013 plan, as of September 30, 2014; and
- 209,102 shares of common stock reserved for future issuance under the 2013 purchase plan, as of September 30, 2014.

In addition, the initial share reserves under the 2013 plan and the 2013 purchase plan are subject to automatic annual increases in accordance with the terms of the plans. Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that any of these options are exercised, new options are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

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SELECTED FINANCIAL DATA

The following selected financial data should be read together with Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and related notes, each incorporated by reference into this prospectus. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future and results of interim periods are not necessarily indicative of the results for the entire year.

The selected statement of operations data for the years ended December 31, 2012 and 2013 and the selected balance sheet data as of December 31, 2012 and 2013 are derived from our audited consolidated financial statements incorporated by reference into this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2013. The selected statement of operations data for the nine months ended September 30, 2013 and 2014, and the selected balance sheet data as of September 30, 2014 are derived from our unaudited financial statements incorporated by reference into this prospectus from our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014. The unaudited financial statements have been prepared on a basis consistent with our audited consolidated financial statements incorporated by reference in this prospectus and include, in our opinion, all adjustments, consisting only of normal recurring adjustments, necessary for the fair presentation of the financial information in those statements.

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2012	2014	2013
			(unaudited)	
	(in thousands, except per share data)			
Statement of Operations Data:				
Revenue	$	$	$	$
Operating expenses:				
Research and development	11,061	11,065	12,424	8,825
General and administrative	6,704	3,947	6,822	5,363
Total operating expenses	17,765	15,012	19,246	14,188
Loss from operations	(17,765)	(15,012)	(19,246)	(14,188)
Other income (expense):				
Interest income	234	194	319	219
Interest expense	(449)		(315)	(335)
Other income (expense), net	(207)	(164)	(266)	(192)
Total other income (expense)	(422)	30	(262)	(308)
Net loss	$ (18,187)	$ (14,982)	$ (19,508)	$ (14,496)
Net loss attributable to common stockholders	$ (18,187)	$ (14,982)	$ (19,508)	$ (14,496)
Net loss per share attributable to common stockholders, basic and diluted[(1)]	$ (23.02)	$ (27.58)	$ (1.50)	$ (18.37)
Weighted average common shares outstanding, basic and diluted[(1)]	790	543	13,008	789

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	As of December 31,		As of September 30,
	2013	2012	2014
	(in thousands)		(unaudited)
Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 16,438	$ 29,383	$ 66,589
Working capital[2]	11,583	27,147	61,104
Total assets	18,776	30,008	68,125
Total debt[3]	5,047		4,082
Convertible preferred stock	74,806	74,806	
Total stockholders equity (deficit)	(64,704)	(47,523)	59,791

(1) For further details on the calculation of basic and diluted net loss per share attributable to common stockholders, see Note 3 to our consolidated financial statements incorporated by reference into this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2013.
(2) We define working capital as current assets less current liabilities.
(3) Total debt includes the current and long-term portion of our debt.

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BUSINESS

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of novel, injectable pain therapies. We are targeting anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, or OA, a type of degenerative arthritis. Our broad and diversified portfolio of product candidates addresses the OA pain treatment spectrum, from moderate to severe pain, and provides us with multiple opportunities to achieve our goal of commercializing novel, targeted pain therapies.

Our lead product candidate, FX006, is a first-in-class injectable, sustained-release, intra-articular, or IA, meaning in the joint, steroid treatment for patients with moderate to severe OA pain. FX006 combines a commonly administered steroid, triamcinolone acetonide, or TCA, with poly lactic-co-glycolic acid, referred to as PLGA, to provide sustained therapeutic concentrations in the joint and persistent analgesic effect. We specifically designed FX006 to address the limitations of current IA therapies by providing long-lasting, local analgesia while avoiding systemic side effects, which are effects that occur throughout the body as a result of drug that is released from the site of injection into circulating blood. In a completed Phase 2b dose-ranging clinical trial, FX006 has demonstrated clinically meaningful and significantly better pain relief compared to the current injectable standard of care.

In April 2014, we initiated a pivotal Phase 2b clinical trial of FX006 to further identify a safe and well-tolerated dose of FX006 that demonstrates superior pain relief to placebo. The pivotal Phase 2b clinical trial is a multi-center, randomized, double-blind study in approximately 300 patients with OA of the knee and will assess the safety, tolerability and efficacy of certain doses of FX006. Patients are being randomized and treated with a single injection of FX006 (20 mg and 40 mg are being tested) or placebo and will be evaluated for up to 24 weeks. The primary outcome measure will be the weekly mean of the average daily pain intensity score compared to placebo at 12 weeks using an 11-point numerical rating scale. Secondary endpoints will include WOMAC, PGIC, CGIC, time to onset of pain relief, rescue medication consumption and responder status.

On September 16, 2014, the U.S. Food and Drug Administration, or FDA, notified us that they had placed a clinical hold on the FX006 investigational new drug application, or IND, due to a single occurrence of what was then reported as septic arthritis in a patient in the clinical trial. The subsequent clinical hold letter from the FDA requested that we:

- determine whether the study drug was the source of infection by recovering both the specific study drug vial used in the treatment of the patient who experienced the infection, as well as unused study drug vials from the clinical site where the patient was injected, and test both for contamination, and
- explore other potential causes for infection, including a compromise of sterile procedures during injection.

In accordance with these FDA requests, we performed various contamination tests through a certified third-party sterility testing firm and determined that there was no contamination in any of the used or unused vials. As a result, we concluded that the FX006 drug product was not contaminated. We also explored other potential causes of possible infection including contamination during the preparation or administration of FX006. Following consultations with the principal investigator, study coordinator and person that administered the injection at the clinical site, we did not find any indication that sterile procedures were compromised during the injection. There have been no other infections noted in the approximately 100 other patients dosed with FX006 in this trial.

On October 28, 2014, we received notification that based upon the highly atypical nature of the patient s clinical presentation as it relates to septic arthritis and the patient s subsequent clinical course which was most consistent with rheumatoid arthritis, the principal investigator had changed the initial serious adverse event diagnosis from septic arthritis, possibly related to study drug treatment, to inflammatory arthritis, unrelated to

study drug treatment. This information was promptly shared with the FDA. It is assumed that the original, and only, positive synovial fluid culture obtained from this patient was a false positive, which occurs in approximately 5% of such cases. Thus there have been no confirmed diagnoses of septic arthritis and no serious adverse events related to drug treatment among the more than 300 patients treated with FX006 in all clinical trials to date.

On December 1, 2014, the FDA notified us that it had lifted the clinical hold on FX006. As a result, we immediately resumed recruitment and dosing in the pivotal Phase 2b trial of FX006, and we expect to receive top-line data from the trial in the second half of 2015.

In 2014, the FDA informed us that it will consider our on-going pivotal Phase 2b trial as one of two pivotal efficacy trials required for registration of a single-dose administration of FX006. In addition, the FDA informed us that a second placebo-controlled pivotal trial would be sufficient to support the filing of a new drug application, or NDA, for single-dose administration of FX006 and that data from a repeat-dose safety trial would not be required. As a result, we plan to initiate a placebo-controlled Phase 3 trial of FX006 in early 2015 and expect to develop and file repeat-dose safety data in a supplemental NDA after an approval and launch of FX006 for single-dose administration. The Phase 3 clinical trial of FX006 will be an international, multi-center, randomized, blinded, single-dose study in 450 patients with OA of the knee. It will have a three arm design that includes a 40 mg dose of FX006, placebo and a 40 mg dose of immediate-release TCA. The primary objective of the trial will be to provide the second pivotal efficacy dataset against placebo at 12 weeks for an NDA submission, however patients will continue to be evaluated through 24 weeks. In addition, the trial will provide a key comparative dataset against the current standard of care, immediate-release TCA.

We believe that FX006 has the potential to be a superior front line injectable treatment for OA pain management compared to existing therapies by providing safe, more effective and sustained pain relief to patients. We believe the following attributes make FX006 an attractive development candidate:

A first-in-class injectable, IA, sustained-release treatment for patients with moderate to severe OA pain that has demonstrated in clinical trials to date:

- clinically meaningful and significantly better pain relief compared to the current injectable standard of care;
- persistent therapeutic concentrations of drug in the joint and durable efficacy; and
- an attractive safety profile with limited systemic exposures and the potential for fewer side effects.

Among the largest analgesic effects seen in OA clinical trials.

Strong proprietary position through a combination of patents, trade secrets and proprietary know-how, as well as eligibility for marketing exclusivity.

Well-defined Section 505(b)(2) of the Federal Food, Drug and Cosmetics Act, or FDCA, regulatory pathway seeking approval for a novel formulation of the same dose of the already approved immediate-release steroid used by orthopedists and rheumatologists.

Familiarity of orthopedists and rheumatologists with IA injections utilizing the same steroid in the same dose.

Potential for pharmacoeconomic benefits due to superior efficacy and durability and the potential to delay costly and invasive total joint replacement, also referred to as total joint arthroplasty, or TJA.

Our other product candidates include FX007 for the treatment of post-operative pain and FX005 for the treatment of end-stage OA patients. FX007 is a locally administered TrkA receptor antagonist that is designed to provide persistent relief of post-operative pain, including in patients who have undergone TJA. We are conducting preclinical local toxicology experiments and plan to initiate a proof of concept, or PoC, clinical trial for FX007 following the generation of the preclinical data. FX005 is a sustained-release p38 MAP, or mitogen-

activated protein, kinase inhibitor which has both analgesic and anti-inflammatory effects. FX005 successfully completed a Phase 2a PoC clinical trial demonstrating significant pain relief and function improvement. We will continue to evaluate further development of FX005 taking into consideration, among other factors, our available capital resources.

We have worldwide commercialization rights to all of our therapeutic candidates. We also have an exclusive worldwide license agreement with Southwest Research Institute, or SwRI, with respect to the use of SwRI s proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including FX006. We intend to market our products in the United States through our own sales force targeting specialty physicians, including orthopedists and rheumatologists. Outside of the United States, we are exploring selective partnerships with third parties for the development and commercialization of our product candidates. Each of our product candidates and our PLGA formulation technology is protected through a combination of patents, trade secrets and proprietary know-how, and we intend to seek marketing exclusivity for any approved products.

OA is a type of degenerative arthritis that is caused by the progressive breakdown and eventual loss of cartilage in one or more joints. Arthritis is the most common cause of disability in the United States and OA is the most common joint disease, affecting 27 million Americans, with numbers expected to grow as a result of aging, obesity and sports injuries. Recent data suggest that OA accounts for over $185 billion of annual healthcare expenditures in the United States, which does not include loss of productivity costs. We estimate that by 2030, 45 million people will have OA. OA commonly affects large weight-bearing joints like the knees and hips, but also occurs in the shoulders, hands, feet and spine. Patients with OA suffer from joint pain, tenderness, stiffness and limited movement. As the disease progresses, it becomes increasingly painful and debilitating, culminating, in many cases, in the need for TJA.

Current therapies for OA are suboptimal, and, because there is no cure for the disease, controlling pain and delaying surgery are the primary goals for treatment regimens. Oral drugs, such as non-steroidal anti-inflammatory drugs, or NSAIDs, including COX II inhibitors, and Cymbalta, as well as topical NSAIDs, are used to treat early-stage OA pain but have limited effect on pain and, given the amount and frequency of use in OA patients, are associated with serious side effects. For example, NSAIDs have shown increased risk of serious cardiovascular, or CV, thrombotic events, myocardial infarction, and stroke. Furthermore, this class of drugs can cause serious gastrointestinal, or GI, adverse events, including bleeding, ulceration and perforation of the stomach or intestines. These serious side effects are particularly worrisome because OA patients often have co-existing medical conditions, including diabetes and hypertension. For patients with moderate to severe OA pain, IA medicines, such as immediate-release steroids and hyaluronic acid, or HA, injected into the joint, are generally considered safe, but leave the joint rapidly and fail to produce or maintain meaningful pain relief. For patients who progress to end-stage OA, physicians prescribe opioids, which, in addition to the risk of addiction, have numerous systemic side effects, such as respiratory depression, hypotension and constipation, and cause a higher incidence of falls and fractures in older OA patients. As a result of these suboptimal therapies, many OA patients experience persistent and worsening pain, which often culminates in the decision for TJA, a painful and expensive procedure. Further, because the initial joint replacement wears out over time, the younger the patient is at the time of the joint replacement, the more likely it is that he or she will require repeat surgery in their lifetime.

We project that by 2030 approximately 23.5 million of the 45 million OA patients will have knee OA. According to IMS Health, each year over four million OA patients in the United States receive IA steroid injection treatments in the knee, hip, shoulder, hand and foot, with over three million of these being knee injections. In 2012 the number of patients that received knee injections of IA steroids increased approximately 12%. We estimate that an additional 1.3 million patients received knee injections of IA HA, which the FDA has approved for use only in the knee. Sales of HA in the United States were approximately $700 million in 2013, the vast majority of which we believe were related to knee therapy. Our clinical trials to date have treated patients with knee OA, which represents the most common joint treated with IA therapies.

While worldwide sales of HA injections are approaching $2 billion, recent negative guidance from specialty societies (e.g. the American Academy of Orthopedic Surgeons, or AAOS, and the Osteoarthritis Research

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Society International, or OARSI) may begin to put downward pressure on HA sales. For example, Sanofi Biosurgery, which sells the market leading HA treatment, Synvisc, reported a 7% drop in U.S. net sales during the first nine months of 2014 when compared to the first nine months of 2013. This could be in part due to the fact that select payer groups have limited reimbursement for the entire class of HA products.

Given the limitations of current therapies, we believe FX006, if successfully commercialized, would provide an attractive therapeutic alternative. Clinical trials to date for FX006 have demonstrated clinically meaningful and significantly better pain relief compared to the current injectable standard of care, persistent therapeutic concentrations of drug in the joint and durable efficacy, and an attractive safety profile with limited systemic exposures and the potential for fewer side effects.

Our Strategy

Our goal is to cost-effectively develop and commercialize novel therapies that will provide safe and substantial analgesia, or pain relief. Initially, we intend to develop a diverse portfolio of product candidates for the treatment of OA and post-operative pain where we believe there are significant unmet needs. The principal elements of our strategy to accomplish this goal are the following:

Focus on novel product candidates that provide long-lasting analgesia locally while avoiding systemic side effects. We intend to develop anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with OA and post-operative pain. Many OA patients will eventually require IA injection therapies to control their pain as the disease progresses. Currently available IA steroids, none of which is formulated for sustained release, leave the joint rapidly and confer pain relief that typically wanes after two to four weeks. Since, by medical practice, steroids are not typically injected more frequently than every three months, patients can experience months of pain during that time. While the benefits of HA injections generally last for a longer period of time than steroid injections, they are only marginally more effective than placebo. As a result, we believe there is a significant unmet medical need for persistent, effective and safe OA pain relief that can be addressed by IA sustained-release injection therapies. We have therefore formulated our IA product candidates, FX006 and FX005, with the goal of achieving effective drug concentrations in the joint for months, while avoiding significant plasma concentrations of drug that have been linked to systemic side effects. FX007 is being developed to treat post-operative pain and is being formulated to remain in the tissues for a sufficient period of time to effectively treat patients experiencing post-operative pain.

Mitigate development risk and expedite regulatory timeline to product approval. We seek to mitigate development risk by selecting product candidates with validated mechanisms of action. Each of our product candidates also utilizes a unique mechanism of action for achieving analgesia and/or anti-inflammatory effects, which diversifies development risk across multiple targets. In addition, for FX006 and FX005, our sustained-release technology employs PLGA delivery systems, which are already used in approved sustained-release drug products outside of OA and in approved surgical devices. Because FX006 incorporates an already approved steroid in PLGA, it qualifies for the Section 505(b)(2) NDA pathway under the FDCA, which can be an expeditious, cost-effective means to seek product approval, as well as potentially to expand indications for this product candidate. Section 505(b)(2) of the FDCA enables the applicant to rely, in part, on published literature or the FDA s findings of safety and efficacy for an existing product in support of its application.

Target multiple points in the OA pain treatment spectrum. To maximize the likelihood of bringing products to market successfully, our product candidates target different elements of the OA treatment continuum. FX006 is targeted for front line IA therapy in patients with moderate to severe OA pain with the potential to replace IA steroids and HA, FX005 is targeted for patients who progress to end-stage disease as an alternative to opioids and FX007 is targeted for patients with post-operative pain, including those undergoing TJAs.

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Retain commercial rights in the United States and selectively partner outside of the United States. Because IA therapies in the United States are administered by a relatively small number of specialists, particularly orthopedists and rheumatologists, we believe that we can cost-effectively commercialize our product candidates, if approved, with our own specialty sales and marketing organization in the United States, and thereby retain more of the commercial value of these product candidates. In prior years, Genzyme Corp., which has been acquired by Sanofi, supported sales of Synvisc utilizing a sales force of approximately 100 representatives. We believe we can establish an effective U.S. commercial organization with our own specialty sales force of approximately 60 to 100 representatives that target orthopedists and rheumatologists. Outside of the United States, we are exploring selective partnerships with third parties for the development and commercialization of our product candidates.

Osteoarthritis

Overview

Osteoarthritis, also referred to as degenerative joint disease, is the most common joint disease in the United States, affecting 27 million Americans, with numbers expected to grow as a result of aging, obesity and sports injuries.

With the U.S. population between the ages of 45 and 64 having grown 31.5% from 2000 through 2010 and accounting for 26.4% of the total population, we expect changing demographics will likely contribute to a growing number of OA patients.

Approximately 35.0% of U.S. adults are obese, which increases the risk of developing OA.

Knee injury is common, particularly among young athletes, and increases the risk of developing OA by more than fivefold.

As an example, one in two Americans is expected to develop symptomatic knee OA, the most common form of OA, during their lifetime, according to the U.S. Centers for Disease Control and Prevention. Recent research estimates that the average age of physician-diagnosed knee OA has fallen by 16 years, from age 72 in the 1990s to age 56 in the 2010s. According to the same research, Americans between the ages of 35 and 84 in the early 2010s will account for approximately 6.5 million new cases of knee OA over the next decade.

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There is no cure for OA. As a result, current treatments are intended to address symptoms, in particular relief of pain and improvement in functional status, and to delay TJA. The therapeutic regimen for OA becomes increasingly invasive with progression of the disease, culminating, in many cases, in TJA. In addition, because patients are being diagnosed with OA earlier in their lives, many patients will require repeat TJAs.

Current Treatments for OA

Early-Stage OA Treatments. In early disease, treatment begins with non-pharmacologic therapy including exercise, weight control and physical therapy. As the disease progresses, physicians prescribe pharmacologic therapy, beginning with acetaminophen and progressing to oral NSAIDs, including COX II inhibitors, topical NSAIDs or Cymbalta. Available oral therapies have serious side effects. For example, Cymbalta may have a role in worsening depression and the emergence of suicidality in certain patients. In addition to their serious side effects, oral drugs provide limited pain relief and eventually become insufficient to control OA pain for many patients as the disease progresses.

IA Injection Treatments. When non-pharmacologic therapy and oral pain medications prove inadequate, physicians typically transition patients to IA injections. Steroids are first line IA therapy and when steroid therapy does not provide sufficiently durable pain relief, patients may progress to IA HA, a significantly more expensive therapy with only marginally greater effect than placebo. TCA, the steroid used in FX006, is among the most commonly prescribed IA steroid injections. In 2012, the number of patients that received steroid injections in the knee, the most commonly injected OA joint, increased approximately 12.0% to 3 million patients. We estimate that approximately 1.3 million patients received knee injections of HA in 2012. Sales of HA in the United States in 2013 were approximately $700 million, with a cost to the patient per treatment ranging from $500 to $1,000. Worldwide, HA sales were approaching $2 billion as of 2012.

End-Stage Treatments. When patients progress to the point where IA injection therapies fail to adequately control OA pain, physicians may prescribe opioids as a medicine of last resort.

TJA and Post-Operative Pain Treatments. Due to severe pain that can no longer be controlled therapeutically, many patients opt to have TJA, which is costly and painful. One of the most prevalent TJA procedures in the United States is total knee arthroplasty. Compared to existing drug therapy, total knee arthroplasty

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is very expensive, costing between $25,000 and $35,000 on average, and as many as 20.0% of patients are dissatisfied with the outcome of this procedure. The earlier a patient receives TJA, the more likely the patient may need repeat replacement surgery in following years. In 2009, inpatient costs exceeded $9 billion per year in the United States for total knee arthroplasty alone and based on some estimates the number of total knee arthroplasties is expected to increase sixfold between 2011 and 2030. Our own market research has indicated that healthcare payors would be willing to reimburse additional OA therapies that have the potential to delay the need for TJA.

Limitations of Current Treatments for OA

Current therapies for OA are suboptimal. Oral drugs, such as NSAIDs, while they may offer adequate analgesia for early-stage OA pain, are associated with serious side effects such as gastrointestinal bleeding and cardiovascular events, and, importantly, are eventually ineffective at managing OA pain as the disease progresses.

IA therapies, including steroids and HA preparations, are generally well-tolerated but provide pain relief that is insufficient or inadequate in duration. All IA therapies approved for OA are immediate-release suspensions or solutions that leave the joint within hours to days and are absorbed systemically, which may result in undesirable side effects. For example, IA immediate-release steroid injections are associated with elevation of blood glucose in diabetics, which can be of clinical concern. While IA steroids demonstrate large initial analgesic effects relative to other therapies, pain relief typically wanes after several weeks as a result of the IA steroids leaving the joint quickly. In addition, current standards of care dictate that IA steroid suspensions not be administered more frequently than once every three months. Based on internal analysis, we believe approximately 44.0% of patients receiving IA immediate-release steroids are unsatisfied with the duration of benefit.

Despite U.S. sales of approximately $700 million in 2013, IA HA therapies, which are approved only for treatment in the knee, produce only marginally more effective pain relief than placebo and may have no discernible effect on a patient s ability to carry out their daily activities. In treatment guidelines for knee OA published in May 2013, the AAOS concluded that current published studies do not show any clinically effective response for HA injections. As a result, the guidelines do not recommend HA treatment for symptomatic knee OA and, most recently, certain insurance carriers are no longer providing policy coverage of HA and this may begin to put downward pressure on HA sales.

For patients with advanced disease, opioids are the medicine of last resort. Opioids, however, are associated with significant side effects, particularly when administered chronically. These side effects include serious dependency and abuse potential, respiratory depression and cardiac events and, increasingly, deaths from unintentional overdose.

For patients undergoing surgery, control of post-operative pain is an important priority. Numerous post-operative pain treatments exist, including local injection of existing drugs at the time of surgical wound closure, opioids, intravenous acetaminophen and NSAIDs and femoral nerve blocks, but these all have limitations in terms of inadequate magnitude and duration of pain relief, troublesome side-effects, such as increased risk of CV and GI events, or functional impairment.

In summary, current therapies for OA pain are inadequate and do not address the desire among physicians and healthcare payors to manage pain for longer periods of time, which can delay TJA. In addition, existing pain therapies provide suboptimal post-operative pain relief. As such, we believe there is a significant commercial opportunity for (i) a front line IA therapy that is well-tolerated and can deliver significant and durable analgesia to patients with moderate to severe pain, (ii) a novel and potent analgesic IA therapy that can provide safe and effective pain relief for end-stage OA patients prior to TJA, and (iii) a novel therapy that safely provides persistent post-operative pain relief.

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The Flexion Portfolio

Our product candidates are designed to deliver established anti-inflammatory and analgesic effects directly to the site of disease, optimizing sustained local drug concentration to achieve a durable and clinically meaningful response. These product candidates are also designed to limit systemic exposure to the drugs and minimize systemic toxicities, a major concern in the many OA patients with comorbidities, which are co-existing medical conditions. We believe that our portfolio of product candidates has the potential to offer safe, durable pain relief and functional improvement for patients across the OA pain treatment spectrum. Moreover, by more effectively controlling and reducing pain over longer periods of time, our therapies, notably FX006, may result in delaying costly TJA procedures in OA patients.

Our sustained-release technology allows us to incorporate pharmaceuticals in PLGA microspheres for administration of FX006 and FX005. PLGA is a proven sustained-release delivery vehicle that is metabolized to carbon dioxide and water as it releases drug in the IA space and is used in approved drug products and surgical devices. The technology is designed to enable novel formulations of pharmaceuticals by providing controlled, sustained release of drugs over time, and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates. Key to the success of our IA therapies is the ability to maintain persistent therapeutic concentrations of drug in the joint, while minimizing systemic exposure. We believe we are the first company to administer PLGA microspheres into a human joint, and preclinical and clinical data suggest that FX006, as well as FX005, may provide local therapeutic concentrations that could last for at least three months and result in very low systemic concentrations of drug. The Phase 2a clinical trial of FX006 provides direct evidence that following a single injection, therapeutic concentrations of TCA are maintained locally (in the joint) for at least six weeks, while very low concentrations of TCA enter systemic circulation. Furthermore, clinical data from the completed Phase 2b dose-ranging clinical trial of FX006 and the Phase 2a clinical trial of FX005 suggest that following a single injection, both drug candidates can provide local pain relief and functional improvement for 12 weeks while producing very low systemic concentrations and attractive systemic safety profiles. Together these data suggest that the local delivery of drug from PLGA microspheres as demonstrated by FX006 and FX005 has the potential to sustain prolonged, local therapeutic effects while reducing the potential for systemic side effects.

Our portfolio currently consists of three product candidates which address the OA treatment spectrum:

FX006 is an intra-articular, sustained-release steroid treatment that combines TCA with PLGA to provide sustained therapeutic concentrations in the joint and persistent analgesic effect, and was specifically designed to address the limitations of current IA therapies by providing long lasting, local analgesia while avoiding systemic side effects. In a completed Phase 2b dose-ranging clinical trial, FX006 demonstrated clinically meaningful and significantly better pain relief compared to the current standard of care and was very well-tolerated.

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FX007 is a preclinical, small-molecule TrkA receptor antagonist designed to address post-operative pain. We are conducting preclinical local toxicology experiments and plan to initiate a PoC clinical trial for FX007 following the generation of the additional preclinical data.

FX005 is a sustained-release p38 MAP, or mitogen-activated protein, kinase inhibitor that has both analgesic and anti-inflammatory properties. In a Phase 2a PoC clinical trial, FX005 demonstrated significant effects on both pain relief and functional improvement and was very well-tolerated. We believe FX005 may prove to be an effective therapy for OA patients with end-stage disease.

The following chart illustrates the current status of development of our product candidates, for which we have worldwide commercialization rights:

We believe our product candidates and technology will be protected primarily through a combination of patents, trade secrets and proprietary know-how, and we intend to seek marketing exclusivity for any approved products. A composition of matter patent has been issued by the USPTO for FX006, with a patent term until 2031. Method of manufacturing and method of use claims have been filed in Divisional applications. Considerable expertise and effort was required to carry out the large body of original work underlying the formulation of FX006, including experimenting with, and observing the effects of, over 50 steroid and PLGA formulations. We believe our extensive know-how and trade secrets relating to the manufacturing process for FX006, including those that relate to precise pharmaceutical release profiles, represent a competitive advantage.

FX006 Front Line IA Therapy for Patients with Moderate to Severe OA Pain

Overview

FX006 is a steroid, TCA, formulated for sustained-release, delivered via IA injection and designed to treat moderate to severe OA pain. FX006 combines commonly administered TCA with PLGA, the cornerstone of our injectable IA sustained-release technology.

To date, three clinical trials have been conducted to test FX006 against immediate-release TCA injection. A total of 302 patients were enrolled in these three clinical trials, of which 236 patients received FX006 and 66 patients received immediate-release TCA. In a completed Phase 2b dose-ranging clinical trial of patients with knee OA, FX006 demonstrated clinically meaningful and significant improvements in pain relief and functional status relative to a commercially available 40 mg immediate-release TCA. Data from this completed 12-week Phase 2b dose-ranging clinical trial show that FX006 has a well-tolerated systemic safety profile that is

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indistinguishable from the standard of care immediate-release steroid. Further, the local safety profile for FX006 in the completed 12-week Phase 2b dose-ranging clinical trial was attractive and comparable to that seen with the same dose of immediate-release steroid comparator.

Our clinical data suggest that IA administration of FX006 produces a more controlled release of TCA from the site of injection than immediate-release TCA, prolonging local exposure to TCA while reducing systemic exposure. A pharmacodynamic clinical trial has also demonstrated that FX006 avoids the marked suppression of the hypothalamic-pituitary-adrenal, or HPA, axis (which determines the body s ability to make its own naturally occurring steroids) seen with commercially available steroid suspensions. Preclinical data demonstrate that single doses are well tolerated and, in an inflammatory arthritis rat model, have the potential to prevent joint damage more effectively than the immediate-release comparator. We have conducted two pharmacokinetic clinical trials that compared the duration of FX006 to immediate-release TCA in the joint by measuring synovial fluid concentrations in patients with OA following a single IA administration. TCA concentrations in the joint were determined at 6, 12, 16 and 20 weeks following injection depending on the trial design. The data from these clinical trials show that at 6 and 12 weeks, both the FX006 10 mg and 40 mg dose groups had measurable concentrations of drug in synovial fluid. In contrast, the 40 mg immediate-release TCA dose group at 6 and 12 weeks had concentrations of drug that were below the lower limit of quantitation. The FX006 40 mg dose group also demonstrated readily measurable concentrations of drug at 16 weeks, which fell to below the lower limit of quantitation at 20 weeks. These data will be used to define the dosing interval for repeat injection.

We are conducting a Phase 2b clinical trial of FX006 and expect to report topline data for the trial in the second half of 2015. In 2014, the FDA informed us that it will consider our on-going pivotal Phase 2b trial as one of two pivotal efficacy trials required for registration of a single-dose administration of FX006. In addition, the FDA informed us that a second placebo-controlled pivotal trial would be sufficient to support the filing of an NDA for single-dose administration of FX006 and that data from a repeat-dose safety trial would not be required. As a result, we plan to initiate a placebo-controlled Phase 3 trial of FX006 in early 2015 and expect to develop and file repeat-dose safety data in a supplemental NDA after approval and launch of FX006 for single-dose administration.

We have a composition of matter patent in the United States that covers FX006 and has an expiration date in 2031. The FX006 composition of matter patent is the result of several unique discoveries relating to a narrow drug load specification, a certain release profile of polymers, specific polymer weights and ratios and clinical efficacy observed within a dose-range.

FX006 Development Program

Study FX006-2011-001. In June 2013, we announced results from a Phase 2b dose-ranging clinical trial in 228 patients with knee OA assessing the safety, tolerability and efficacy of FX006. The clinical trial was conducted at a total of 22 sites in Australia, Canada and the United States. The objective of the study was to identify a safe and well-tolerated dose of FX006 that demonstrates superiority to immediate-release TCA and to provide an assessment of the magnitude and duration of pain relief, while differentiating it from current front line IA therapy.

229 patients were randomized and 228 patients were treated with a single IA injection of 10, 40, or 60 mg of FX006 or 40 mg of immediate-release TCA, the labeled dose and current standard of care. Each patient was evaluated for a total of 12 weeks. The primary outcome measure was the weekly mean of the average daily pain intensity score as assessed using an 11-point numerical rating scale, with zero being no pain and 10 being pain as bad as you can imagine. The primary efficacy endpoint was the change from baseline to each of weeks 8, 10 and 12 for that primary outcome measure. Secondary endpoints included change from baseline in the primary outcome measure for each week not addressed in the primary endpoint, time to onset of analgesia, responder status, pain, stiffness and function measured using the Western Ontario and McMaster Universities Osteoarthritis Index, known in the industry as WOMAC, patient global impression of change, or PGIC, clinical global impression of change, or CGIC, and rescue medication consumption.

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The responder status endpoint was based upon three responder analyses:

- the proportion of patients meeting the OMERACT-OARSI (Outcome Measures in Rheumatology-Osteoarthritis Research Society International) responder criteria which uses a combination of pain, function and patient assessment to derive a composite endpoint;
- the proportion of patients achieving a greater than 30% improvement from baseline in the primary outcome measure; and
- the proportion of patients achieving a greater than 20% improvement from baseline in the primary outcome measure.

The rescue medication consumption endpoint was based upon the mean number of rescue medication tablets (i.e. acetaminophen) used per week to provide additional pain relief.

The WOMAC Osteoarthritis Index is an osteoarthritis-specific questionnaire completed by the patient that consists of 24 questions covering the areas of pain, stiffness and physical function.

PGIC is a single item questionnaire that uses a 7-point scale (1= very much improved; 7= very much worse) to measure the patient s impression of change regarding his or her overall status.

CGIC is a single item questionnaire that uses a 7-point scale (1= very much improved; 7= very much worse) to measure the physician s impression of change regarding a patient s overall status.

The clinical trial design of our completed Phase 2b dose-ranging clinical trial for FX006 is outlined as follows:

Treatment arms were well-balanced with respect to demographic and baseline characteristics, with a mean baseline average daily pain score of 6.4 to 6.6. With respect to the primary outcome measure, the FX006 40 mg dose was significantly better than immediate-release TCA at improving pain relief beginning at week 5 and continuing to week 10 ($p<0.05$ at each time point) (see Figure 1). The FX006 40 mg dose also demonstrated significant improvement compared to immediate-release TCA in the average change from baseline in the primary outcome measure across weeks 1 to 12 ($p=0.0382$) (see Figure 1) and in key secondary outcomes including pain, stiffness, function, PGIC, CGIC and responder status at week 8 ($p<0.05$). The 10 mg dose of FX006 produced effects in the primary outcome measure that were consistently improved relative to immediate-release TCA but of lessor magnitude than those produced by the 40 mg dose. In clinical trials, the p-value is the probability that the result was obtained by chance. For example, a p-value of 0.10 would indicate that there is a 10% likelihood that the observed results could have happened at random. By convention, a p-value that is less than 0.05 is considered statistically significant.

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The performance of the 60 mg dose in the primary outcome measure and secondary outcome measure did not represent a material improvement relative to the 40 mg dose, and following week 6, the 60 mg dose was numerically inferior to the 40 mg dose (see Figure 2). Based on subsequent investigation, we believe that the inferior pain relief achieved by the 60 mg dose compared to lower doses of FX006 after week 6 was the result of the increased concentration of PLGA microspheres in the 60 mg dose. Following injection, we expect that this resulted in aggregates. Aggregation is associated with a more acidic microenvironment which results in accelerated degradation of PLGA microspheres causing premature release of TCA. We have separately observed in our synovial PK study (see Figure 5) that TCA concentrations in joint fluid six weeks after injection of 60 mg of FX006 are substantially lower than that seen with the 40 mg dose. Taken together, we believe that the inferior pain relief achieved by the 60 mg dose compared to lower doses of FX006 after week 6 reflects the likelihood that the majority of TCA in the 60 mg dose group was released in the first six weeks. In this exploratory dose-ranging study, the statistical analysis assumed that the magnitude of pain relief would increase with dose. This was not the case and, for that reason, the primary endpoint was not achieved.

Figure 1: Weekly Mean of Average Daily Pain Intensity Scores

# indicates p<0.1 for comparison of FX006 40 mg compared with immediate-release TCA; * indicates p<0.05; ** indicates p<0.01

Figure 2: Weekly Mean of Average Daily Pain Intensity Scores

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All treatments were well-tolerated and there were no drug-related serious adverse events (see Figure 3). Adverse events, or AEs, were generally mild to moderate and unrelated to study drug. Local knee-related AEs, laboratory assessments, electrocardiograms and vital signs were unremarkable and similar across all treatments.

Figure 3: FX006 Phase 2b Summary of Adverse Events

	FX006 10 mg N=58	FX006 40 mg N=59	FX006 60 mg N=60	TCA IR 40 mg N=51
	n (%)	n (%)	n (%)	n (%)
Number of Patients with at Least 1 TEAE	27 (46.6)	33 (55.9)	34 (56.7)	28 (54.9)
Number of Patients with at Least 1 Serious TEAE	0	2 (3.4)*	1 (1.7)	0
Number of Patients with at Least 1 TEAE Leading to Study Withdrawal	1 (1.7)	0	0	0
Number of Patients with TEAEs by Maximum Severity				
Mild	17 (29.3)	20 (33.9)	19 (31.7)	14 (27.5)
Moderate	9 (15.5)	13 (22.0)	15 (25.0)	12 (23.5)
Severe	1 (1.7)	0	0	2 (3.9)
Number of Patients with TEAEs by Maximum Relationship	17 (29.3)	24 (40.7)	22 (36.7)	15 (29.4)
Not Related				
Unlikely	3 (5.2)	4 (6.8)	5 (8.3)	4 (7.8)
Possibly Related	3 (5.2)	2 (3.4)	4 (6.7)	3 (5.9)
Probably Related	2 (3.4)	3 (5.1)	2(3.3)	5 (9.8)
Definitely Related	2 (3.4)	0	1 (1.7)	1 (2.0)
Possibly, Probably, or Definitely Related	7 (12.1)	5 (8.5)	7 (11.7)	9 (17.6)

= Treatment Emergent Adverse Event
TEAE
artery disease and stroke - both judged to be not related to drug treatment
*Coronary
abscess - judged to be not related to drug treatment
*Axillary

Studies FX006-2011-002 and FX006-2013-005.

We have completed two Phase 2a multi-center clinical trials in patients with OA evaluating systemic pharmacokinetics, systemic pharmacodynamics, and/or local pharmacokinetics (in the synovial fluid of the joint) of FX006 compared to immediate-release TCA.

FX006-2011-002 was a double-blind study in which 24 patients were randomized to single IA injections of 10, 40, or 60 mg of FX006 or 40 mg of immediate-release TCA. Each patient was evaluated for a total of six weeks following treatment. Safety was evaluated and specimens were collected for plasma drug concentration and cortisol (the body s naturally occurring steroid) measurements during one 48-hour in-patient period (day 1-2), two 24-hour in-patient periods (days 14-15 and 42-43) and seven out-patient visits (days 3, 4, 5, 8, 22, 29 and 36). Synovial fluid was also collected via aspiration on day 1 just prior to study treatment administration and again at week 6.

FX006-2013-005 was an open-label study initiated following the completion of Study FX006-2011-001 (Phase 2b dose-ranging study), in which it was demonstrated that therapeutic effect at a 40 mg dose of FX006 persisted for at least 12 weeks. The purpose of study FX006-2013-005 was

to establish duration of exposure to TCA from FX006 in the joint, and in so doing, support the definition of dosing interval for repeat administration.

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Fifty patients with OA of the knee were assigned sequentially to one of five groups to receive a single IA injection of either 10 or 40 mg of FX006 or 40mg of immediate-release TCA. Synovial fluid was collected via aspiration on day 1 just prior to study treatment administration, and again at weeks 12, 16 or 20 depending on the group assignment.

In combination, these two studies provide the following characterization of the pharmacokinetics and pharmacodynamics of FX006 relative to immediate release TCA, the current standard of care:

- The 40 mg dose of FX006 produced maximal plasma concentrations (peak plasma concentrations measured over the given sampling period) that were 30-fold lower than immediate release TCA (see Figure 4).

- During the first three days following injection (the period during which maximal plasma concentrations occur), the immediate-release TCA 40 mg dose reduced serum cortisol by almost 90%. In contrast, the FX006 40 mg dose produced a reduction of approximately 40% in serum cortisol, a magnitude that is typically not associated with adverse effects.

- Direct measures in synovial fluid (fluid found in the cavity of a synovial joint, in this case the knee) of TCA concentrations at weeks 6, 12, 16 and 20 demonstrated the following (see Figure 5):

  - At weeks 6 and 12, immediate release TCA produced synovial fluid concentrations of TCA that were below the level of quantitation.

  - At weeks 6, 12 and 16, the 40 mg dose of FX006 was associated with measurable levels of TCA. At Week 20, the level of TCA dropped below the level of quantitation.

  - At weeks 6 and 12, the 10 mg dose of FX006 produced measurable concentrations that were less than those produced by the 40 mg dose.

  - The 40 mg dose of FX006 was associated with synovial TCA concentrations at weeks 12, 16 and 20 which we believe are permissive of re-administration.

Overall, these results suggest that IA administration of FX006 produced a more controlled release of TCA from the site of injection, prolonging local exposure to TCA while reducing systemic exposure to TCA relative to immediate-release TCA. While synovial fluid concentrations produced by 40 mg of FX006 at weeks 12 and beyond are permissive of repeat administration, the final definition of dosing interval will take into account the persistence of analgesic effect beyond 12 weeks. The ongoing pivotal Phase 2b study will assess efficacy through week 24.

Figure 4. Plasma TCA Concentrations over Time

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Figure 5. Synovial TCA Concentrations over Time

Other On-Going and Planned Studies

In April 2014, we initiated a pivotal Phase 2b clinical trial of FX006 to further identify a safe and well-tolerated dose of FX006 that demonstrates superior pain relief to placebo. The pivotal Phase 2b clinical trial is a multi-center, randomized, double-blind study in approximately 300 patients with OA of the knee and will assess the safety, tolerability and efficacy of certain doses of FX006. Patients are being randomized and treated with a single injection of FX006 (20 mg and 40 mg doses are being tested) or placebo and will be evaluated for up to 24 weeks. The primary outcome measure will be the weekly mean of the average daily pain intensity score compared to placebo at 12 weeks using an 11-point numerical rating scale. Secondary endpoints will include WOMAC, PGIC, CGIC, time to onset of pain relief, rescue medication consumption and responder status.

On September 16, 2014, the FDA notified us that they had placed a clinical hold on the FX006 IND due to a single occurrence of what was then reported as septic arthritis in a patient in the clinical trial. The subsequent clinical hold letter from the FDA requested that we:

- determine whether the study drug was the source of infection by recovering both the specific study drug vial used in the treatment of the patient who experienced the infection, as well as unused study drug vials from the clinical site where the patient was injected, and test both for contamination, and
- explore other potential causes for infection, including a compromise of sterile procedures during injection.

In accordance with these FDA requests, we performed various contamination tests through a certified third-party sterility testing firm and determined that there was no contamination in any of the used or unused vials. As a result, we concluded that the FX006 drug product was not contaminated. We also explored other potential causes of possible infection including contamination during the preparation or administration of FX006. Following consultations with the principal investigator, study coordinator and person that administered the injection at the clinical site, we did not find any indication that sterile procedures were compromised during the injection. There have been no other infections noted in the approximately 100 other patients dosed with FX006 in this trial.

On October 28, 2014, we received notification that based upon the highly atypical nature of the patient s clinical presentation as it relates to septic arthritis and the patient s subsequent clinical course which was most

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consistent with rheumatoid arthritis, the principal investigator had changed the initial serious adverse event diagnosis from septic arthritis, possibly related to study drug treatment, to inflammatory arthritis, unrelated to study drug treatment. This information was promptly shared with the FDA. It is assumed that the original, and only, positive synovial fluid culture obtained from this patient was a false positive, which occurs in approximately 5% of such cases. Thus there have been no confirmed diagnoses of septic arthritis and no serious adverse events related to drug treatment among the more than 300 patients treated with FX006 in all clinical trials to date.

On December 1, 2014, the FDA notified us that it had lifted the clinical hold on FX006. As a result, we immediately resumed recruitment and dosing in the pivotal Phase 2b trial of FX006, and we expect to receive top-line data from the trial in the second half of 2015.

We also plan to launch a Phase 3 trial of FX006 in early 2015. The Phase 3 clinical trial of FX006 will be an international, multi-center, randomized, blinded, single-dose study in 450 patients with OA of the knee. It will have three arms that include a 40 mg dose of FX006, placebo and a 40 mg dose of immediate-release TCA, and patients will be evaluated for a total of 24 weeks. The primary objective of the trial will be to provide the second pivotal efficacy dataset against placebo at 12 weeks for an NDA submission. In addition, the trial will provide a key comparative dataset against the current standard of care, immediate-release TCA. Specifically, the primary outcome measure will be the weekly mean of the average daily pain intensity score compared to placebo at 12 weeks using an 11-point numerical rating scale. Secondary endpoints will include a comparison to immediate-release TCA at 8, 10 and 12 weeks, WOMAC, PGIC, CGIC, time to onset of pain relief, rescue medication consumption and responder status.

FX006 Regulatory Strategy

In 2014, the FDA informed us that it will consider our on-going Phase 2b trial of FX006 as one of two pivotal efficacy trials required for registration of a single-dose administration of FX006. In addition, the FDA informed us that a second placebo-controlled pivotal trial would be sufficient to support the filing of an NDA for single-dose administration of FX006 and that data from a repeat-dose safety trial would not be required. As a result, we plan to initiate a placebo-controlled Phase 3 trial of FX006 in early 2015 and expect to develop and file repeat-dose safety data in a supplemental NDA after an approval and launch of FX006 for single-dose administration.

FX007 For Post-Operative Pain

Overview

FX007 is a small molecule TrkA receptor antagonist that is in development for the persistent relief of post-operative pain. TrkA is the receptor for nerve growth factor, commonly known as NGF, a small peptide that is released following tissue injury. NGF binds to TrkA on the surface of pain sensing neurons and renders these cells more responsive to external stimuli. In recent clinical trials of Pfizer s monoclonal antibody, tanezumab, systemic blockade of NGF demonstrated marked analgesia in a variety of painful conditions. Additionally, human genetic studies demonstrated that patients with a mutation in the TrkA gene have congenital insensitivity to pain. These data indicate that interruption of the NGF-TrkA pathway produces a profound analgesic effect, and in preclinical pharmacology experiments, FX007 has demonstrated both high affinity for the TrkA receptor and analgesic effects in OA and post-operative pain. However, systemic and persistent blockade of NGF has been associated with rapidly progressive OA requiring TJA. FX007 is being developed for acute, local administration, which has the potential to avoid side effects associated with chronic systemic use.

Post-operative pain is usually most severe in the first few days following the completion of a surgical procedure and is a response to tissue damage during surgery which stimulates peripheral nerves that signal the brain to produce a sensory and physiological response. Numerous studies reveal that the incidence and severity of post-operative pain is primarily determined by the type of surgery, duration of surgery and the pain treatment choice following surgery.

Unrelieved acute pain causes patient suffering and can lead to other complications, which delays recovery from surgery and may result in higher healthcare costs. This is particularly true with respect to post-operative

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TJA pain, which can compromise rehabilitation and result in poor outcomes. According to the Agency for Healthcare Research and Quality, aggressive prevention of the onset of pain is better than treatment of pain because, once established, pain is more difficult to suppress. Current multimodal therapy for post-operative pain includes administration of local anesthetics to the wound combined with the systemic administration of opioid and NSAID analgesics. Opioids are associated with a variety of unwanted and potentially severe side effects, such as respiratory depression, hypotension and constipation, and many physicians seek alternatives to opioids for their patients. These side effects may require additional medications or treatments and prolong a patient s stay in the post-anesthesia care unit and the hospital or ambulatory surgery center, thereby increasing costs significantly. The use of injectable NSAIDs, such as ketorolac and ibuprofen, is severely limited in the post-operative period because they increase the risk of bleeding and gastrointestinal and renal complications.

There are approximately 51 million surgeries performed in the United States each year, and the global post-operative pain market was estimated to be $5.9 billion in 2010. Despite the size of this market, however, post-operative pain management remains a challenge for healthcare providers, with studies reporting that up to 80% of patients experience inadequate pain relief after surgery. Given the limitations of current post-operative therapies, we are developing FX007 as a superior alternative to manage post-operative pain. The blockade of the NGF-TrkA pathway results in highly effective analgesia. Additionally, acute local administration has the potential to avoid the side-effects associated with systemic and persistent blockade of NGF.

We have a composition of matter patent in the United States that covers the TrkA receptor antagonist and has an expiration date in 2028.

FX007 Development Program

FX007 is being developed to treat post-operative pain with target duration for analgesia of 36 to 72 hours. As a result, unlike FX005 and FX006 for OA pain, in which the goal is months of pain relief, we do not believe it will be necessary to formulate FX007 with PLGA, which should expedite development of this compound.

We are conducting preclinical local toxicology experiments and plan to initiate a PoC clinical trial for FX007 following the generation of the preclinical data.

FX005 For End-Stage OA Pain

Overview

FX005 is intended as therapy for patients with end-stage OA pain, particularly those patients awaiting TJA, as an alternative to opioids. FX005 is a p38 MAP kinase inhibitor formulated for sustained-release delivered via IA injection, which is designed to have both analgesic and anti-inflammatory benefits without the systemic side effects of oral p38 MAP kinase inhibitors. p38 MAP kinase is an enzyme in an inflammatory cascade that up regulates in response to stress and culminates in the elaboration of multiple proinflammatory cytokines, including interleukin 1 and tumor necrosis factor, as well as enzymes like matrix metalloproteinases that have the potential to destroy cartilage. In other studies, multiple oral p38 MAP kinase inhibitors have been evaluated in inflammatory diseases and pain and, while efficacy has been demonstrated, serious toxicity affecting multiple organ systems has been frequently observed. For example, a recent clinical study of an orally administered p38 MAP kinase inhibitor in OA demonstrated pain relief comparable to oxycodone but was associated with concerning side effects, including QTc prolongation which could increase the risk of arrhythmias. Because FX005 leverages the same PLGA technology used in

FX006 in order to achieve persistent therapeutic concentrations of drug in the joint while maintaining very low plasma concentrations, it may have the potential to provide durable pain relief while avoiding p38 MAP kinase inhibitor systemic side effects. We believe the preclinical and clinical data we have generated to date support this potential.

We have a composition of matter patent in the United States that covers the p38 MAP kinase inhibitor and has an expiration date in 2028. We have also filed a composition of matter patent application for the novel

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formulation of FX005, which, if issued as a patent, is expected to expire in 2029. Like FX006, we have manufacturing know-how and trade secrets that we believe will provide us with additional proprietary advantages for FX005.

FX005 Development Program

In May 2012, FX005 completed a Phase 2a clinical trial in which 70 patients were randomized to FX005 and 70 patients were randomized to placebo. The Phase 2a clinical trial demonstrated positive effects of FX005 on both pain and function. These effects increased substantially in a sub-population of patients with higher baseline pain scores.

Study FX005-2010-001. A Phase 2a clinical trial in 140 patients with knee OA was conducted as a multi-center, randomized, double-blind, placebo-controlled trial and consisted of a single ascending dose phase, or SAD Phase, followed by a single dose PoC phase, or PoC Phase. In the SAD Phase of the study, escalating doses of 1, 10, and 45 mg of FX005 were compared to blank PLGA microspheres and diluent in three cohorts of twelve patients, with six patients receiving FX005, three patients receiving blank PLGA microspheres and three patients receiving diluent in each cohort. Diluent is a placebo containing all components of the FX005 formulation except the active drug and the PLGA microspheres. Each patient in the SAD Phase was followed for safety and pharmacokinetics for six weeks after a single IA injection. FX005 was well-tolerated at each dose level and, as a result, the highest dose of 45 mg was advanced to the next phase.

In the PoC Phase, 52 patients were randomized to receive 45 mg of FX005, 26 patients were randomized to receive blank PLGA microspheres as a placebo control, and 26 patients were randomized to receive diluent as a placebo control, each as a single IA injection. Each patient was followed for 12 weeks after the injection for safety, pharmacokinetics, and efficacy. The primary endpoint was the change from baseline in the WOMAC pain subscale at four weeks. Secondary efficacy assessments included the WOMAC function subscale and responder status. FX005 demonstrated pain relief and functional improvement at four weeks, and the absolute magnitude of effect in both subscales was persistent through 12 weeks. These effects were substantially enhanced in a prespecified exploratory subset analysis of patients with high baseline pain. FX005 also demonstrated efficacy in responder analysis. Overall, FX005 was well-tolerated systemically and local tolerability was similar to that documented for marketed HA preparations.

Repeat dose toxicology studies demonstrated that FX005 can be associated with synovial inflammation, articular cartilage damage and alterations to joint structure. These findings were not present in animals treated with blank PLGA microspheres, so toxicity appears to be specific to the p38 MAP kinase inhibitor itself. To guide the appropriate future development path for FX005, additional toxicology studies using lower doses of FX005 were conducted to determine the appropriate dose level.

These additional toxicology studies showed that at the human equivalent dose of 3 and 1 mg, there was no evidence of the damage to cartilage that had been associated with doses greater than or equal to 10 mg. Based on this, we expect that any further development of FX005, if any, would involve a dose substantially lower than the doses studied in the previously-conducted Phase 2a clinical trial. We will continue to evaluate further development of FX005 taking into consideration, among other factors, our available capital resources.

Manufacturing

We believe that the multifaceted nature of PLGA manufacturing and the limited number of capable contract manufacturing companies that offer PLGA manufacturing provides a competitive advantage. The technology is designed to enable novel formulations of pharmaceuticals by

providing controlled, sustained release of drugs over time and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates.

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We currently do not have manufacturing facilities and thus utilize contract manufacturers to produce our drug substances and drug products used for preclinical and clinical supplies. Manufacture of PLGA microspheres is a complex process and there are a limited number of contract manufacturing sites with PLGA experience. Our injectable IA immediate-release technology allows us to incorporate pharmaceuticals in PLGA microspheres for administration of FX006 and FX005. Following extensive development programs, we have generated formulations of FX006 and FX005 designed to sustain local concentrations of drug in the joint for several months. The FX005 and FX006 microsphere PLGA formulations have gone through numerous iterations and have been optimized to provide a controlled diffusion of drug over an extended period of time. In developing this unique combination of manufacturing process and formulation we have established numerous trade secrets that relate to precise pharmaceutical release profiles.

FX006. The active pharmaceutical ingredient in FX006, TCA, is manufactured and supplied by Farmabios SpA in accordance with current good manufacturing practice standards, or cGMP. This supplier is subject to regular inspections by the FDA. The microspheres finished product is manufactured by Evonik Corporation, or Evonik. Evonik is a global, commercial-scale supplier of cGMP-compliant bioabsorbable polymers for a wide variety of medical devices and implantable/injectable sustained-release products. Their materials are components of marketed pharmaceutical and medical device products in the United States, Europe, India and Asia.

FX007. The active ingredient for FX007 is manufactured by AstraZeneca. Existing inventory of drug substance is from AstraZeneca and is suitable for preclinical and early clinical development. We are in the process of identifying a new supplier to manufacture drug substance for use in later-phase manufacture of clinical supplies and commercial product.

FX005. The drug substance in FX005 is currently manufactured by Cambridge Major Laboratories. The microsphere-based finished drug product and associated diluent are manufactured by Evonik.

Commercial Strategy

We intend to build a commercial infrastructure in the United States to effectively support the commercialization of FX006, FX007 and FX005, in advance of anticipated drug approval of FX006. We believe that we can cost effectively promote FX006 to the approximately 9,000 orthopedists and rheumatologists who perform more than 75% of OA treatment injections in the United States with a targeted sales force of approximately 60 to 100 sales representatives. Support for this team will include sales management, internal sales support, distribution support and an internal marketing group. Additional requisite capabilities will include focused management of key accounts such as managed care organizations, group purchasing organizations and government accounts.

Of patients who are treated for OA, it is estimated that 70% of OA patients receive IA injections from orthopedic surgeons or sports medicine specialists. An additional 6% and 7% of patients receive IA injections from physical medicine and rehabilitation (PM&R) specialists and rheumatologists, respectively. Finally, the remaining 17% of IA injections are administered by a wider array of physicians, the largest subgroup being general practitioners. We believe we can effectively cover all specialties and successfully execute our future commercial plans using a cost-efficient strategy, particularly given that orthopedists and rheumatologists are familiar with IA injections utilizing the same steroid in the same dose.

FX006 demonstrates clinically meaningful and significantly better pain relief and functional status compared to a commercially available immediate-release TCA. We believe FX006 s prolonged analgesia may delay the need for TJA, a costly, highly-invasive procedure with a protracted recovery time. Our own market research has indicated that healthcare payors would be willing to reimburse any additional OA therapies that have the potential for pharmacoeconomic benefits reflecting differential efficacy and durability and the potential to delay costly

and invasive TJAs. As a result of both increased patient satisfaction and the potential to delay TJA, we believe FX006 will be priced competitively with existing HA therapies.

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Outside of the United States, we are exploring selective partnerships with third parties for the development and commercialization of our products.

Competition

Overview

Our industry is highly competitive and subject to rapid and significant technological change. The large size and expanding scope of the pain market makes it an attractive therapeutic area for biopharmaceutical businesses. Our potential competitors include pharmaceutical, biotechnology and specialty pharmaceutical companies. Several of these companies have robust drug pipelines, readily available capital and established research and development organizations. We believe our success will be driven by the ability to actively manage a portfolio of assets that remains highly focused on OA patients and their needs.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, durability, safety, price and the availability of reimbursement from government and other third party payors. We believe we will compete favorably by having:

- best-in-class product candidates that have validated mechanisms of action for pain relief;
- sustained-release technology that enable our therapies to maintain persistent therapeutic concentrations in the joint and provide durable efficacy; and
- product candidates with attractive safety profiles with limited systemic exposures and the potential for fewer side effects.

FX006 Competition

Immediate-release steroids and HA are currently the two marketed classes of IA products that would compete with FX006. Immediate-release steroids are generic and widely used as a first line therapy, but leave the joint rapidly after injection and have efficacy that typically wanes within several weeks. FX006 has demonstrated that it persists in the joint at therapeutic concentrations for at least six weeks following injection, whereas there is no measurable immediate-release TCA in the joint by that time. FX006 also provides prolonged analgesia significantly better than that seen with immediate-release TCA. In addition to immediate-release steroids, FX006 will compete with HA in patients considering something beyond an immediate-release steroid injection. HA therapy, which has demonstrated only marginal pain relief over placebo in knee OA patients, generated U.S. sales of approximately $700 million in 2013. The magnitude of pain relief demonstrated by FX006 to date is much greater than that seen in historic HA clinical trials. Also on the market are platelet rich plasma injections, but these require on site preparation from blood drawn from the patient, have generated questionable efficacy in controlled clinical trials and are unlikely to be a broadly embraced therapeutic option for OA patients. Because platelet rich plasma is a therapy derived from the individual patient s blood, it does not require and has not received FDA review or approval.

In addition to marketed IA medications for OA, other companies have OA product candidates in advanced stages of clinical development. These IA products include Fidia Farmaceutici S.p.A s Hymovis, a physical hydrogel based on HA with properties that appear to be similar to most approved HA products, and Ampio Pharmaceuticals, Inc. s Ampion. Ampion is a derivative of human serum albumin, is described as having anti-inflammatory properties and is formulated for immediate-release. It is currently in Phase 3 clinical trials, and the 3 month data suggest it has an HA-like efficacy profile. We believe that other programs, such as Orthotrophix s TPX-100, Carbylan BioSurgery, Inc. s Hydros-TA, Merck Serono s FGF-18 and Allergan, Inc. s botulinum toxin, have not yet entered Phase 3 clinical trials. Autologous cartilage transplantation products, like Carticel, are appropriate for focal defects in cartilage, not the kind of diffuse disease that is seen with OA. Eupraxia s EP-104 is a pre-clinical/Phase 1 therapy that combines an unapproved carrier technology (Plexis) with a steroid (fluticasone) that is not commonly used for the treatment of knee OA. Stem cell approaches to OA are being explored, but these are earlier in development, bear significant technical risks and it remains to be seen how applicable they will be to the treatment of OA.

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Finally, there are many new oral therapies in development for OA pain, but we believe these therapies are likely to expose patients to systemic safety risks greater than that of FX006.

FX007 Competition

Numerous post-operative pain treatments exist, including local administration with combinations of existing analgesic and anti-inflammatory drugs at the time of surgical wound closure, opioids, intravenous acetaminophen and NSAIDs and femoral nerve blocks. However, these all have limitations in terms of inadequate magnitude and duration of pain relief, serious side effects or functional impairment. Pacira Pharmaceuticals has more recently launched EXPAREL®, a product that combines bupivacaine with the DepoFoam® drug delivery platform to provide up to 24 hours of postsurgical pain control following a single intraoperative administration.

FX005 Competition

FX005 would compete mainly against oral opioids, as patients require very strong analgesic therapy for end-stage OA pain. Opioids have numerous systemic side effects, including addiction and constipation, and also cause a higher incidence of falls and fractures in an older OA patient population. Competitors for FX005 include new formulations of existing opioids, including Janssen Pharmaceuticals, Inc. s Nucynta ER and Johnson & Johnson s OROS. For patients with end-stage disease, monoclonal anti-NGF antibodies have the potential to offer powerful pain relief, but in controlled clinical trials these agents were associated with accelerated progression to joint replacement and were placed on clinical hold for the treatment of OA by the FDA in 2010. At the present time, we are not aware of any ongoing trials of monoclonal anti-NGF antibodies in OA.

Intellectual Property/Patents and Proprietary Rights

Intellectual Property and Exclusivity

We seek to protect our product candidates and our technology through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity and contractual restrictions on disclosure.

Patents and Patent Applications

Our policy is to seek to protect the proprietary position of our product candidates by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. U.S. patents generally have a term of 20 years from the earliest effective date of the application.

As of September 30, 2014, we exclusively license (i) one U.S. patent and its foreign counterparts directed to FX007 and (ii) one U.S. patent, one U.S. patent application and their foreign counterparts directed to FX005. In addition, we own one U.S. patent, two pending U.S. applications, and counterpart foreign patent applications, along with one pending international application and one pending U.S. provisional patent application, all directed to our FX006 product candidate. Our issued U.S. patent directed to FX006 relates to its composition of matter and has an expiration date in 2031. The FX006 composition of matter patent is the result of several unique discoveries relating to a narrow drug load specification, a certain release profile of polymers, specific polymer weights and ratios and clinical efficacy observed within a dose-range. Further, for our FX006 product candidate, we have foreign patent applications pending in Australia, Canada, Europe, Japan, China and other foreign countries. Our two related pending U.S non-provisional applications could result in additional claims expiring in 2031 and an additional pending international application, if pursued as a non-provisional international application whereby patents, if granted, based on this international application would have an expiration in 2034. One pending provisional application directed to our FX006 product candidate could, if pursued as a non-provisional patent application, result in a patent expiring in 2035.

For our FX007 product candidate, there is one issued U.S. patent covering the TrkA antagonist compound, FX007, which is owned by AstraZeneca and to which we have an exclusive license. This patent is scheduled to

expire in 2028. We have also licensed counterpart foreign patents that have granted in over 50 countries, which include Australia, Canada and other countries, such as Chile and the Philippines. These patents in Australia, Canada and multiple European countries are scheduled to expire in 2026. We have licensed counterpart patent applications that are pending in Brazil, Ecuador, Egypt, India, Norway, Pakistan, Uruguay, Venezuela, Argentina, Indonesia and Thailand.

For our FX005 product candidate, there is one issued U.S. patent covering the p38 compound, FX005, which is owned by AstraZeneca and to which we have an exclusive license. This patent is scheduled to expire in 2028. We have also licensed counterpart foreign patents that have granted in over 50 countries, which include Australia, Canada, and other countries. The patents in Australia, Canada and multiple European countries are scheduled to expire in 2024. We have also licensed counterpart patent applications that are pending in Argentina, Brazil, Egypt, Indonesia, Norway, Uruguay, Thailand and Venezuela. In addition, we have licensed a patent application for the novel formulation of FX005 a patent, if issued based on this application, would be expected to expire in 2029. Foreign equivalents of this patent have been granted in multiple European countries and more recently in Mexico and South Africa, and have been allowed in Israel and Russia and are pending in several other countries.

We have other patent applications on formulations or uses of compounds that are not relevant to our current programs in development.

Trade Secrets and Proprietary Information

The FX005 and FX006 microsphere PLGA formulations have gone through numerous iterations and have been optimized to deliver the drug substance with a controlled diffusion of drug over an extended period of time. In developing this unique combination of manufacturing process and formulation, we have established numerous trade secrets, including those that relate to a precise pharmaceutical release profile. In addition, due to the complexity of the sustained-release technology and the time, costs and technical risks involved in demonstrating bioequivalence through clinical trials, we believe that the ability of manufacturers to gain market approval for generic alternatives to our products upon expiration of our patents and FDA exclusivity will be challenging.

We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees to execute Proprietary Information, Inventions, Non-Solicitation, and Non-Competition Agreements upon the commencement of their employment. Consultants and other advisors are required to sign consulting agreements. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Further, we require confidentiality agreements from entities that receive our confidential data or materials.

License Agreements

We have entered into license agreements with AstraZeneca for the license of FX007 and FX005.

AstraZeneca FX007. On September 3, 2010, we entered into an exclusive license agreement with AstraZeneca for FX007, which was subsequently amended on March 17, 2014. The agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense, subject to certain conditions described below) under AstraZeneca s patent rights and certain know-how covering FX007. We paid

AstraZeneca a non-refundable fee following execution of the agreement and will owe up to an aggregate of $21 million upon the achievement of certain regulatory and development milestones for a first licensed product for OA indications or up to an aggregate of $15 million upon the achievement of certain regulatory and

development milestones for a first licensed product for non-OA indications. Upon commercialization of a product that results from the technology licensed under the agreement, we will owe AstraZeneca tiered royalty payments on net sales based on a percentage ranging from low single digits to low double digits, depending on the volume of sales of the applicable product, as well as up to $75 million in additional payments based on the achievement of certain sales milestones. Our obligation to pay royalties to AstraZeneca will continue on a country-by-country basis until the later to occur of 12 years following the first commercial sale of the applicable product in the applicable country, or the date that the product is no longer covered by AstraZeneca s patent rights or any applicable data or marketing exclusivity periods in such country.

Under the terms of the agreement, we may not grant sublicenses except in the territory of Japan prior to the achievement of a specified development milestone. In addition, the agreement provides that in the event we desire to offer rights to FX007 to a third party prior to the achievement of a specified development milestone, we must make certain diligence materials available to AstraZeneca, and AstraZeneca will have the right to make an offer to re-acquire rights to FX007. In such circumstances, we are not required to accept AstraZeneca s offer, but we may not enter into an agreement with a third party containing financial terms and conditions that on the whole are more favorable to the third party than the terms and conditions last offered by AstraZeneca.

Unless earlier terminated, the agreement will continue in effect for as long as we are obligated to pay royalties to AstraZeneca, after which the licenses granted to us will survive and become royalty-free, perpetual and irrevocable. AstraZeneca has the right to terminate the agreement if we fail to use commercially reasonable efforts to develop, commercialize and sell licensed products in major markets (subject to a good-faith negotiation and cure period) or if we or any of our affiliates or sublicensees institute, prosecute or otherwise participate in any proceeding challenging the AstraZeneca patent rights that are licensed under the agreement. AstraZeneca also has a right to terminate the agreement in the event of a change of control of us prior to the achievement of a specified development milestone, unless we pay a fee to AstraZeneca (which can be offset against future milestone payments), in which case this termination right will be forfeited. We have the right to terminate the agreement in its entirety, or on a country-by-country basis, for any reason upon three months prior written notice to AstraZeneca. In addition, either party may terminate the agreement in the event of the other party s uncured material breach of the agreement, or in the event of the other party s bankruptcy or insolvency.

AstraZeneca FX005. On June 12, 2009, we entered into an exclusive license agreement with AstraZeneca for FX005. The agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) under AstraZeneca s patent rights and certain know-how covering FX005. We paid AstraZeneca a non-refundable fee upon execution of the agreement and will owe up to an aggregate of $17 million upon the achievement of certain regulatory and development milestones for a first licensed product for OA indications or up to an aggregate of $11 million upon the achievement of certain regulatory and development milestones for a first licensed product for non-OA indications. Upon commercialization of a product that results from the technology licensed under the agreement, we will owe AstraZeneca tiered royalty payments on net sales based on a percentage ranging from low to high single digits, depending on the volume of sales of the applicable product, as well as up to $45 million in additional payments based on the achievement of certain sales milestones. Our obligation to pay royalties to AstraZeneca will continue on a country-by-country basis until the later to occur of 12 years following the first commercial sale of the applicable product in the applicable country, or the date that the product is no longer covered by AstraZeneca s patent rights or any applicable data or marketing exclusivity periods in such country.

The agreement provides that in the event we desire to offer rights to FX005 to a third party prior to the achievement of a specified development milestone, we must make certain diligence materials available to AstraZeneca and AstraZeneca will have the right to make an offer to re-acquire rights to FX005. However, pursuant to a separate letter agreement entered into between the parties on December 3, 2012, AstraZeneca agreed to waive this right for a specified period.

Unless earlier terminated, the agreement will continue in effect for as long as we are obligated to pay royalties to AstraZeneca, after which the licenses granted to us will survive and become royalty-free, perpetual

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and irrevocable. AstraZeneca has the right to terminate the agreement if we fail to use commercially reasonable efforts to develop, commercialize and sell licensed products in major markets (subject to a good-faith negotiation and cure period) or if we or any of our affiliates or sublicensees institute, prosecute or otherwise participate in any proceeding challenging the AstraZeneca patent rights that are licensed under the agreement. We have the right to terminate the agreement in its entirety, or on a country-by-country basis, for any reason upon three months prior written notice to AstraZeneca. In addition, either party may terminate the agreement in the event of the other party s uncured material breach of the agreement, or in the event of the other party s bankruptcy or insolvency. AstraZeneca initially had a right to terminate the agreement in the event of a change of control of us prior to the achievement of a specified development milestone for FX005. However, AstraZeneca agreed to waive this right pursuant to the separate letter agreement described above. Pursuant to the same letter agreement, we are now free to assign our rights under the agreement to our affiliates or to a third party in connection with a change of control.

In addition to our license agreements related to FX007 and FX005, we also have an exclusive worldwide license agreement with SwRI with respect to the use of SwRI s proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including FX006.

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. FX006 and any other drug candidate that we develop must be approved by the FDA before they may be legally marketed in the United States and by the corresponding foreign regulatory agencies before they may be legally marketed in foreign countries.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the FDCA and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA s refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, or other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

performance of adequate and well-controlled human clinical trials according to the FDA s laws and regulations pertaining to the conduct of human clinical studies, collectively referred to as Good Clinical Practices, or GCP, and according to the International Conference of Harmonization, or ICH, GCP guidelines, to establish the safety and efficacy of the proposed drug for its intended use;

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submission to the FDA of an NDA for a proposed new drug;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA s cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity;

potential FDA audit of the non-clinical and clinical trial sites that generated the data in support of the NDA; and

FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the non-clinical testing stage, also referred to as preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non- compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical trials involve the administration of the drug candidate to healthy subjects or patients with the target disease under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor s control. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA s regulations which reflect the ICH GCP requirements. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the Phase 3 clinical trials that they believe will support approval of the new drug.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or

life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted only in patients having the specific disease.

Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease.

Phase 3. The drug is administered to an expanded patient population in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Generally, at least two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA. In some cases, the FDA has approved a drug based on the results of a single adequate and well-controlled Phase 3 study of excellent design and which provided highly reliable and statistically strong evidence of important clinical benefit, such as an effect on survival, and where a confirmatory study would have been difficult to conduct on ethical grounds.

Post-approval studies, also referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

Progress reports detailing the status of drug development and results of the clinical trials must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects or patients. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the drug has been associated with unexpected serious harm to study subjects.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug 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 drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Processes

The results of product development, preclinical studies and clinical trials for the claimed indications in all relevant pediatric subpopulations and the support for dosing and administration for each pediatric subpopulation for which the product is safe and effective, are contained in an NDA. The FDA may grant deferrals for submission of pediatric data or full or partial waivers after the initial submission of a pediatric study plan following an end of Phase 2 meeting unless otherwise agreed upon by the FDA and the sponsor. In addition, descriptions of the manufacturing process and controls, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are also submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins

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an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 12 months after submission of an NDA in which to complete its initial review of a standard NDA and respond to the applicant, and eight months for a priority review NDA. The FDA does not always meet its PDUFA goal dates for review of standard and priority review NDAs. The review process and the PDUFA goal date may be extended by additional three month review periods whenever the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and 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. During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA will inspect the facilities at which the product is to be manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities 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 sites to assure compliance with FDA regulations regarding conduct of clinical trials for the product s trials. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information.

The NDA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data, which could delay, limit or prevent regulatory approval. The FDA will issue a complete response letter if the agency decides not to approve the NDA. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post approval studies, referred to as Phase 4 testing, which involves clinical trials designed to further assess a product s safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Post-Approval Requirements

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product,

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providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising requirements include, among other things, standards for direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug s approved labeling (known as off-label use), rules for conducting industry-sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA s cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA. These restrictions may include suspension of a product until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a consent decree of permanent injunction, which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third party payors. Third party payors include government payor programs at the federal and state levels, including Medicare and Medicaid, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our drug candidates may not be considered medically necessary or cost-effective. A payor s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The cost of pharmaceuticals continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and

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efficacy. If these third party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

Healthcare Reform

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The Medicare Modernization Act expanded Medicare coverage for drug purchases by the elderly by establishing Medicare Part D and introduced a new reimbursement methodology based on average sales prices for physician administered drugs under Medicare Part B. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class under the new Medicare Part D program. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement rate that we receive for any of our approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, collectively, PPACA, 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 healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among other things, PPACA revises the definition of average manufacturer price for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may

require us to modify our business practices with healthcare practitioners, and a significant number of provisions are not yet, or have only recently become, effective. Although it is too early to determine the effect of PPACA, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. For example, on August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation s automatic reduction to several government programs. These reductions, which began in 2013, include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, 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 have a material adverse effect on our customers and accordingly, our financial operations.

We expect that PPACA, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenue. 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 products.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, and state and local governments. For example, various activities, including but not limited to sales, marketing and scientific/educational grant programs, must comply with the anti-fraud and abuse provisions of the Social Security Act, the federal Anti-Kickback Statute, the federal False Claims Act and similar state laws, each as amended. Failure to comply with such requirements could potentially result in substantial penalties to us. Even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend against enforcement or litigation, in light of the fact that there is significant enforcement interest in pharmaceutical companies in the United States, and some of the applicable laws are quite broad in scope.

The federal Anti-Kickback Statute prohibits any person, including a prescription drug manufacturer (or a party acting on its behalf), from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce or reward either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. The term remuneration is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain business arrangements from prosecution, the exemptions and safe harbors are drawn narrowly and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices

may not in all cases meet all of the criteria for safe harbor protection from federal Anti-Kickback Statute liability. The reach of the Anti-Kickback Statute was broadened by PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal healthcare 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. Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute, and some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payor, not only the Medicare and Medicaid programs in at least some cases, and do not contain safe harbors.

The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third party payor and not merely a federal healthcare program. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare numbers when detailing the provider of services, improper promotion of off-label uses (i.e., uses not expressly approved by FDA in a drug s label), and allegations as to misrepresentations with respect to the services rendered. Our future activities relating to the reporting of discount and rebate information and other information affecting federal, state and third party reimbursement of our future products, and the sale and marketing of our future products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance. Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third party payors. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation by both the federal government and the states in which we conduct our business. For example, HIPAA and its implementing regulations established uniform federal standards for certain covered entities (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included expansion of HIPAA s privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, referred to as HITECH, which became effective on February 17, 2010. Among other things, HITECH makes HIPAA s privacy and security standards directly applicable to business associates independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and

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gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney s fees and costs associated with pursuing federal civil actions. We may also be subject to various federal and state marketing expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported. Compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, or register their sales representatives, as well as prohibiting pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and prohibiting certain other sales and marketing practices. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise comply with these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities.

Where our activities involve foreign government officials, they may also potentially be subject to the Foreign Corrupt Practices Act. If we seek to have a product covered in the United States by the Medicaid programs, various obligations, including government price reporting, are required under the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended, which generally require products to be offered at substantial rebates/discounts to such programs and certain purchasers. In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Many of our current as well as possible future activities are potentially subject to federal and state consumer protection and unfair competition laws. We must also comply with laws that require clinical trial registration and reporting of clinical trial results on the publicly available clinical trial databank maintained by the National Institutes of Health at www.ClinicalTrials.gov. We are subject to various environmental, health and safety regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous substances. From time to time, and in the future, our operations may involve the use of hazardous materials.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private qui tam actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

U.S. Marketing Exclusivity

Hatch-Waxman Exclusivity. Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of other companies seeking to reference another company s

NDA. If the new drug is a new chemical entity subject to an NDA, the FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a Section 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, such as new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. 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 effectiveness.

Pediatric Exclusivity. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to any existing exclusivity period or patent term. This six-month exclusivity may be granted by the FDA based on the completion of a pediatric clinical trial in accordance with provisions of the FDCA.

Europe/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our future products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application, or CTA, must be submitted to each country s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country s requirements, the clinical trial described in that CTA may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with the ICH GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. In the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations: the Community MA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use, a body of the European Medicines Agency, or the EMA, and which is valid throughout the entire territory of the EEA; and the National MA, which is issued by the competent authorities of the Member States of the EEA and only authorizes marketing in that Member State s national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The

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Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. The National MA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member state, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a national MA in all the Member States where the authorization was sought. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees

As of September 30, 2014, we had 21 full-time employees. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Research and Development

We invested $11.1 million, $11.1 million and $8.2 million in research and development in the years ended December 31, 2013, 2012 and 2011, respectively.

Facilities

Our offices are located at an 11,754 square foot leased facility in Burlington, MA used primarily for corporate functions. The lease expires in October 2016. We believe that our existing facility is sufficient for our needs for the foreseeable future.

Legal Proceedings

We are not currently a party to any material legal proceedings.

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MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information regarding our current executive officers and directors as of October 31, 2014:

Name	Age	Position(s)
Executive Officers and Key Employees		
Michael D. Clayman, M.D.	62	President, Chief Executive Officer, Director and Co-Founder
Neil Bodick, M.D., Ph.D.	67	Chief Medical Officer and Co-Founder
Frederick W. Driscoll	64	Chief Financial Officer
Non-Employee Directors		
Patrick J. Mahaffy[(2)(3)]	51	Chairman of the Board of Directors
Samuel D. Colella[(2)(3)]	74	Director
Heath Lukatch, Ph.D.[(2)(3)]	47	Director
Sandesh Mahatme[(1)]	49	Director
Ann Merrifield[(1)]	63	Director
Alan Milinazzo[(1)]	55	Director
Andrew J. Schwab[(1)]	43	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Michael D. Clayman, M.D. Dr. Clayman was a co-founder and has served as our President, Chief Executive Officer, and as one of our directors since our inception in 2007. Dr. Clayman also serves on the board of directors of Akebia Therapeutics, Inc., a biopharmaceutical company. Previously, Dr. Clayman had a lengthy career at Eli Lilly and Company, a global pharmaceutical company, where he was most recently Vice President, Lilly Research Laboratories, and General Manager of Chorus, Lilly s early-phase development accelerator. During his career at Lilly, Dr. Clayman also led its Global Regulatory Affairs division, the Cardiovascular Discovery Research and Clinical Investigation, Research and Development at Advanced Cardiovascular Systems, a medical device subsidiary of Lilly, the Internal Medicine Division, the Lilly Clinic, Lilly s dedicated Phase 1 unit, and served as Chair of Lilly s Bioethics Committee. Prior to his tenure at Lilly, Dr. Clayman was an Assistant Professor in the School of Medicine at the University of Pennsylvania, where his research centered on the immunopathogenesis of renal disease. Dr. Clayman is the recipient of the Physician Scientist Award from the National Institutes of Health. Dr. Clayman earned a B.A., cum laude, from Yale University and an M.D. from the University of California, San Diego School of Medicine. Following an internship and residency in Internal Medicine at the University of California, San Francisco Moffitt Hospitals, Dr. Clayman completed clinical and research fellowships in Nephrology at the University of Pennsylvania. Our board of directors believes that Dr. Clayman s clinical and research experience, along with his more than 20 years of experience in pharmaceutical development, qualifies him to serve on our board of directors.

Neil Bodick, M.D., Ph.D. Dr. Bodick was a co-founder and has served as our Chief Medical Officer since our inception in 2007. Previously, Dr. Bodick was at Eli Lilly and Company, where he founded Chorus and served as Chief Medical Officer and Chief Operating Officer. Prior to that, Dr. Bodick was responsible for early-phase clinical investigation at Lilly Research Laboratories. Dr. Bodick also was Assistant Professor in the School of Medicine at the University of Pennsylvania, where his research centered on the development of computer-based systems to support

image-intensive diagnosis. Dr. Bodick holds 13 patents in the areas of neuroscience and computer science and is the recipient of the Biomedical Research Service Award and the New Investigator

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Research Award from the National Institutes of Health. Dr. Bodick earned an A.B. from Cornell University, a Ph.D. in neuroscience from Columbia University, an M.D. from the Albert Einstein College of Medicine and an M.B.A. from the Wharton School of the University of Pennsylvania.

Frederick W. Driscoll. Mr. Driscoll has served as our Chief Financial Officer since May 2013. Mr. Driscoll also serves on the board of directors of OXiGENE, Inc., a biopharmaceutical company. Prior to joining us, Mr. Driscoll was Chief Financial Officer at Novavax, Inc., a publicly traded biopharmaceutical company since 2009. Previously, Mr. Driscoll also served as Chief Financial Officer from 2007 to 2008, and subsequently Chief Executive Officer from 2008 to 2009, at Genelabs Technologies, Inc., a publicly traded biopharmaceutical and diagnostics company, Chief Financial Officer at Astraris, Inc., a private biotechnology company, from 2006 to 2007, and Chief Executive Officer at OXiGENE, Inc., a biopharmaceutical company, from 2002 to 2006. Mr. Driscoll earned a bachelor s degree in accounting and finance from Bentley University.

Non-Employee Directors

Patrick J. Mahaffy. Mr. Mahaffy has served as one of our directors and as Chairman of our board of directors since 2009. Mr. Mahaffy has served as the President, Chief Executive Officer, and a director of Clovis Oncology, Inc., a biopharmaceutical company, since 2009, and also serves on the board of directors of Orexigen Therapeutics, Inc., a biopharmaceutical company. Previously, Mr. Mahaffy served as President and Chief Executive Officer and as a member of the board of directors at Pharmion Corporation, a pharmaceutical company that he founded in 2000 and sold to Celgene Corporation in 2008. From 1992 through 1998, Mr. Mahaffy was President and Chief Executive Officer of NeXagen, Inc. and its successor, NeXstar Pharmaceuticals, Inc., a biopharmaceutical company. Prior to that, Mr. Mahaffy was a Vice President at the private equity firm E.M. Warburg Pincus and Co. He is also a trustee of Lewis and Clark College. Mr. Mahaffy earned a B.A. in international affairs from Lewis and Clark College and an M.A. in international affairs from Columbia University. Our board of directors believes that Mr. Mahaffy s experience and expertise in the pharmaceutical industry qualifies him to serve on our board of directors.

Samuel D. Colella. Mr. Colella has served as one of our directors since 2008. Mr. Colella is a Managing Director of Versant Ventures, a healthcare venture capital firm he co-founded in 1999, and has been a general partner of Institutional Venture Partners since 1984. Mr. Colella currently serves as Chairman of the Board of Fluidigm Corporation, a biotechnology tools company, and is a member of the board of directors of Genomic Health, Inc., a molecular diagnostics company, and the boards of several private companies. Mr. Colella served on the board of directors of Alexza Pharmaceuticals, Inc., a pharmaceutical company, from 2002 to 2012 and Jazz Pharmaceuticals, Inc., a biopharmaceutical company, from 2003 to 2012. Mr. Colella earned a B.S. in business and engineering from the University of Pittsburgh and an M.B.A. from Stanford University. Our board of directors believes that Mr. Colella s broad understanding of the life science industry and his extensive experience in working with emerging private and public companies qualifies him to serve on our board of directors.

Heath Lukatch, Ph.D. Dr. Lukatch has served as one of our directors since 2012. Dr. Lukatch is employed as a Partner at Novo Ventures (US) Inc., which provides certain consultancy services to Novo A/S, a Danish limited liability company that manages investments and financial assets. Dr. Lukatch joined Novo Ventures (US) Inc. in 2006. He currently serves as Chairman of the board of directors of Inogen, Inc., a publicly traded medical technology company. He is also currently a member of the board of directors of a number of private companies. Prior to joining Novo Ventures (US) Inc., Dr. Lukatch was a Managing Director responsible for biotechnology venture investments at Piper Jaffray Ventures and SightLine Partners, a private equity firm and spin off of Piper Jaffray Ventures, from 2001 to 2006. Prior to joining Piper Jaffray Ventures, Dr. Lukatch worked as a strategy consultant with McKinsey & Company, a consulting firm. Dr. Lukatch also served as co-founder and chief executive officer of AutoMate Scientific, Inc., a biotechnology instrumentation company and held scientific positions with Chiron Corporation, a biotechnology company, Roche Bioscience, a healthcare company, and Cetus Corporation, a biotechnology company. Dr. Lukatch received his Ph.D. in Neuroscience from Stanford University where he was a DOD USAF Fellow, and his B.A. in Biochemistry from the University of California at Berkeley. Our board of directors believes that his extensive industry experience, his experience

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with venture capital investments, and his experience of serving on the board of directors for several biopharmaceutical and healthcare companies qualifies Dr. Lukatch to serve on our board of directors.

Sandesh Mahatme. Mr. Mahatme has served as one of our directors since 2014. Since November 2012, Mr. Mahatme has served as Senior Vice President, Chief Financial Officer at Sarepta Therapeutics, Inc., a publicly traded biopharmaceutical company. From January 2006 to November 2012, Mr. Mahatme worked at Celgene Corporation, a publicly traded biopharmaceutical company, where he served in various roles, including Senior Vice President of Corporate Development, Senior Vice President of Finance, Corporate Treasurer and Head of Tax. While at Celgene, Mr. Mahatme built the treasury and tax functions before establishing the Corporate Development Department, focused on strategic, targeted initiatives including commercial development in emerging markets, acquisitions, licensing and global manufacturing expansion. From 1997 to 2005 Mr. Mahatme worked for Pfizer Inc., a pharmaceutical company, where he served in senior roles in business development and corporate tax. Mr. Mahatme started his career at Ernst & Young LLP where he advised multinational corporations on a broad range of transactions. Mr. Mahatme earned LL.M. degrees from Cornell Law School and NYU School of Law and is a member of the New York State Bar Association. Our board of directors believes that Mr. Mahatme s financial expertise qualifies him to serve on our board of directors.

Ann Merrifield. Ms. Merrifield has served as one of our directors since 2014. From December 2012 to July 2014, Ms. Merrifield served as President and Chief Executive Officer of PathoGenetix, Inc., a privately held health technology company, which voluntarily filed for Chapter 7 bankruptcy in July 2014. Prior to joining PathoGenetix, Ms. Merrifield served an 18-year tenure at Genzyme Corporation, a diversified, global biotechnology company. At Genzyme, Ms. Merrifield served most recently as President of Genzyme Biosurgery, where she led global business strategy across a complex portfolio of biologics, therapeutic devices and combination products, and was previously Vice President of Marketing, General Manager and President of Genzyme Genetics, where she played an instrumental role in developing and shaping its diagnostic business. Prior to joining Genzyme, Ms. Merrifield was a Partner at Bain and Company, a global strategy consulting firm, and an Investment Officer at Aetna Life & Casualty. She currently serves as a director of InVivo Therapeutics Holdings Corp., a publicly traded biotechnology company, and as a trustee of MassMutual Premier, Select and MML Series Investment Funds. Ms. Merrifield earned a B.A. in Zoology and a Master of Education from The University of Maine, and an M.B.A. from the Amos Tuck School of Business at Dartmouth College. Our board of directors believes that Ms. Merrifield s commercial expertise specifically in the intra-articular injection field qualifies her to serve on our board of directors.

Alan Milinazzo. Mr. Milinazzo has served as one of our directors since 2011. Since January 2013, Mr. Milinazzo has served as President, Chief Executive Officer and a director of InspireMD, a medical device company. Previously, Mr. Milinazzo served as President and Chief Executive Officer of Orthofix International N.V., a Nasdaq-listed medical device company, until August 2011, a position he was promoted to in 2006 after being hired a year earlier as Chief Operating Officer. He also served as a director of Orthofix International N.V. from December 2006 until June 2012. From 2002 to 2005, Mr. Milinazzo was the General Manager of Medtronic, Inc. s coronary and peripheral vascular businesses. Mr. Milinazzo also spent 12 years as an executive with Boston Scientific Corporation in numerous roles, including Vice President of Marketing for SCIMED Europe. Mr. Milinazzo has over 20 years of experience in management and marketing, including positions with Aspect Medical Systems and American Hospital Supply. Our board of directors believes that Mr. Milinazzo s more than two and a half decades of experience in the life sciences sector qualifies him to serve on our board of directors.

Andrew J. Schwab. Mr. Schwab has served as one of our directors since 2009. Mr. Schwab is a founder and Managing Partner of 5AM Ventures, a life sciences venture capital firm, and has served on the boards of directors at several private life sciences companies. Prior to founding 5AM Ventures in 2002, Mr. Schwab was a Principal at Bay City Capital, a life sciences venture capital firm. Previously, Mr. Schwab was Vice President of Business Development at Digital Gene Technologies, Inc. and a Vice President in the life science investment banking group of Montgomery Securities. Mr. Schwab earned a B.S. with honors in genetics and ethics from Davidson College. Our board of directors believes that Mr. Schwab s venture capital and financial services background and prior service on other boards of directors qualifies him to serve on our board of directors.

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Board Composition

Our business and affairs are organized under the direction of our board of directors, which currently consists of eight members. The primary responsibilities of our board of directors are to provide oversight, strategic guidance, counseling and direction to our management. Our board of directors meets on a regular basis and additionally as required. After review of all relevant identified transactions or relationships between each director, or any of his or her family members, and the Company, its senior management and its independent auditors, our board of directors has affirmatively determined that, with the exception of Dr. Clayman, all of our directors are independent directors within the meaning of the applicable Nasdaq Listing Rules.

Our board of directors is divided into three classes, as follows:

- Class I, which consists of Dr. Clayman, Mr. Mahatme and Ms. Merrifield, whose terms will expire at our annual meeting of stockholders to be held in 2015;
- Class II, which consists of Mr. Colella and Mr. Schwab, whose terms will expire at our annual meeting of stockholders to be held in 2016; and
- Class III, which consists of Dr. Lukatch, Mr. Mahaffy and Mr. Milinazzo, whose terms will expire at our annual meeting of stockholders to be held in 2017.

At each annual meeting of stockholders, the successors to directors whose terms then expire will serve until the third annual meeting following their election and until their successors are duly elected and qualified. The authorized size of our board of directors is currently nine members. The authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed between the three classes so that, as nearly as possible, each class will consist of one-third of the directors. This classification of the board of directors may have the effect of delaying or preventing changes in our control or management. Our directors may be removed for cause by the affirmative vote of the holders of at least 66 2/3% of our voting stock.

Board Leadership Structure

Our board of directors is currently chaired by Mr. Mahaffy. As a general policy, our board of directors believes that separation of the positions of Chairman and Chief Executive Officer reinforces the independence of the board of directors from management, creates an environment that encourages objective oversight of management s performance and enhances the effectiveness of the board of directors as a whole. As such, Dr. Clayman serves as our President and Chief Executive Officer while Mr. Mahaffy serves as our Chairman of the board of directors but not as an officer. We expect and intend the positions of Chairman of the board of directors and Chief Executive Officer to continue to be held by two individuals in the future.

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. The board of directors does not have a standing risk management committee, but rather administers this oversight function directly through the board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

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Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee.

Audit Committee

Our audit committee consists of Mr. Mahatme, Ms. Merrifield, Mr. Milinazzo and Mr. Schwab. Our board of directors has determined that each of the members of our audit committee satisfies the Nasdaq Stock Market and SEC independence requirements. Mr. Mahatme serves as the chair of our audit committee. The functions of this committee include, among other things:

- evaluating the performance, independence and qualifications of our independent auditors and determining whether to retain our existing independent auditors or engage new independent auditors;
- reviewing and approving the engagement of our independent auditors to perform audit services and any permissible non-audit services;
- monitoring the rotation of partners of our independent auditors on our engagement team as required by law;
- prior to engagement of any independent auditor, and at least annually thereafter, reviewing relationships that may reasonably be thought to bear on their independence, and assessing and otherwise taking the appropriate action to oversee the independence of our independent auditor;
- reviewing our annual and quarterly financial statements and reports, including the disclosures contained under the caption Management s Discussion and Analysis of Financial Condition and Results of Operations, and discussing the statements and reports with our independent auditors and management;
- reviewing with our independent auditors and management significant issues that arise regarding accounting principles and financial statement presentation and matters concerning the scope, adequacy and effectiveness of our financial controls;
- reviewing with management and our auditors any earnings announcements and other public announcements regarding material developments;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding financial controls, accounting or auditing matters and other matters;
- preparing the report that the SEC requires in our annual proxy statement;
- reviewing and providing oversight of any related-person transactions in accordance with our related person transaction policy and reviewing and monitoring compliance with legal and regulatory responsibilities, including our code of business conduct and ethics;

reviewing our major financial risk exposures, including the guidelines and policies to govern the process by which risk assessment and risk management is implemented;

reviewing on a periodic basis our investment policy; and

reviewing and evaluating on an annual basis the performance of the audit committee, including compliance of the audit committee with its charter.

Our board of directors has determined that Mr. Schwab qualifies as an audit committee financial expert within the meaning of SEC regulations and meets the financial sophistication requirements of the Nasdaq Listing Rules. In making this determination, our board has considered Mr. Schwab s previous and current experience in investment banking and financial oversight roles. Both our independent registered public accounting firm and management periodically meet privately with our audit committee.

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Compensation Committee

Our compensation committee consists of Mr. Colella, Dr. Lukatch and Mr. Mahaffy. Mr. Mahaffy serves as the chair of our compensation committee. Our board of directors has determined that each of the members of our compensation committee is a non-employee director, as defined in Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code, and satisfies the Nasdaq Stock Market independence requirements. The functions of this committee include, among other things:

- reviewing, modifying and approving (or if it deems appropriate, making recommendations to the full board of directors regarding) our overall compensation strategy and policies;
- reviewing and approving the compensation and other terms of employment of our executive officers;
- reviewing and approving performance goals and objectives relevant to the compensation of our executive officers and assessing their performance against these goals and objectives;
- reviewing and approving (or if it deems it appropriate, making recommendations to the full board of directors regarding) the equity incentive plans, compensation plans and similar programs advisable for us, as well as modifying, amending or terminating existing plans and programs;
- evaluating risks associated with our compensation policies and practices and assessing whether risks arising from our compensation policies and practices for our employees are reasonably likely to have a material adverse effect on us;
- reviewing and approving (or if it deems it appropriate, making recommendations to the full board of directors regarding) the type and amount of compensation to be paid or awarded to our non-employee board members;
- establishing policies with respect to votes by our stockholders to approve executive compensation as required by Section 14A of the Exchange Act and determining our recommendations regarding the frequency of advisory votes on executive compensation;
- reviewing and assessing the independence of compensation consultants, legal counsel and other advisors as required by Section 10C of the Exchange Act;
- administering our equity incentive plans;
- establishing policies with respect to equity compensation arrangements;
- reviewing the competitiveness of our executive compensation programs and evaluating the effectiveness of our compensation policy and strategy in achieving expected benefits to us;
- reviewing and approving the terms of any employment agreements, severance arrangements, change in control protections and any other compensatory arrangements for our executive officers;

reviewing the adequacy of its charter on a periodic basis;

reviewing with management and approving our disclosures under the caption Compensation Discussion and Analysis in our periodic reports or proxy statements to be filed with the SEC;

preparing the report that the SEC requires in our annual proxy statement; and

reviewing and assessing on an annual basis the performance of the compensation committee.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Mr. Colella, Dr. Lukatch and Mr. Mahaffy. Our board of directors has determined that each of the members of this committee satisfies the Nasdaq Stock Market independence requirements. Mr. Colella serves as the chair of our nominating and corporate governance committee. The functions of this committee include, among other things:

identifying, reviewing and evaluating candidates to serve on our board of directors consistent with criteria approved by our board of directors;

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determining the minimum qualifications for service on our board of directors;

evaluating director performance on the board and applicable committees of the board and determining whether continued service on our board is appropriate;

evaluating, nominating and recommending individuals for membership on our board of directors;

evaluating nominations by stockholders of candidates for election to our board of directors;

considering and assessing the independence of members of our board of directors;

developing a set of corporate governance policies and principles, including a code of business conduct and ethics, periodically reviewing and assessing these policies and principles and their application and recommending to our board of directors any changes to such policies and principles;

considering questions of possible conflicts of interest of directors as such questions arise;

reviewing the adequacy of its charter on an annual basis; and

annually evaluating the performance of the nominating and corporate governance committee.

Compensation Committee Interlocks and Insider Participation

We have established a compensation committee which has and will make decisions relating to compensation of our executive officers. Our board of directors has appointed Mr. Colella, Dr. Lukatch and Mr. Mahaffy to serve on the compensation committee. None of these individuals has ever been an executive officer or employee of ours. None of our executive officers currently serves, or has served during the last completed fiscal year, on the compensation committee or board of directors of any other entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2011 to which we have been a party, in which the amount involved in the transaction exceeded $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described in our filings with the SEC set forth under Incorporation of Certain Information by Reference .

Preferred Stock Financings

December 2012 Series B Preferred Stock Financing

In December 2012, we entered into a Series B Preferred Stock Purchase Agreement pursuant to which we issued and sold to investors an aggregate of 17,736,786 shares of our Series B convertible preferred stock at a purchase price of $1.1275 per share, for aggregate consideration of $20.0 million.

March 2011 and February 2012 Additional Closings of Series A Preferred Stock Financing

In March 2011, we issued and sold to investors an aggregate of 13,000,000 shares of our Series A convertible preferred stock at a purchase price of $1.00 per share, for aggregate consideration of $13.0 million. These shares were sold and issued in an additional closing pursuant to a Share Purchase Agreement originally entered into between the Company and the investors in September 2009, or the 2009 Purchase Agreement. In February 2012, at an additional closing pursuant to the 2009 Purchase Agreement, we issued and sold to investors an aggregate of 13,093,464 additional shares of our Series A convertible preferred stock at a purchase price of $1.00 per share, for aggregate consideration of $13.1 million.

The participants in the convertible preferred stock financings described above included the following holders of more than 5% of our capital stock or entities affiliated with them. The following table presents the number of shares issued to these related parties in these financings:

Participants[1]	Series A Preferred Stock Issued in March 2011 and February 2012	Series B Preferred Stock Issued in December 2012
5% or Greater Stockholders		
Versant Venture Capital III, L.P. and its affiliates[2]	8,656,148	3,153,677
Sofinnova Capital VI FCPR	6,458,265	2,116,562
Pfizer Inc.	5,812,438	1,904,905
5AM Ventures II, L.P. and its affiliates[3]	5,166,613	1,693,249
Novo A/S		8,868,393

(1) Additional details regarding these stockholders and their equity holdings is provided in Principal Stockholders.

(2) Represents shares held by Versant Venture Capital III, L.P. and Versant Side Fund III, L.P.
(3) Represents shares held by 5AM Ventures II, L.P. and 5AM Co-Investors II, L.P.

Some of our directors are associated with participants in the convertible preferred stock financings described above, as indicated in the table below:

Director	Principal Stockholder
Samuel D. Colella	Versant Venture Capital III, L.P. and its affiliates
Heath Lukatch, Ph.D.	Novo A/S
Andrew J. Schwab	5AM Ventures II, L.P. and its affiliates

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Investor Rights, Voting and Co-Sale Agreements

In connection with our preferred stock financings, we entered into amended and restated investor rights, voting and right of first refusal and co-sale agreements containing registration rights, information rights, voting rights and rights of first refusal, among other things, with certain holders of our convertible preferred stock and certain holders of our common stock. These stockholder agreements terminated upon the closing of our initial public offering, except for the registration rights granted under our amended and restated investor rights agreement in December 2012 between us and the investors listed therein, or the Investor Rights Agreement, as more fully described below under the heading Description of Capital Stock Registration Rights.

Services Agreement with Stockholder Affiliate

We previously entered into a services agreement with Euro Ventures, Inc., or Euro Ventures, pursuant to which Euro Ventures provided general business consulting services to us, including consulting relating to general business development, assistance with our financial strategy and assistance with respect to clinical development and strategic matters, in exchange for a monthly consulting fee. Euro Ventures is an affiliate of Versant Venture Capital III, L.P., our largest stockholder. The services agreement was terminated in 2011. From January 1, 2010 until the time of termination, we paid Euro Ventures an aggregate of $729,495 in fees for the performance of services under the services agreement.

Participation in our Initial Public Offering

Certain of our pre-IPO stockholders purchased an aggregate of approximately 1,230,769 shares of our common stock in our initial public offering at a price of $13.00 per share, or approximately $16.0 million in the aggregate.

Purchaser	Initial Public Offering Shares
Versant Venture Capital III, L.P. and its affiliates	307,692
Sofinnova Capital VI FCPR	230,769
Novo A/S	692,308

Certain of our current and former directors have affiliations with the investors that participated in the initial public offering described above, as indicated in the table below:

Director	Principal Stockholder
Samuel D. Colella	Versant Venture Capital III, L.P. and its affiliates[2]
Heath Lukatch, Ph. D.	Novo A/S

Employment Arrangements

We have entered into employment arrangements with our executive officers, as more fully described in our filings with the SEC.

Stock Options Granted to Executive Officers and Directors

We have granted stock options to our executive officers and directors, as more fully described in our filings with the SEC.

Indemnification Agreements

We have entered into, and intend to continue to enter into, separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our amended and restated bylaws. These agreements, among other things, require us to indemnify our directors and executive officers for

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certain expenses, including attorneys fees, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of their services as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder s investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Policies and Procedures for Transactions with Related Persons

We have adopted a written related-person transactions policy that sets forth our policies and procedures regarding the identification, review, consideration and oversight of related-person transactions. For purposes of our policy only, a related-person transaction is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any related person are participants involving an amount that exceeds $120,000.

Transactions involving compensation for services provided to us as an employee, consultant or director are not considered related-person transactions under this policy. A related person is any executive officer, director or a holder of more than 5% of our common stock, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee (or, where review by our audit committee would be inappropriate, to another independent body of our board of directors) for review. The presentation must include a description of, among other things, the material facts, the direct and indirect interests of the related persons, the benefits of the transaction to us and whether any alternative transactions are available. To identify related-person transactions in advance, we rely on information supplied by our executive officers, directors and certain significant stockholders. In considering related-person transactions, our audit committee or other independent body of our board of directors takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director s independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and

the terms available to or from, as the case may be, unrelated third parties or to or from our employees generally.

In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding beneficial ownership of our capital stock by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

The percentage ownership information under the column entitled Before offering is based on 15,627,288 shares of common stock outstanding as of October 31, 2014. The percentage ownership information under the column entitled After offering is based on the sale of 5,040,000 shares of common stock in this offering. The table below does not reflect purchases of shares in this offering by certain existing investors affiliated with certain of our directors. See Underwriting.

The following table is based upon information supplied by officers, directors and certain principal stockholders and Schedules 13G filed with the SEC. We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable on or before December 30, 2014, which is 60 days after October 31, 2014. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Except as otherwise noted below, the address for each person or entity listed in the table is c/o Flexion Therapeutics, Inc., 10 Mall Road, Suite 301, Burlington, Massachusetts 01803.

Name and address of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5% or greater stockholders			
Versant Venture Capital III, L.P. and its affiliates[1] 1700 Owens Street, Suite 541 San Francisco, CA 94158	3,206,807	20.52%	15.52%
Sofinnova Capital VI FCPR[2] 16-18 rue de 4 Septembre	2,105,491	13.47%	10.19%

75002 Paris, France			
Pfizer Inc.[3]. 235 E. 42nd Street New York, NY 10017	1,687,250	10.80%	8.16%
5AM Ventures II, L.P. and its affiliates[4] 2200 Sand Hill Road, Suite 110 Menlo Park, CA 94025	1,512,076	9.68%	7.32%
Novo A/S[5] Tuborg Havnevej 19 DK-2900 Hellerup Denmark	1,783,131	11.41%	8.63%

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Name and address of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
Directors and named executive officers			
Michael D. Clayman, M.D.[6]	781,955	4.97%	3.77%
Neil Bodick, M.D., Ph.D.[7]	547,331	3.49%	2.64%
Frederick Driscoll[8]	53,556	*	*
Patrick J. Mahaffy[9]	44,324	*	*
Samuel D. Colella [10]	3,213,557	20.55%	15.54%
Heath Lukatch, Ph.D.			
Sandesh Mahatme			
Ann Merrifield			
Alan Milinazzo[11]	23,278	*	*
Andrew J. Schwab[12]	1,518,826	9.71%	7.35%
All current executive officers and directors as a group (10 persons)[13]	5,405,461	33.94%	25.78%

* Represents beneficial ownership of less than one percent.

(1) Includes (a) 2,803,385 shares of common stock held by Versant Venture Capital III, L.P., (b) 14,739 shares of common stock held by Versant Side Fund III, L.P. and (c) 388,683 shares of common stock held by Versant Development Fund III, LLC. Brian G. Atwood, Ross A. Jaffe, M.D., Samuel D. Colella, Donald B. Milder, Rebecca B. Robertson, Bradley J. Bolzon, Ph.D., William J. Link, Ph.D., Charles M. Warden, and Barbara N. Lubash, as managing directors of Versant Ventures III, LLC, share voting and investment authority over the shares held by Versant Venture Capital III, L.P. and Versant Side Fund III, L.P. Versant Venture Capital III, L.P. is the majority member of Versant Development Fund III, LLC.

(2) Represents shares of common stock held by Sofinnova Capital VI FCPR. Sofinnova Partners SAS, a French corporation and the management company of Sofinnova Capital VI FCPR, may be deemed to have sole voting and investment power, and Dennis Lucquin, Antoine Papiernik, Rafaèle Tordjman, M.D., Ph.D. and Monique Saulnier, the managing partners of Sofinnova Partners SAS, may be deemed to have shared voting and investment power with respect to such shares.

(3) Represents shares of common stock held by Pfizer Inc.

(4) Includes (a) 1,454,679 shares of common stock held by 5AM Ventures II, L.P. and (b) 57,397 shares of common stock held by 5AM Co-Investors II, L.P. John D. Diekman, Andrew J. Schwab and Scott M. Rocklage are managing members of 5AM Partners II LLC, the general partner of 5AM Ventures II L.P. and 5AM Co-Investors II L.P., and as such, share voting and investment authority over the shares held by 5AM Ventures II L.P. and 5AM Co-Investors II L.P.

(5) Represents shares of common stock held by Novo A/S, or Novo. Novo is a Danish limited liability company. The board of directors of Novo, which consists of Sten Scheibye, Göran Ando, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, has shared investment and voting control with respect to the shares held by Novo and may exercise such control only with the support of a majority of the members of the Novo board of directors. As such, no individual member of the Novo board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo. Dr. Lukatch, a member of our board of directors, is employed as a Partner of Novo Ventures (US) Inc., which provides certain consultancy services to Novo. Dr. Lukatch is not deemed a beneficial owner of, and does not have a reportable pecuniary interest in, the shares held by Novo.

(6) Includes 273,661 shares of common stock held by Dr. Clayman and 95,011 shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014. Also includes 24,600 shares of common stock held by the Michael D. Clayman Irrevocable Trust, of which Dr. Clayman s spouse is trustee. Also includes 388,683 shares of common stock held by Versant Development Fund III, LLC. Dr. Clayman is a manager and minority member of Versant Development Fund III, LLC. Dr. Clayman disclaims any beneficial ownership of the shares held by Versant Development Fund III, LLC except to the extent of his pecuniary interest in these shares.

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(7) Includes 86,937 shares of common stock held by Dr. Bodick and 71,711 shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014. Also includes 388,683 shares of common stock held by Versant Development Fund III, LLC. Dr. Bodick is a manager and minority member of Versant Development Fund III, LLC. Dr. Bodick disclaims any beneficial ownership of the shares held by Versant Development Fund III, LLC except to the extent of his pecuniary interest in these shares.
(8) Represents shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014.
(9) Represents shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014.
(10) Includes the shares of capital stock held by the Versant Ventures entities referred to in footnote (1) above. Mr. Colella disclaims any beneficial ownership of the shares held by these entities except to the extent of his pecuniary interest in these entities. Also includes 6,750 shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014.
(11) Represents shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014.
(12) Includes the shares of capital stock held by the 5AM Ventures entities referred to in footnote (4) above. Mr. Schwab disclaims any beneficial ownership of the shares held by these entities except to the extent of his pecuniary interest in these entities. Also includes 6,750 shares of common stock issuable upon the exercise of options exercisable within 60 days of October 31, 2014.
(13) Includes 5,104,081 shares held by all current executive officers and directors as a group and 301,380 shares that all current executive officers and directors as a group have the right to acquire from us within 60 days of October 31, 2014 pursuant to the exercise of stock options. The shares held by Versant Venture Capital III, L.P. and Versant Side Fund III, L.P., which are deemed to be beneficially owned by Mr. Colella, and the shares held by Versant Development Fund III, LLC, which are deemed to be beneficially owned by Drs. Bodick and Clayman and Mr. Colella, are counted only once in this total.

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DESCRIPTION OF CAPITAL STOCK

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock, par value $0.001 per share and 10,000,000 shares of preferred stock, par value $0.001 per share.

As of September 30, 2014, there were outstanding:

- 15,627,288 shares of common stock; and
- options exercisable for up to 420,974 shares of common stock.

As of September 30, 2014, we had 27 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

The following description of our capital stock is not complete and is subject to and qualified in its entirety by our amended and restated certificate of incorporation and amended and restated bylaws, each filed as an exhibit to our Current Report on Form 8-K filed with the SEC on February 19, 2014, and by the relevant provisions of the Delaware General Corporation Law.

Common Stock

Voting

Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

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Preferred Stock

Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. As of September 30, 2014, there were no shares of preferred stock outstanding, and we have no current plans to issue any shares of preferred stock.

Registration Rights

Certain holders of our common stock, or their transferees, are entitled to the registration rights set forth below with respect to registration of the resale of such shares under the Securities Act pursuant to the Investor Rights Agreement by and among us and certain of our stockholders.

Demand Registration Rights

The holders of a majority of the registrable securities, as defined in the Investor Rights Agreement, have the right to make up to two demands that we file a registration statement under the Securities Act covering the majority of registrable securities then outstanding (or a lesser portion if the anticipated aggregate offering price of securities requested to be sold under such registration statement would exceed $10.0 million, net of underwriting discounts and commissions), subject to specified exceptions.

Form S-3 Registration Rights

If we are eligible to file a registration statement on Form S-3, holders of registrable securities have the right to demand that we file a registration statement on Form S-3 so long as the aggregate amount of securities to be sold under the registration statement on Form S-3 is at least $2.0 million, subject to specified exceptions, conditions and limitations.

Piggyback Registration Rights

If we register any securities for public sale, holders of registration rights will have the right to include their shares in the registration statement. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement, but not below 30% of the total number of shares requested by the holders to be included in the registration statement, except this offering in which the holders have waived any and all rights to have their shares included.

Expenses of Registration

Generally, we are required to bear all registration and selling expenses incurred in connection with the demand, piggyback and Form S-3 registrations described above, other than underwriting discounts and commissions.

Expiration of Registration Rights

The demand, piggyback and Form S-3 registration rights discussed above will terminate three years following the closing of our initial public offering or, as to a given holder of registrable securities, when such holder is able to sell all of their registrable securities in a single 90-day period under Rule 144 of the Securities Act, or Rule 144.

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Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation, Our Bylaws and Delaware Law

Delaware Anti-Takeover Law

We are subject to Section 203 of the Delaware General Corporation Law, or Section 203. Section 203 generally prohibits a public Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the time that such stockholder became an interested stockholder, unless:

- prior to such time the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);

provide that the authorized number of directors may be changed only by resolution of the board of directors;

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provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;

divide our board of directors into three classes;

require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;

provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder s notice;

do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose); and

provide that special meetings of our stockholders may be called only by the chairman of the board, our Chief Executive Officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 66 2/3% of our then outstanding common stock.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the symbol FLXN.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar s address is P.O. Box 43078, Providence, Rhode Island 02940.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to our initial public offering in February 2014, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of our outstanding options, could adversely affect prevailing market prices from time to time and could impair our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of September 30, 2014, upon the completion of this offering, shares of common stock will be outstanding, assuming no exercise of the underwriters option to purchase additional shares and no exercise of options. Of those shares, all of the shares sold in this offering and all other outstanding shares of our common stock will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144, may only be sold in compliance with the limitations described below.

Rule 144

In general, under Rule 144 as currently in effect, any person who is not an affiliate of ours and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, provided current public information about us is available. In addition, under Rule 144, any person who is not an affiliate of ours and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares without regard to whether current public information about us is available. A person who is an affiliate of ours and who has beneficially owned restricted securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of restricted shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 206,673 shares immediately after this offering; or
- the average weekly trading volume of our common stock on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 pursuant to Rule 144 with respect to the sale.

Sales of restricted shares under Rule 144 held by our affiliates are also subject to requirements regarding the manner of sale, notice and the availability of current public information about us. Rule 144 also provides that affiliates relying on Rule 144 to sell shares of our common stock that are not restricted shares must nonetheless comply with the same restrictions applicable to restricted shares, other than the holding period requirement.

Rule 701

In general, under Rule 701 of the Securities Act, any of our stockholders who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement before we became subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act is eligible to resell those shares in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirements of Rule 144, and a non-affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about the issuer.

As of September 30, 2014, options to purchase a total of 1,238,973 shares of common stock were outstanding, of which 420,974 were vested. Of the total number of shares of our common stock issuable under these options, 833,477 are subject to contractual lock-up agreements with the underwriters described below under Underwriting .

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Lock-Up Agreements

We, along with our directors, executive officers and the entities affiliated with our directors, as well as certain of our existing stockholders, have agreed that for a period of 90 days after the date of this prospectus, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, other than with respect to 16,000 shares held by one of our executive officers which shares will not be subject to such restrictions. Upon expiration of the lock-up period, certain of our stockholders will have the right to require us to register their shares under the Securities Act. See Registration Rights below.

Certain of our employees, including our executive officers and/or directors, may in the future enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange Act. Sales under any trading plan entered into by our executive officers and/or directors in the future, if any, would not be permitted until the expiration of the lock-up agreements relating to the offering described above, other than with respect to 16,000 shares held by one of our executive officers which shares will not be subject to such restrictions.

Registration Rights

The holders of a substantial number of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. See Description of Capital Stock Registration Rights.

Equity Incentive Plans

Shares of our common stock reserved for issuance under our 2013 equity incentive plan and our 2013 employee stock purchase plan are available for sale in the open market, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes that may be relevant to Non-U.S. Holders in light of their particular circumstances, does not deal with foreign, state and local tax consequences and does not address U.S. federal tax consequences other than income and estate taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code, such as financial institutions (except to the extent specifically set forth below), insurance companies, persons subject to the alternative minimum tax, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below), persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy, persons who are subject to the alternative minimum tax or the Medicare contribution tax, partnerships and other pass-through entities, and investors in such pass-through entities or an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation). Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and U.S. Department of the Treasury, or Treasury, regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

The following discussion is for general information only and is not tax advice. Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that has not been excluded from this discussion and is not a U.S. Holder. A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is includable in gross income for U.S. federal income tax purposes regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to

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provide us with a properly executed IRS Form W-8BEN or W-8BEN-E, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, or other appropriate form, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a non-taxable return of capital to the extent of your adjusted basis and will first reduce your adjusted basis in our common stock, but not below zero, and then will be treated as gain and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a non-resident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets (which include U.S. real property interests). We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than 5% of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder s holding period, and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, unless a specific treaty exemption applies, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30%

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rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

Information Reporting Requirements and Backup Withholding

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or W-8BEN-E or otherwise establishes an exemption. The backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds from a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or W-8BEN-E or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

If backup withholding is applied to you, you should consult with your own tax advisor to determine if you are able to obtain a tax benefit or credit with respect to such backup withholding.

Foreign Accounts

A U.S. federal withholding tax of 30% may apply to dividends and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules), including when the foreign financial institution holds our common stock on behalf of a Non-U.S. Holder, unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which may include certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing these withholding and reporting requirements may be subject to different rules. This U.S. federal withholding tax of 30% may also apply to dividends and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding direct and indirect U.S. owners of the entity. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such tax. Holders are encouraged to consult with their own tax advisors regarding the possible implications of this withholding on their investment in our

common stock.

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The withholding provisions described above generally apply to payments of dividends on our common stock and will apply to payments of gross proceeds from a sale or other disposition of our common stock on or after January 1, 2017.

Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

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UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table.

Name	Number of Shares
BMO Capital Markets Corp.	2,142,000
RBC Capital Markets, LLC	1,638,000
Needham & Company, LLC	655,200
Janney Montgomery Scott LLC	302,400
Summer Street Research Partners	302,400
Total	5,040,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

The underwriters propose to offer the shares of our common stock directly to the public at the public offering price set forth on the cover of this prospectus and to certain dealers at that price less a concession not in excess of $0.612 per share. After the initial offering of the shares, the offering price and the selling concession may be changed by the underwriters.

Certain existing investors affiliated with certain of our directors have agreed to purchase shares of our common stock in this offering at the public offering price.

The underwriters have an option to buy up to an additional 756,000 shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise this option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above, and the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Paid by Flexion Therapeutics, Inc.	
	No Exercise	Full Exercise
Per share	$ 1.02	$ 1.02
Total	5,140,800	5,911,920

We estimate that the total expenses of this offering payable by us will be approximately $500,000. We have also agreed to reimburse the underwriters for certain of their expenses, in an amount of up to $10,000, as set forth in the underwriting agreement.

Lock-Up Agreements

We, our officers and directors, and certain of their affiliated entities have agreed that, subject to specified limited exceptions, for a period of 90 days from the date of this prospectus, we and they will not, without the

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prior written consent of BMO Capital Markets, dispose of or hedge any shares or any securities convertible into or exchangeable for our common stock, other than with respect to 16,000 shares held by one of our executive officers which shares will not be subject to such restrictions. BMO Capital Markets in its sole discretion may release any of the securities subject to these lock-up agreements at any time.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the symbol FLXN .

Stabilization, Short Positions

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the over-allotment option, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

Covered short sales are sales of shares in an amount up to the number of shares represented by the underwriters over-allotment option.

Naked short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters over-allotment option.

Covering transactions involve purchases of shares either pursuant to the underwriters over-allotment option or in the open market in order to cover short positions.

To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

To close a covered short position, the underwriters must purchase shares in the open market or must exercise the over-allotment option. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the

price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of

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investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an offer of securities to the public in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or Corporations Act) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

you confirm and warrant that you are either:

a sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;

a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant s certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

a person associated with the company under section 708(12) of the Corporations Act; or

a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this document is void and incapable of acceptance; and

you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers.* The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

released, issued, distributed or caused to be released, issued or distributed to the public in France; or

used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and

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Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Japan

The shares offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a

foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

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LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, San Diego, California. Cooley LLP currently owns 3,075 shares of our common stock. The underwriters are being represented by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2013 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the shares of common stock being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC s website at www.sec.gov. You may also read and copy any document we file with the SEC at its Public Reference Room at 100 F Street NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. You may also request a copy of these filings, at no cost, by writing us at 10 Mall Road, Suite 301, Burlington, MA 01803 or telephoning us at (781) 305-7777.

We are subject to the information reporting requirements of the Exchange Act and file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information are available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.flexiontherapeutics.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is incorporated by reference in, and is not part of, this prospectus.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus.

We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-36287):

- our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on March 28, 2014;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014, filed with the SEC on May 12, 2014, August 8, 2014 and November 14, 2014; and
- our Current Reports on Form 8-K filed with the SEC on February 19, 2014, March 3, 2014, June 12, 2014, June 17, 2014, July 24, 2014, September 2, 2014, September 3, 2014 and September 17, 2014 .

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents by writing us at 10 Mall Road, Suite 301, Burlington, MA 01803 or telephoning us at (781) 305-7777. We also maintain a website at www.flexiontherapeutics.com, at which you may access our reports and other documents we file with the SEC. However, unless otherwise noted, the information contained in, or that may be accessed through, our website is not part of this prospectus.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

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Flexion Therapeutics, Inc.

5,040,000 Shares

Common Stock

Prospectus

December 11, 2014

Through and including January 5 , 2015 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

BMO Capital Markets RBC Capital Markets

Needham & Company

Janney Montgomery Scott Summer Street Research Partners