Flexion Therapeutics Inc
Form 424B4
December 12, 2014
Table of Contents

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

Table of Contents

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.

TABLE OF CONTENTS

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

	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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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;

Table of Contents

- 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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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

21

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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;