Transformative Medicine...

Where It Matters

flexion

2017 ANNUAL REPORT

To Our Shareholders:

Flexion was founded in 2007, and for the past decade, we have been focused on developing medicines that matter for patients in need. On October 6, 2017, we achieved a key goal with the U.S. Food and Drug Administration's approval of ZILRETTA®, the first extended-release, intra-articular therapy for the management of osteoarthritis (OA) knee pain. This approval was transformative in many dimensions.

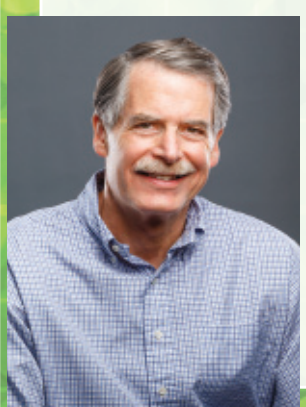
Most immediately, Flexion transitioned from a "development organization" to a full-fledged "commercial enterprise." Between October 6th and November 20th, we introduced ZILRETTA into our distribution channels; we hired, trained and deployed our entire field organization; and we launched a comprehensive marketing program to educate and inform prescribers about ZILRETTA's unique product profile and ensure it is positioned in the market for long-term success.

Flexion Therapeutics is a biopharmaceutical company focused on the discovery, development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions. ZILRETTA® (triamcinolone acetonide extended-release injectable suspension), the company's flagship product, received approval from the U.S. Food and Drug Administration on October 6, 2017 and the company initiated the full commercial launch of ZILRETTA on November 20, 2017. The company's core values are focus, ingenuity, tenacity, transparency and fun. Flexion was named one of the Boston Business Journal's 2017 Best Places to Work and one of the Top Places to Work in Massachusetts by The Boston Globe.

Beyond the launch of ZILRETTA, 2017 was replete with important accomplishments which strengthened Flexion. We advanced our clinical development and life cycle management plans for ZILRETTA; fortified ZILRETTA's patent estate; expanded our product pipeline; and bolstered Flexion's financial position. Notable highlights include:

- **Completed enrollment** in a clinical trial to evaluate the safety of repeat administration of ZILRETTA. Earlier this year, we reported initial data showing 95% of patients achieved clinical benefit after a single administration and approximately 92% of evaluable patients elected to receive a second administration between Weeks 12 and 24;
- **Completed enrollment** in a clinical trial to evaluate the pharmacokinetics (PK) and safety of concurrent injections of ZILRETTA in patients with bilateral OA of the knee;
- **Initiated enrollment** in a randomized, open-label Phase 2 clinical trial to evaluate the PK and safety of ZILRETTA in patients with OA of the shoulder or hip (known as the "SHIP" study);
- **Presented the full data set** from a Phase 2 clinical trial of ZILRETTA in patients with Type 2 diabetes and OA of the knee at the American Diabetes Association's 77th Scientific Sessions. The data demonstrated that ZILRETTA was not associated with the significant rise in blood glucose seen following an immediate-release steroid injection in patients with Type 2 diabetes and OA of the knee;
- **Received from the U.S. Patent and Trademark Office** two new patents (U.S. Patent Numbers 9,555,048 and 9,555,047) covering ZILRETTA's Method of Use and Method of Manufacturing, with terms extending into 2031;
- **Acquired the rights to FX201**, a locally administered, pre-clinical gene therapy candidate which may hold the potential to provide relief from OA related knee pain for at least a year and arrest disease progression; and
- **Conducted two separate financings** in 2017. In May, we completed an offering of convertible senior notes due in 2024, providing gross proceeds of approximately $201 million. In October, we completed a follow-on public offering and issued 5,520,000 shares of common stock which were sold at a price of $25.50, resulting in total gross proceeds of $140.8 million.

We pride ourselves on the strength of our corporate culture, and Flexion has been repeatedly recognized as one of the best places to work in the Boston area. We believe this provides a real competitive advantage, enabling us to attract and retain genuinely outstanding professionals who are unquestionably critical to our success. Today those teams of talented individuals are advancing our commercial strategy with a passion and drive that I believe is unrivalled in the industry. We are in the enviable position of having the resources needed to execute a world-class commercial launch which will establish a strong foundation for ZILRETTA in 2018 and position it for success for years to come. This is only possible because of you, our shareholders.



On behalf of the patients we serve, thank you for your invaluable support.

Michael D. Clayman, MD

Michael D. Clayman, MD
President and CEO

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

FORM 10-K

(MARK ONE)

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

For the fiscal year ended December 31, 2017

or

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

For the transition period from to

Commission file number 001-36287

Flexion Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-1388364**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
10 Mall Road, Suite 301 Burlington, Massachusetts	**01803**
(Address of principal executive offices)	**(Zip Code)**

(781) 305-7777
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	**The NASDAQ Stock Market LLC**

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant based on the last reported sales price of the common stock on June 30, 2017 was approximately $557,701,832.

The number of outstanding shares of the registrant's common stock as of March 1, 2018 was 37,619,452.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2018 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant's fiscal year ended December 31, 2017.

FLEXION THERAPEUTICS, INC.
FORM 10-K—ANNUAL REPORT
For the Fiscal Year Ended December 31, 2017

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PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or this Annual Report, contains "forward-looking statements"— that is, statements related to future, not past, events—as defined in Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that reflect our current expectations regarding our future development activities, results of operations, financial condition, cash flows, performance and business prospects, and opportunities, as well as assumptions made by, and information currently available to, our management. Forward-looking statements include any statement that does not directly relate to a current or historical fact. We have tried to identify forward-looking statements by using words such as "believe," "may," "could," "will," "estimate," "continue," "anticipate," "intend," "seek," "plan," "expect," "should," or "would." Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: we have incurred significant losses since our inception and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability; we have generated limited revenue from ZILRETTA®, and have not received regulatory approval for any other product candidates; we may require additional capital prior to completing development and commercializing any of our product candidates in development; we may be unable to successfully commercialize ZILRETTA or any of our other product candidates; we rely on third parties to manufacture and conduct the clinical trials of ZILRETTA and our development-stage product candidates, which could limit our commercialization efforts or delay or limit their future development or regulatory approval; we may be unable to adequately maintain and protect our proprietary intellectual property assets, which could impair our commercial opportunities; and other risks detailed below in "Item 1A. Risk Factors."

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

Item 1. Business

Unless the content requires otherwise, references to "Flexion," "Company," "we," "our," and "us," in this Annual Report refer to Flexion Therapeutics, Inc. and our subsidiary, Flexion Therapeutics Securities Corporation.

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, or OA, a type of degenerative arthritis. On October 6, 2017, the U.S. Food and Drug Administration, or FDA, approved ZILRETTA® (triamcinolone acetonide extended-release injectable suspension), as the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA pain of the knee. ZILRETTA is a non-opioid therapy that employs our proprietary microsphere technology to provide pain relief over 12 weeks. We established a full field sales force of Musculoskeletal Business Managers (MBMs) following ZILRETTA's approval. The MBMs were trained, certified and deployed in the field as of November 20, 2017, when they began the process of informing and educating prescribing clinicians about ZILRETTA.

ZILRETTA combines a commonly administered steroid, triamcinolone acetonide, or TA, with poly lactic-co-glycolic acid, referred to as PLGA, delivering a 32 mg dose of TA to provide extended therapeutic concentrations in the joint and persistent analgesic effect. Both the magnitude and duration of pain relief provided by ZILRETTA in clinical trials were clinically meaningful with the magnitude of pain relief amongst the largest seen to date in OA clinical trials. ZILRETTA is not intended for repeat administration, as the efficacy and safety of repeat administration of ZILRETTA have not been evaluated. The overall frequency of treatment-related adverse events in these trials was similar to those observed with placebo and no drug-related serious adverse events were reported.

Based on the strength of our pivotal and other clinical trials, we believe that ZILRETTA represents an important new treatment option for the millions of patients in the U.S. who are in need of safe and effective extended relief from OA knee pain. ZILRETTA is uniquely distinguished by the following attributes:

- in the Phase 3 trial,
  - statistically significant pain relief against placebo (saline) as measured by the weekly mean of the Average Daily Pain, or ADP, score:
    - demonstrated at week 12, the primary endpoint, a p-value of <0.0001, 2-sided, with benefits extending through week 16; and
    - at each week beginning at week 1 and continuing through week 12 nearly 60% of patients reported no pain or mild pain;
  - statistically significant change from baseline as compared to placebo in weekly ADP intensity score through week 12 as measured by the area under effect curve ($p<0.0001$) (demonstrating a 50% reduction from baseline);
  - numeric improvement when compared with placebo and immediate-release TA at each time point through 12 weeks on exploratory measures – WOMAC A (pain), WOMAC B (stiffness) and WOMAC C (function) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale;
  - reduced rescue medicine consumption compared with placebo and immediate-release TA (exploratory endpoint); and
  - was superior to placebo, but the difference between ZILRETTA and immediate-release TA as measured by ADP was not statistically significant;
- an acceptable safety profile with side effects similar to placebo;

- statistically significant ($p<0.05$, 2-sided) reduction in the rise of blood glucose compared to that observed following immediate-release TA injection in patients with Type 2 diabetes who also have knee OA as measured by change in average blood glucose from baseline to 72 hours post injection; and
- persistent concentrations of drug in the joint.

In summary, ZILRETTA has demonstrated significant, durable relief for OA knee pain and, as such, addresses an important unmet need among patients, physicians and healthcare payers. We believe that ZILRETTA has the potential to be prescribed as a first-line IA medicine for OA knee pain.

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 more than 30 million Americans, and these numbers are expected to grow as a result of aging, obesity and sports injuries. 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 total joint arthroplasty, or TJA.

Because there is no cure for OA, controlling pain and delaying surgery are the primary goals of prescribing clinicians. Oral drugs, such as non-steroidal anti-inflammatory drugs, or NSAIDs, including COX II inhibitors, and serotonin and norepinephrine reuptake inhibitors, or SNRIs, as well as topical NSAIDs, are used to treat early-stage OA pain but have limited effect 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 well-tolerated, but they leave the joint rapidly and often fail to produce or maintain clinically meaningful pain relief. Physicians may prescribe opioids, which in addition to the serious risk of addiction and abuse, have numerous serious side effects including respiratory depression, hypotension, constipation, cardiac events and, increasingly, deaths from unintentional overdose. As a result of these limitations, many OA patients experience persistent and worsening pain, which often culminates in the decision to have 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.

According to IQVIA, in 2016 approximately 5 million patients in the United States received an IA injection treatment for knee OA with approximately 4.3 million of these patients being treated with immediate-release steroids. Furthermore, despite negative guidance from prominent medical societies, including the American Academy of Orthopedic Surgeons and Osteoarthritis Research Society International that hyaluronic acid (HA) is an ineffective treatment for knee OA, and the growing number of payers that no longer reimburse for the entire class of HA products, HA sales in the United States were approximately $977 million in 2017, with a cost per treatment ranging from $430 to $1,300. Our market research indicates that, given the limitations of immediate-release steroids and HA, physicians are open to new treatment options which can provide their patients with extended pain relief.

Our pipeline includes FX101 and FX201. FX101 is a PLGA-based extended-release formulation of fluticasone, a well-established corticosteroid, which aims to provide at least six months of pain relief from OA of large joints. FX101 is a pre-clinical stage program. The results of our ongoing and planned early studies will inform our decision on the next steps of the development process. FX201 is a gene therapy candidate designed to stimulate the production of an anti-inflammatory protein, interleukin-1 receptor antagonist (IL-1Ra), with the goal of providing at least one year of pain relief from OA of the knee. Based on its mechanism of action, we believe FX201 also has the potential to possibly arrest disease progression. FX201 is also a pre-clinical stage program, and subject to positive data from our ongoing and planned early studies and the initiation and successful completion of Good Laboratory Practice (GLP) toxicology studies, we plan to file an Investigational New Drug Application (IND) in 2019.

We have worldwide commercialization rights for ZILRETTA and our product candidates, FX101 and FX201. 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 ZILRETTA. 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. In addition, we own or have rights to various trademarks, copyrights and trade names used in our business, including FLEXION™ and ZILRETTA®. Our logos and trademarks are the property of Flexion Therapeutics, Inc. All other brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsement or sponsorship of us, by the trademark or trade dress owners.

Our Strategy

Our goal is to cost-effectively develop and commercialize novel, locally administered medicines that can safely and effectively address significant unmet medical needs. The principal elements of our strategy include the following:

- ***Focus initially on novel biopharmaceutical candidates that provide long-lasting analgesia locally while minimizing the potential for systemic side effects.*** We are currently focusing on anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with OA. Many OA patients will eventually require IA injection therapies to control their pain as the disease progresses. Immediate-release IA steroids leave the joint rapidly and typically fail to confer pain relief of sufficient magnitude or duration. Since, by medical practice, steroids are not injected more frequently than every three months, patients can experience a recurrence in, or increasing, pain during that time. While some patients may obtain benefit from HA injections, they are not recommended for OA pain by the American Academy of Orthopaedic Surgeons (AAOS) based on a lack of efficacy. ZILRETTA was specifically designed to provide persistent and effective OA pain relief with an acceptable safety profile. It is formulated using our proprietary PLGA-based microsphere technology to slowly and continuously release drug in the joint for over 12 weeks, avoiding significant plasma concentrations of drug.
- ***Build a robust pipeline of additional locally administered therapies to address musculoskeletal conditions.*** We seek to build a pipeline of additional product candidates and to mitigate development risk by selecting product candidates that have at least demonstrated efficacy in animal models of disease or have validated mechanisms of action. In 2017, we established the Flexion Innovation Lab in Woburn, Massachusetts to support our development activities, including our two active pipeline programs, FX101 and FX201. We aim to further build the pipeline through internal development and the selective addition of external opportunities.
- ***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 effectively commercialize ZILRETTA in the United States with our own sales and marketing organization, and thereby retain more of the commercial value of this product. We established a full field sales force of MBMs following ZILRETTA's approval on October 6, 2017. The MBMs were trained, certified and deployed in the field as of November 20, 2017, when they began the process of informing and educating prescribing clinicians about ZILRETTA. While we believe that the United States represents the most attractive market for ZILRETTA, we continue to evaluate opportunities and potential partnerships to develop and commercialize ZILRETTA in territories outside the United States where we believe there is the potential for value-based pricing and reimbursement.

Osteoarthritis

Overview

OA, also referred to as degenerative joint disease, is the most common joint disease in the United States according to the U.S. Centers for Disease Control, affecting more than 30 million Americans. These numbers are only expected to grow in the years ahead as a result of aging, obesity and sports injuries.

- With the U.S. population between the ages of 45 and 64 having grown 32% from 2000 through 2010 and accounting for 26% of the total population, we expect changing demographics will likely contribute to a growing number of OA patients.
- Approximately 35% of U.S. adults are obese, which increases the risk of developing OA.
- Knee injury is common, particularly amongst young athletes, and increases the risk of developing OA later in life by more than fivefold.
- OA accounts for over $185 billion of annual healthcare expenditures, which does not include loss of productivity costs.
- As reported in an Osteoarthritis Research Society International (OARSI) white paper (Nov 2016), “subjects in the US with symptomatic radiographic knee OA were 23% more likely to die prematurely than people free from OA independent of age, sex, and race”.

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

OA is a progressive disease for which there is no cure. As a result, current treatments are intended to address the symptoms of OA, in particular, relief of pain and improvement in functional status. The therapeutic regimen for OA becomes increasingly invasive with progression of the disease, culminating, in many cases, in TJA. In addition, because patients are being diagnosed with OA earlier in their lives, many patients will require repeat TJAs. Because the decision to have TJA is based in large part on intractable pain and functional impairment, we believe that the development of new therapies which can meaningfully and durably relieve pain and improve function could potentially delay TJA.

Common Treatments for OA

In early-stage disease, treatment begins with non-pharmacologic therapy including exercise, weight control and physical therapy. As the disease progresses, physicians prescribe pharmacologic therapy, beginning with acetaminophen and progressing to oral NSAIDs, including COX II inhibitors, topical NSAIDs or SNRIs. Physicians may also treat OA pain with opioids, which are prescribed to approximately 50% of patients suffering from OA pain. However, they have very serious drawbacks and are generally considered to be a suboptimal therapy for chronic non-cancer pain, like that associated with osteoarthritis.

When non-pharmacologic therapy and oral pain medications prove inadequate, physicians typically transition patients to IA injections. Immediate-release steroids have historically served as the first line IA therapy, and when these no longer provide sufficiently durable pain relief, patients may progress to IA HA, a significantly more expensive therapy with only marginally greater effect than placebo. TA, the corticosteroid used in ZILRETTA, is amongst the most commonly prescribed IA corticosteroid injections.

Due to severe pain that can no longer be controlled therapeutically, many patients opt to have TJA, which is costly and painful. One of the most prevalent TJA procedures in the United States is total knee arthroplasty. Compared to existing drug therapy, total knee arthroplasty is very expensive, with average costs ranging between $25,000 and $50,000, and as many as 30% of patients are dissatisfied with the outcome of this procedure. The earlier a patient receives TJA, the more likely it is that the patient will need repeat replacement surgery in following years. In 2010, inpatient costs exceeded $13 billion per year in the United States for total knee arthroplasty alone

and based on some estimates the number of total knee arthroplasties is expected to increase six-fold to 3.5 million procedures per year between 2011 and 2030. Our own market research has indicated that healthcare payers would be willing to reimburse additional OA therapies that have the potential to delay the need for TJA.

Limitations of Common Treatments for OA

Oral therapies, such as NSAIDs, may offer adequate analgesia for early-stage OA pain, but they may be associated with serious side effects such as gastrointestinal bleeding, cardiovascular events and other adverse events. For example, SNRIs may have a role in worsening depression and the emergence of suicidality in certain patients. In addition to their serious side effects, oral drugs may provide limited pain relief and eventually can become insufficient to control OA pain for many patients as the disease progresses.

IA therapies, including immediate-release steroids and HA preparations, are generally well-tolerated but provide pain relief that is often insufficient or inadequate in duration. Historically, all IA steroid therapies approved for OA are immediate-release suspensions or solutions that leave the joint within hours to days, and they are rapidly absorbed systemically, which may result in undesirable side effects. For example, IA immediate-release steroid injections are associated with a rapid elevation of blood glucose in diabetics, which can be of clinical concern. While IA steroids demonstrate large initial analgesic effects relative to other therapies, as a result of leaving the joint quickly, IA steroids typically fail to confer pain relief of sufficient magnitude or duration. In addition, current clinical practice dictate that IA steroid suspensions not be administered more frequently than once every three months. Based on internal analysis, we believe approximately 44% of patients receiving IA immediate-release steroids are unsatisfied with the duration of benefit.

Despite U.S. sales of approximately $977 million in 2016 and 2017 sales estimated to exceed $1 billion, IA HA therapies, which are approved only for treatment in the knee, produce only marginally more effective pain relief than placebo and may have no discernible effect on a patient's ability to carry out their daily activities. In treatment guidelines for non-operative management of knee OA published in May 2013, the AAOS concluded that data from then-current published studies did not show clinically meaningful effectiveness for HA injections. As a result, the guidelines do not recommend HA treatment for symptomatic knee OA due to lack of efficacy and, most recently, certain insurance carriers are no longer providing policy coverage of HA.

While the consequences from the overuse and abuse of opioids are well-known, these powerful medicines are still commonly prescribed for OA related pain, despite the fact that they are not an effective treatment for this chronic condition. A recent study estimated that as many as 70% of patients who are prescribed a medicine for OA pain will receive an opioid, and we believe this is a reflection of the fact that physicians have so few effective treatment options. We believe that the growing societal awareness of the risks posed by opioids may make new treatment options attractive for patients and physicians seeking non-opioid alternatives. Beyond the significant concerns related to the potential for overuse, abuse and unintentional overdose, opioid use is also associated with a host of other serious side effects including, respiratory depression, hypotension, constipation, cardiac events and, increasingly, death.

The Flexion Extended-Release Technology

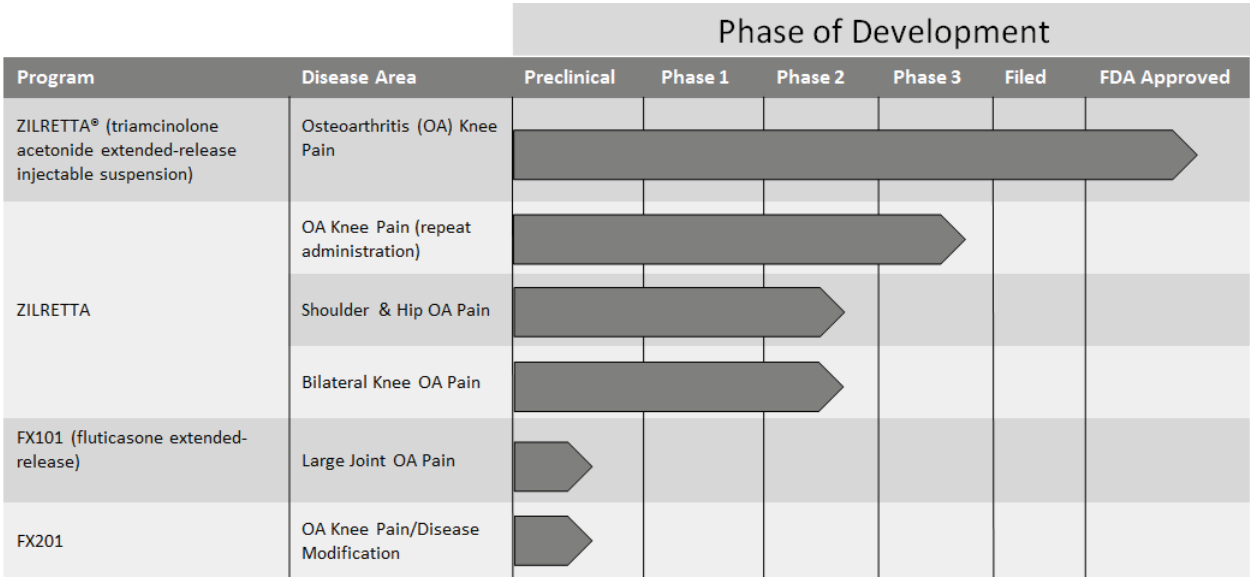
Our extended-release technology allows us to incorporate active pharmaceutical ingredients in PLGA microspheres. We believe we are the first company to administer PLGA microspheres into a human joint. PLGA is a proven extended-release delivery vehicle that is metabolized to carbon dioxide and water as it releases drug in the IA space and is used in other approved drug products and surgical devices. The technology is designed to enable novel formulations of pharmaceuticals by providing extended-release of drugs over time and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates. Key to the success of our IA therapies is the ability to maintain persistent concentrations of drug in the joint, while minimizing systemic exposure. Utilizing our PLGA microsphere technology, ZILRETTA is the first and only approved extended-release, IA therapy for patients confronting OA-related knee pain.

We believe ZILRETTA and our technology will be protected primarily through a combination of patents, trade secrets and proprietary know-how, and we intend to seek marketing exclusivity for any approved products. A composition of matter patent has been issued by the United States Patent and Trademark Office, or U.S. PTO, for

ZILRETTA, with a patent term into 2031. The U.S. PTO has also issued two patents directed at the methods of manufacturing and using ZILRETTA with patent terms into 2031. Considerable expertise and effort was required to carry out the large body of original work underlying the formulation of ZILRETTA, including experimenting with, and observing the effects of over 50 steroid and PLGA formulations. We believe our extensive know-how and trade secrets relating to the manufacturing process for ZILRETTA, including those that relate to precise pharmaceutical release profiles, represent a competitive advantage.

The Flexion Pipeline

Our pipeline strategy is to continue to study ZILRETTA in other areas and, if feasible, expand ZILRETTA's label to include additional indications and broaden its scope of administration, and build a robust pipeline of additional locally administered therapies to address musculoskeletal conditions, with an initial focus on OA.



FX101 (fluticasone ER)

FX101 utilizes our proprietary microsphere technology to create an extended-release formulation of fluticasone, a well-known corticosteroid, within a PLGA matrix. The approach builds on our deep experience and expertise in developing and commercializing microsphere-based, extended-release therapies. We are assessing whether FX101 holds the potential to deliver meaningful OA pain relief for at least six months. FX101 has been designed to provide sustained duration of analgesia after local administration of extended release formulation, while potentially minimizing systemic side effects. The results of our ongoing and planned early studies will inform our decision on the next steps of for the program.

FX201

FX201 is an IA gene therapy candidate which is designed to induce the local production of interleukin-1 receptor antagonist (IL-1Ra), an anti-inflammatory protein. Following injection of FX201, its genetic material is incorporated into local cells, and IL-1Ra is expressed in response to inflammation in the joint tissues. Inflammation is a known cause of pain, and chronic inflammation is thought to play a major role in the progression of OA. By persistently suppressing inflammation, FX201 has the potential to both reduce pain and possibly arrest disease progression. Based on preclinical data, we believe a single injection of FX201 could enable expression of IL-1Ra in an osteoarthritic joint for at least a year. Pending successful results from additional preclinical studies and our GLP toxicology studies, we intend to file an IND and initiate a proof-of-concept clinical trial in 2019. We acquired the rights to FX201 via a definitive agreement with GeneQuine Biotherapeutics GmbH, or GeneQuine, and have an exclusive license to the underlying intellectual property rights for human use of FX201 from Baylor College of Medicine.

ZILRETTA – FDA Approved Product for the Management of OA Knee Pain

Regulatory Developments

On October 6, 2017, ZILRETTA (triamcinolone acetonide extended-release injectable suspension) received approval from the FDA for the management of OA pain of the knee. ZILRETTA is the first and only approved extended-release, IA therapy for OA knee pain. It is a non-opioid medicine that employs our proprietary microsphere technology to provide proven pain relief over 12 weeks. The approval was based upon data from the pivotal Phase 3 clinical trial, a randomized, double-blind study which evaluated 486 patients at 37 centers worldwide.

ZILRETTA's label reflects its strong safety profile and states the most commonly reported adverse reactions (incidence ≥1%) in clinical studies included sinusitis, cough and contusions. We believe ZILRETTA's extended-release profile may also provide effective treatment for OA pain of the shoulder and OA pain of the hip and have initiated a clinical trial to investigate it in these joints.

Summary of Active and Key Completed Clinical Trials

Prior to approval, we completed seven clinical trials evaluating ZILRETTA (also known as FX006) against either immediate release triamcinolone acetonide crystalline suspension (TAcs), placebo (saline), or both in patients with OA of the knee. In total, 424 patients were treated with a single IA injection (32mg) of ZILRETTA in those trials.

We currently have three active ZILRETTA clinical trials:

- In February 2017, we initiated an open-label, Phase 3b trial to evaluate the safety of repeat administration of ZILRETTA in patients with OA of the knee. The 208 study participants received an initial IA injection of ZILRETTA on day 1 followed by evaluation at weeks 12, 16, 20 and 24 to determine their eligibility for a second IA injection of ZILRETTA. Participants who received a repeat administration of ZILRETTA will be followed for a total of 52 weeks after the initial injection, regardless of when the second injection was administered. At specified times throughout the study, participants undergo physical examinations, knee assessments and X-rays.

  In January 2018, we reported initial data showing that of the 205 evaluable patients, 95% (195/205) experienced clinical benefit by week 12 following the initial injection of ZILRETTA, as determined by self-assessment and with the agreement of their physician. In the trial, 92% (179/195) of eligible patients received a second dose of ZILRETTA between weeks 12 and 24. The full study results are expected in the third quarter of 2018.

- In December 2017, we enrolled the first patient in a trial to evaluate the pharmacokinetics and safety of concurrent injections of ZILRETTA in patients with bilateral OA of the knee. The open-label, Phase 2 study is randomized (1:1) with patients receiving either two IA injections of 32 mg ZILRETTA or two 40 mg injections of immediate-release TA. The study was fully enrolled with 24 patients in January 2018 and results are anticipated in the second quarter of 2018.

- Also in December 2017, we announced a study to evaluate the pharmacokinetics and safety of ZILRETTA in patients with OA of the shoulder or hip. Known as the "SHIP" study, patients are randomized (1:1) to receive either a single IA injection of 32 mg ZILRETTA or 40 mg immediate-release TA. The open-label, Phase 2 trial is expected to recruit approximately 48 patients in total, comprised of 24 patients with OA of the shoulder and 24 patients with OA of the hip. We expect to report top-line results of the study in the second half of 2018.

Key Completed Studies

In November 2016, we announced top-line results from a clinical trial to assess the effects of ZILRETTA on the blood glucose levels of adults with OA of the knee who also have Type 2 (adult) diabetes. The objective of the double-blind, randomized, parallel group, single-dose study was to examine if ZILRETTA had effects on blood glucose levels that differ from immediate-release TA. Investigators from seven study sites enrolled 33 patients,

randomized 1:1 to receive a single IA injection of 32 mg ZILRETTA or 40 mg immediate-release TA. Blood glucose levels were evaluated for a total of three weeks (one week prior to injection and two weeks post injection) using a continuous glucose monitoring device. Patients returned for follow-up visits at day 8, day 15 and day 43 (week 6). The primary endpoint compared the change in average glucose values from the period of 72 hours before to the period of 72 hours after injection with ZILRETTA versus immediate-release TA. The data demonstrate that ZILRETTA is associated with a statistically significant (p-value of <0.05, 2-sided) and clinically relevant reduction in the rise of blood glucose compared to that observed following TA injection in patients who also have knee OA. In clinical trials, the "p-value" is the probability that the result was obtained by chance. For example, a "p-value" of less than 0.10 (or p<0.10) would indicate that there is a less than 10% likelihood that the observed results could have happened at random. By convention, a "p-value" that is less than 0.05 is considered statistically significant.

In February 2016, we announced top-line results from our pivotal ZILRETTA study, a Phase 3 clinical trial that evaluated 486 patients with moderate to severe OA knee pain. This Phase 3 trial randomized patients 1:1:1 to ZILRETTA 32 mg, immediate release TA 40 mg or placebo (saline) injection. It met its primary endpoint at week 12, demonstrating highly statistically significant (p<0.0001) pain relief against placebo (saline). In addition, ZILRETTA achieved a statistically significant change from baseline as compared to placebo in weekly ADP intensity score through week 12 as measured by the area under effect curve (p<0.0001) (demonstrating a 50% reduction from baseline). It also delivered persistent analgesia against placebo in this trial at each of weeks 1 through 16. Results showed ZILRETTA was superior to placebo on ADP, however a secondary exploratory analysis showed a numeric but not statistically significant difference between ZILRETTA and immediate-release TA for the change from baseline at Week 12 in weekly mean ADP.

In pre-specified exploratory analyses, compared to placebo and immediate-release TA, ZILRETTA also demonstrated numeric improvement at each measured time point through 12 weeks on the Western Ontario and McMaster Universities Osteoarthritis Index, commonly referred to as WOMAC®, subscales for WOMAC A (pain), WOMAC B (stiffness) and WOMAC C (function) and the validated Knee injury and Osteoarthritis Outcome Score, commonly referred to as KOOS, quality of life, or QOL, subscale. WOMAC is a validated, widely accepted questionnaire (in our surveys over 90% of treating orthopedists are familiar with WOMAC whereas only approximately 10% are familiar with the Numeric Rating Scale which forms the basis for the ADP determination) used by healthcare professionals to specifically evaluate the condition of patients with OA of the knee and hip, including pain, stiffness, and physical function of the joints and the KOOS QOL subscale is a validated questionnaire used by healthcare professionals to evaluate the extent to which knee symptoms compromise a patient's quality of life.

The frequency of treatment-related side effects in this study was comparable across all treatment arms. No drug-related serious adverse events were observed and no patients treated with ZILRETTA were discontinued from the study due to a treatment-related side effect. We have submitted the results, which have been accepted, for publication in a peer-reviewed medical journal.

Manufacturing

We believe that the multifaceted nature of PLGA drug product manufacturing and the limited number of capable contract manufacturing companies that offer PLGA drug product manufacturing creates a competitive advantage. The technology is designed to enable novel formulations of pharmaceuticals by providing extended-release of drugs over time and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates.

We utilize contract manufacturers to produce the drug substances and drug products used in ZILRETTA. Manufacture of PLGA microspheres is a complex process and there are a limited number of contract manufacturing sites with PLGA experience. Our proprietary injectable IA extended-release technology allows us to incorporate pharmaceuticals in PLGA microspheres, such as TA, in the case of ZILRETTA, and fluticasone, in the case of FX101, as well as potentially other product candidates. Following extensive development programs, we have established that a single injection of ZILRETTA sustains local concentrations of TA in the joint for several months. The ZILRETTA microsphere PLGA formulation has gone through numerous iterations and has been optimized to release the drug over an extended period of time. In developing this unique combination of manufacturing process and formulation, we have established numerous trade secrets that relate to precise pharmaceutical release profiles.

The active pharmaceutical ingredient in ZILRETTA, TA, is manufactured and supplied by Farmabios SpA in accordance with current good manufacturing practice, or cGMP, standards. This supplier is subject to regular inspections by the FDA. The PLGA material used in the manufacture of ZILRETTA is supplied by Evonik Corporation, or Evonik. In November 2016, we entered into a Supply Agreement with Evonik for the purchase of PLGA for clinical and commercial supply of ZILRETTA. The initial term of the Supply Agreement is until July 2021 and will renew for two successive two year terms upon mutual written consent by both parties. Under the Supply Agreement, we are bound to purchase PLGA from Evonik at certain minimum purchase amounts, which decrease over time, and at a specified price per gram, subject to adjustment from time to time, including due to changes in price indices and in the event the initial term of the Supply Agreement is extended. Upon termination of the Supply Agreement (other than termination due to the bankruptcy of either Evonik or us) we are obligated to pay the costs associated with the binding supply forecast provided to Evonik.

In August 2015, we entered into a Manufacturing Agreement with Patheon U.K. Limited, or Patheon, for the manufacture of clinical and commercial supplies of ZILRETTA finished drug product. In connection with the agreement, Patheon undertook certain technical transfer activities and construction services to prepare its United Kingdom facility for the manufacture of ZILRETTA in dedicated manufacturing suites. The initial term of our Manufacturing Agreement with Patheon is until October 2027. We may terminate this agreement upon one month's notice if a regulatory authority causes the withdrawal from, or halts development of, ZILRETTA (in either case for reasons outside our reasonable control) in the United States or any other market that represents 80% of our overall sales. We may also terminate this agreement at any time for convenience by providing 24 months' notice. Either we or Patheon may terminate this Agreement in the event of (a) an unremedied material breach or bankruptcy of the other party, (b) if a material force majeure event remains uncured for a period of more than 90 days and (c) the granting of a permanent injunction to a third party claiming intellectual property infringement of ZILRETTA in the United States or UK. Upon termination of this agreement, we are obligated to pay for the costs associated with the removal of our manufacturing equipment and for Patheon's termination costs up to a specified maximum amount.

Commercial Strategy

We have established a commercial infrastructure designed to drive the adoption and sales of ZILRETTA with the approximately 9,500 prescribers who treat approximately 70% of patients diagnosed with OA pain of the knee who receive an IA treatment. Of these prescribers, approximately 80% are orthopedists and rheumatologists. We hired our full complement of MBMs immediately following ZILRETTA's approval on October 6, 2017. The MBMs were trained, certified and deployed in the field as of November 20, 2017, when they began the process of informing and educating prescribing clinicians about ZILRETTA. We distribute ZILRETTA solely through a limited network of contracted party specialty distributors and one specialty pharmacy. While we believe that the United States represents the most attractive market for ZILRETTA, we continue to evaluate opportunities and potential partnerships to develop and commercialize ZILRETTA in territories outside the United States where we believe there is the potential for value-based pricing and reimbursement.

Of patients who are treated for OA pain of the knee with an IA injection, we estimate that 55% receive IA injections from orthopedic surgeons. Approximately 8% of patients receive IA injections from physical medicine and rehabilitation (PM&R) specialists and rheumatologists, and approximately 7% of patients are treated by sports medicine specialists. Approximately 12% are treated by primary care physicians. The remaining 18% of IA injections are administered by a wider array of providers, including physician's assistants and nurse practitioners.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. The large size and expanding scope of the pain market makes it an attractive therapeutic area for biopharmaceutical businesses. Our potential competitors include pharmaceutical, biotechnology, medical device and specialty pharmaceutical companies. Several of these companies have robust drug pipelines, readily available capital and established research and development organizations. We believe our success will be driven by our ability to develop and commercialize treatment options that make a meaningful difference for patients with musculoskeletal conditions, beginning with OA.

The key competitive factors that could affect the success of ZILRETTA's launch are likely to be efficacy, safety, price and the availability of reimbursement from government and other third-party payers. Immediate-release steroids and HA are currently the two marketed classes of IA products that compete directly with ZILRETTA.

Also on the market are platelet rich plasma injections, but these require on site preparation from blood drawn from the patient, have generated questionable efficacy in controlled clinical trials, and we believe they are unlikely to be a broadly embraced therapeutic option for OA patients. Because platelet rich plasma is a therapy derived from the individual patient's blood, it does not require and has not received FDA review or approval. For that reason, it is generally not reimbursed by payers and patients must pay out of pocket to receive this therapy.

In addition to marketed IA medications for OA, other companies have OA medical devices and product candidates in advanced stages of clinical development. These IA products include:

- Anika Therapeutics, Inc.'s Cingal®, which is a mixture of Anika's Monovisc and a low dose of a commonly used immediate-release steroid. Anika filed a Pre-Market Application with the FDA for Cingal based on a single pivotal clinical trial. In December 2015, Anika announced that due to the steroid component of the product, it will need to file this product candidate under an NDA.
- Halyard Health, Inc.'s COOLIEF, which is a Cooled Radiofrequency (RF) device used to ablate sensory nerves. In April 2017, Halyard received FDA clearance for COOLIEF to treat patients with chronic moderate to severe OA knee pain and has a trial underway comparing COOLIEF to HA injection (Synvisc-One® (hylan G-F 20)). The estimated primary completion date is Q2 2019.
- Actavis plc/Hanmi Pharmaceuticals Co., Ltd.'s HA product Hyalrheuma, which is an HA preparation.
- TissueGene, Inc.'s Invossa™, which is a combination of human allogeneic chondrocytes and TGF-β1 transfected allogeneic chondrocytes. We believe Invossa is planning to initiate Phase 3 clinical trials in the U.S. in 2018.
- Ampio Pharmaceuticals, Inc.'s Ampion™, which is a derivative of human serum albumin, is described as having anti-inflammatory properties, and is formulated for immediate-release. Ampio stated that Ampion is in Phase 3 development and has not announced a timeline for potentially submitting a BLA.
- Centrexion Therapeutics Corporation's CNTX-4975, which is a synthetic, ultra-pure injection of trans-capsaicin. In February 2018, Centrexion announced that the first patient was treated in a Phase 3 clinical trial for CNTX-4975, and according to clinicaltrials.gov, the study is expected to complete in February 2020.
- We believe that programs such as Orthotrophix's TPX-100, Merck Serono's sprifermin FGF-18, Abbvie's ABT-981, Menarini's MEN16132, Dong-A's DA-5202, Ember Therapeutics BMP-7, Samumed's SM04690, and Allergan, Inc.'s botulinum toxin, have not yet entered Phase 3 clinical trials.
- Eupraxia's EP-104 is a Phase 1 therapy for knee OA that combines an unapproved carrier technology (Plexis) with a steroid (fluticasone).
- Taiwan Liposome Company's TLC599, which is a liposomal formulation of dexamethasone sodium phosphate. TLC599 is currently in Phase 2 clinical development.
- Stem cell approaches to OA are being explored, but these are earlier in development, bear significant technical risks and it remains to be seen how applicable they will be to the treatment of OA.
- A number of investigational nerve growth factor antibodies are in development. Regeneron's fasinumab and Pfizer and Eli Lilly's tanezumab are both in Phase 3 development.

Intellectual Property/Patents and Proprietary Rights

Intellectual Property and Exclusivity

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

Patents and Patent Applications

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

As of January 31, 2018, we owned three U.S. issued patents, two pending U.S. applications, and counterpart foreign patents and patent applications, all directed to ZILRETTA. One issued U.S. patent directed to ZILRETTA relates to its composition of matter and has an expiration date in 2031. A second issued U.S. patent directed to ZILRETTA relates to methods of manufacturing ZILRETTA and has an expiration date in 2031. A third issued U.S. patent directed to ZILRETTA relates to methods of using ZILRETTA and has an expiration date in 2031. The ZILRETTA composition of matter patent is the result of several unique discoveries relating to a narrow drug load specification, a certain release profile of polymers, specific polymer weights and ratios and clinical efficacy observed within a dose-range. The patents directed to ZILRETTA's composition of matter and methods of using ZILRETTA are listed in the FDA Orange Book. The two pending U.S. applications directed at ZILRETTA, if resulting in issued patents, could provide additional claims expiring in 2031 and 2037.

During 2017, we expanded our patent portfolio with additional granted patents related to ZILRETTA outside the United States. In 2017, we had patents granted in Australia, Canada, China, Indonesia and Singapore further expanding to the scope of the previously granted patents in Australia, Japan, New Zealand, Saudi Arabia, South Africa, Taiwan and Ukraine. Generally, these foreign patents are directed to compositions of matter for ZILRETTA, methods of manufacturing ZILRETTA and/or methods of using ZILRETTA, and are similar in scope to the protection in the United States described above. In addition, we have applications pending in Europe and additional countries throughout the world directed to ZILRETTA and related inventions.

We have also exclusively licensed issued patents, owned by SwRI, directed to our proprietary microsphere manufacturing technology used in the production of ZILRETTA. These patents are scheduled to expire in 2025.

As of January 31, 2018, we also have one pending Patent Cooperation Treaty patent application directed to the formulation comprising our FX101 product candidate, as well as one pending U.S. provisional patent application related to FX101. In addition, we have exclusively licensed patents and patent applications owned by Baylor College of Medicine for human applications directed to our FX201 product candidate. The Baylor patents are issued in China and Europe, with expiry dates in 2032, and pending in Australia, Eurasia, India, Japan and the U.S. Finally, we have other patent applications directed to formulations and/or uses of compounds that are not directly relevant to ZILRETTA or our current programs in development.

Trade Secrets and Proprietary Information

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

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

Intellectual Property Agreements

Southwest Research Institute Manufacturing® (SwRI) License

In July 2014, we executed an exclusive worldwide licensing agreement with SwRI to utilize proprietary microsphere manufacturing technologies for production of our extended-release drug candidates, including ZILRETTA. The SwRI technologies employ a uniquely controlled and continuous atomizing technology that facilitated scale-up of commercial supply. This exclusive agreement provides for an expanded field of use in a variety of musculoskeletal disorders, as well as broader polymer and steroid ranges, which offers the flexibility to potentially explore different doses, disease indications, and drug-PLGA combinations. We have no further payment obligations following the amendment executed by the parties in February 2017 and the license remains in effect through patent term expiry.

FX201 Related Agreements

In December 2017, we entered into a definitive agreement with GeneQuine to acquire the global rights to FX201. As part of the asset purchase transaction with GeneQuine, we made an upfront payment of $2 million. We may also be required to make additional milestone payments during the development of FX201, including up to $8.7 million through Phase 2 proof of concept (PoC) and, following successful PoC, up to an additional $54 million in development and global regulatory approval milestone payments. As part of the transaction, we became the direct licensee of certain underlying Baylor College of Medicine (Baylor) patents and other proprietary rights related to FX201 for human applications. The Baylor license agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patent and other proprietary rights directly related to FX201, with a similar non-exclusive license to certain Baylor intellectual property rights that are not specific to FX201. The license agreement with Baylor includes a low single-digit royalty on net sales of FX201 and requires us to use reasonable efforts to develop FX201 according to timelines set out in the license agreement. In December 2017, we also entered into a Master Production Services Agreement with SAFC Carlsbad, Inc., a part of MilliporeSigma, for the manufacturing of pre-clinical and initial clinical supplies of FX201.

Termination of FX007 Agreement

On March 5, 2018, we sent AstraZeneca AB notice that we are terminating the Out-License Agreement between the parties, dated as of September 13, 2010, related to our FX007 pyrazole formulation development program. Pursuant to the terms of the Out-License Agreement, the termination will be effective three months after our delivery of the notice. As previously disclosed, we have discontinued internal development of FX007. Upon termination of the Out-License Agreement, our rights pertaining to FX007 will revert to AstraZeneca and our milestone, royalty and patent maintenance obligations under the agreement will cease.

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing and commercializing.

U.S. Biopharmaceutical Product Development Process

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

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, or other applicable regulations;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's laws and regulations pertaining to the conduct of human clinical studies, collectively referred to as Good Clinical Practices, or GCP, and according to the International Council for Harmonization, or ICH, GCP guidelines, to establish the safety and efficacy of the proposed biopharmaceutical product for its intended use;
- submission to the FDA of an NDA for a proposed new drug product or a Biologics License Application, or BLA, for a biological product;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biopharmaceutical product is produced and tested to assess compliance with the FDA's cGMP requirements, to assure that the facilities, methods and controls are adequate to preserve the biopharmaceutical product's identity, strength, quality and purity;
- potential FDA audit of the non-clinical and clinical trial sites that generated the data in support of the NDA or BLA; and
- FDA review and approval or licensure of the NDA or BLA.

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

Before testing any compounds with potential therapeutic value in humans, the biopharmaceutical product candidate enters the nonclinical testing stage, also referred to as preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the biopharmaceutical product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of the IND application. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biopharmaceutical product candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the biopharmaceutical product candidate to healthy subjects or patients with the target disease under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the

parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA's regulations which reflect the ICH GCP requirements. Further, each clinical trial must be reviewed and approved by an IRB at, or servicing, each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

Clinical trials for biopharmaceutical product candidates are typically conducted in humans in three sequential phases that may overlap. In Phase 1 clinical trials, the biopharmaceutical product is initially introduced into healthy human subjects and tested for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion and clinical pharmacology. In Phase 2 clinical trials, the biopharmaceutical product is evaluated in a limited patient population to identify possible adverse side effects and safety risks, evaluate preliminarily the efficacy of the biopharmaceutical product for specific targeted indications and determine dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease. Once a biopharmaceutical product shows evidence of effectiveness and is found to have an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials are undertaken to more fully evaluate clinical outcomes. In Phase 3 clinical trials, the biopharmaceutical product is administered to an expanded patient population in adequate and well-controlled trials to generate sufficient data to statistically confirm the efficacy and safety of the biopharmaceutical product for approval, to establish the overall risk-benefit profile of the biopharmaceutical product and to provide adequate information for its labeling.

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

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

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

FDA Review and Approval Processes

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

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing and may request additional information rather than accepting the application for filing. Once the application is accepted for filing, the FDA begins an in-depth review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 12 months after submission for a new molecular entity in which to complete its initial review and respond to the applicant, and eight months for a priority review application. In addition, the FDA has 10 months after submission of an NDA for a non-new molecular entity in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority review NDA. The FDA does not always meet its PDUFA goal dates for review of standard and priority review applications. The review process and the PDUFA goal date may be extended by additional three month review periods whenever the FDA requests or the sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

The FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel biopharmaceutical products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the biopharmaceutical product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Before approving an NDA or BLA, the FDA will typically inspect the facilities at which the product is to be manufactured. When an inspection is undertaken, the FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA will typically inspect one or more clinical sites to assure compliance with FDA regulations regarding conduct of clinical trials for the product's trials. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in a complete response letter to the applicant and often will request additional testing or information.

If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, or withdraw the application.

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

Post-Approval Requirements

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

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

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any biopharmaceutical products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payers.

In the United States, third-party payers include federal and state government payer programs, including Medicare and Medicaid, managed care organizations, private health insurers and other organizations. The process for determining whether a third-party payer will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the third-party payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. In addition, our biopharmaceutical products may not be considered medically necessary or cost-effective.

A third-party payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a drug product does not ensure that other payers also will provide coverage or an adequate reimbursement rate for the drug product. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payer interest. We expect that the pharmaceutical industry will continue experiencing pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third-party payers are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

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

Additionally, in order to be eligible for certain federal agencies and grantees to purchase ZILRETTA, or to have it paid for with federal funds under the Medicaid and Medicare Part B programs, we participate in the Department of Veterans Affairs (VA), Federal Supply Schedule (FSS) pricing program. We are obligated through the FSS program to sell ZILRETTA through a FSS contract and charge a price that is no higher than the statutory Federal Ceiling Price (FCP) to four federal agencies (VA, U.S. Department of Defense, Public Health Service, and Coast Guard). The FCP is based on the non-federal Average Manufacturer Price (Non-FAMP), which we will need to calculate and report to the VA on a quarterly and annual basis. These obligations contain extensive disclosure and certification requirements.

Healthcare Reform

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

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

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively PPACA, was enacted as a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of PPACA of importance to our potential drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program, created under Section 6002 of PPACA, and its implementing regulations, that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to Centers for Medicare and Medicaid Services, or CMS, information related to "payments or other transfers of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and that applicable manufacturers and applicable group purchasing organizations report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for non-compliance;
- an FDA-approval framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to numerous provisions of PPACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the Health Care Reform Law or otherwise circumvent some of the requirements for health insurance mandated by PPACA. Further, The Tax Cuts and Jobs Act of 2017, signed into law on December 22, 2017, removed the individual mandate starting in 2019 that required individuals to have insurance or face a penalty. Additionally, on January 23, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees. Congress may consider additional legislation to repeal or replace other elements of PPACA.

We expect that PPACA reform, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, as well as additional downward pressure on the price that we receive for any approved product, including ZILRETTA. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices, including at the federal level several recent U.S. Congressional inquiries and proposed bills designed to, among other things, increase drug pricing transparency, reduce the cost of drugs under Medicare, review relationships between pricing and manufacturer patient assistance programs, and reform government program drug reimbursement methodologies. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payers. At the state level, legislatures have

increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize ZILRETTA and any future products for which we receive regulatory approval.

Accelerated Approval for Regenerative Advanced Therapies

As part of the 21st Century Cures Act, Congress recently amended the FDCA to create an accelerated approval program for regenerative advanced therapies, which include cell therapies, gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Regenerative advanced therapies do not include those gene therapies, human cells, tissues, and cellular and tissue based products regulated solely under section 361 of the Public Health Service Act and 21 CFR Part 1271. The new program is intended to facilitate efficient development and expedite review of regenerative advanced therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. A drug sponsor may request that the FDA designate a drug as a regenerative advanced therapy concurrently with or at any time after submission of an IND. The FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A NDA or BLA for a regenerative advanced therapy may be eligible for priority review or accelerated approval through surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative advanced therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

Other U.S. Healthcare Laws and Compliance Requirements

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

The federal Anti-Kickback Statute prohibits any person or entity, including a prescription drug manufacturer (or a party acting on its behalf), from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce or reward either the referral of business, or the furnishing, recommending, or arranging for the purchase, lease or order of a good, facility, item or service, for which payment may be made under a federal healthcare program, such as the Medicare or Medicaid program. This statute has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers, among others, on the other. The term “remuneration” has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value.

Federal false claims and false statements laws, including the federal False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for items or services, including drugs, for payment to, or approval by, a federal healthcare program, including Medicare or Medicaid. The qui tam provisions of the False Claims Act allow a private individual to bring a civil action on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payer, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government's and/or pharmaceutical industry's voluntary compliance guidelines, state 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, as well as state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Where our activities involve foreign government officials, they may also potentially be subject to the Foreign Corrupt Practices Act, which prohibits companies and individuals from engaging in specified activities to obtain or retain business or to influence a person working in an official capacity. Under the FCPA, it is illegal to pay, offer to pay, or authorize the payment of anything of value to any foreign government official, governmental staff members, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls.

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

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

U.S. Marketing Exclusivity

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

Rest of World Government Regulation

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

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials.

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

Employees

As of December 31, 2017, we had 251 full-time employees. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Research and Development

We invested $51.2 million, $41.3 million, and $32.7 million in research and development in the years ended December 31, 2017, 2016 and 2015, respectively.

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 Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Exchange Act are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. We also regularly post copies of our press releases as well as copies of presentations and other updates about our business on our website at www.flexiontherapeutics.com. Information contained in our website does not constitute a part of this Annual Report or our other filings with the SEC. The SEC maintains an internet site that contains our public filings with the SEC and other information regarding our company, at www.sec.gov. These reports and other information concerning our company may also be accessed at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330.

This Annual Report contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Form 10-K, including logos, artwork and other visual displays, may appear without the ® or TM 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.

ITEM 1A. RISK FACTORS

You should consider carefully the risks described below, together with the other information contained in this Annual Report on Form 10-K and other documents we file with the Securities and Exchange Commission. The risks and uncertainties below are those identified by us as material, but there are also additional risks and uncertainties that we are unaware of that may become important factors that affect us. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected.

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 a limited operating history. To date, we have focused primarily on developing our commercialized product, ZILRETTA. Any additional product candidates we develop will require substantial 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 $137.5 million, $71.9 million, and $46.3 million for fiscal years 2017, 2016, and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $349.2 million. We expect to incur net losses over the next few years as we invest in the commercialization of ZILRETTA and advance our development programs.

We have devoted most of our financial resources to product development, including our nonclinical development activities and clinical trials, and more recently to commercial efforts. 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. The U.S. Food and Drug Administration, or FDA, granted marketing approval and we launched commercial sales of ZILRETTA in the fourth quarter of 2017. We have not generated significant revenues from sales of ZILRETTA and cannot guarantee that our commercialization efforts will result in substantial product revenues.

We also expect to continue to incur substantial and increased expenses as we invest in the commercialization of ZILRETTA, scale up commercial manufacturing of ZILRETTA, conduct additional clinical trials for this product and continue our development activities with respect to ZILRETTA, FX101 and FX201. 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 not generated significant revenue and may never be profitable.

Our ability to generate significant revenue and achieve profitability depends primarily on our ability to successfully commercialize ZILRETTA, as well as our ability to obtain regulatory approval for and commercialize other product candidates. We may never succeed in these activities and may never generate revenues that are significant enough to achieve profitability. Our ability to generate significant revenue from product sales depends heavily on our success in commercializing ZILRETTA and any other product candidates for which we receive regulatory approval.

Because of the numerous risks and uncertainties associated with new pharmaceutical products and development efforts, we are unable to predict the timing or amount of increased expenses, when, or if, we will begin to generate meaningful 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 determine that additional sales and marketing personnel or other resources are necessary to successfully commercialize ZILRETTA or if we face any product liability claims that may be brought against us following the commercial launch of ZILRETTA.

If we are unable to generate significant revenues from product sales, particularly from sales of ZILRETTA, or to maintain an acceptable cost structure related to our operations, we may not become profitable and may need to obtain additional funding to continue operations.

If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs and/or commercialization activities.

Developing and commercializing pharmaceutical products, including conducting preclinical studies and clinical trials, and building and maintaining sales and marketing capabilities, is expensive. We expect our expenses to substantially increase in connection with our ongoing activities, particularly as we expand our sales and marketing activities, commercialize ZILRETTA and advance our clinical programs.

As of December 31, 2017, we had cash, cash equivalents and marketable securities of $423.9 million and working capital of $367.4 million. Based upon our current operating plan, we believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital requirements for at least the next twelve months from the issuance date of the financial statements included in this report. Regardless of our expectations as to how long our 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.

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 scale back or discontinue commercialization of ZILRETTA or the further development of ZILRETTA or 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;
- seek corporate partners to assist in the commercialization of ZILRETTA 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.

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 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 existing indebtedness contains restrictions that limit our flexibility in operating our business. In addition, we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect, which could have a materially adverse effect on our business, or may otherwise be unable to repay our indebtedness as it becomes due.

On August 4, 2015, we entered into a credit and security agreement with MidCap Financial SBIC, LP, or MidCap, as administrative agent, MidCap Funding XIII Trust and Silicon Valley Bank, as agent lenders, to borrow up to $30.0 million and contemporaneously drew down $15.0 million under the credit facility. The credit 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 in the credit agreement could prevent us from pursuing 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 credit 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 a material impairment of the prospect of our repayment of any portion of the amounts we owe under the credit agreement occurs. In the case of a continuing event of default under the credit agreement, the lenders could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted the lenders a security interest under the credit agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the credit agreement are secured by all of our existing and future assets, excluding intellectual property, which is subject to a negative pledge arrangement.

In April 2017, we also issued $201.3 million principal amount of our 3.375% Convertible Senior Notes due 2024, or the 2024 Convertible Notes. The 2024 Convertible Notes will mature on May 1, 2024, unless earlier redeemed, repurchased or converted in accordance with the terms of the indenture governing the notes. If specified bankruptcy, insolvency or reorganization-related events of default occur, or if certain other events of default occur and the trustee or certain holders of the 2024 Convertible Notes elect, the principal of, and accrued and unpaid interest on, all of the then-outstanding 2024 Convertible Notes will automatically become due and payable. In addition, if we undergo certain fundamental change transactions specified in the indenture governing the 2024 Convertible Notes, the holders of the notes may require us to repurchase their notes at a price equal to 100% of the principal amount of the notes, plus any accrued and unpaid interest.

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 or refinance our indebtedness at the time any such repayment or repurchase 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 Commercialization Activities

Our prospects are highly dependent on the successful commercialization of ZILRETTA. To the extent ZILRETTA is not commercially successful, our business, financial condition and results of operations may be materially adversely affected.

ZILRETTA is our only drug that has been approved for sale and it has only been approved for the management of osteoarthritis, or OA, pain of the knee for patients in the United States. We are focusing a significant portion of our activities and resources on ZILRETTA, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize ZILRETTA in the United States.

Successful commercialization of ZILRETTA is subject to many risks. We have never, as an organization, commercialized a product, and there is no guarantee that we will be able to do so successfully with ZILRETTA for its approved indication. There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us.

Market acceptance of ZILRETTA and any other product for which we receive approval, will depend on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the timing of market introduction of the product as well as competitive products;
- the clinical indications for which the product is approved;
- acceptance by physicians, the medical community and patients of the product as a safe and effective treatment;
- the ability to distinguish safety and efficacy from existing, less expensive generic alternative therapies;
- the convenience of prescribing, administrating and initiating patients on the product;
- the potential and perceived advantages of the product over alternative treatments;
- the potential and perceived value of the product 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 payers and government authorities;
- the uptake of ZILRETTA in light of the miscellaneous J-code for reimbursement;

- the prevalence and severity of adverse side effects; and
- the effectiveness of sales and marketing efforts.

With respect to ZILRETTA, while we have established our commercial team and sales force, there are many factors that could cause the commercialization of ZILRETTA to be unsuccessful, including a number of factors that are outside our control. The commercial success of ZILRETTA depends on the extent to which patients and physicians accept and adopt ZILRETTA as a treatment for OA pain of the knee, and we do not know whether our or others' revenue estimates in this regard will be accurate. For example, if the patient population suffering from OA pain of the knee is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to use ZILRETTA, the commercial potential of ZILRETTA will be limited. In addition, if ZILRETTA is not convenient for physicians to use, then it may not achieve widespread adoption, regardless of its efficacy and safety. For example, ZILRETTA must be administered only by a health care professional in an office, clinic or hospital setting. In addition, ZILRETTA requires a multi-step preparation process, which may discourage some physicians from using ZILRETTA. Moreover, ZILRETTA's label indicates that it is not intended for repeat administration; this may negatively impact our commercialization efforts. We also do not know how physicians, patients and payers will respond to the pricing of ZILRETTA in the long-term. In particular, as part of our initial launch strategy we have provided some product as samples during a trial period, and do not know whether physicians that initially use ZILRETTA will continue to do so after using the product samples.

Physicians may not prescribe ZILRETTA and patients may be unwilling to use ZILRETTA if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for ZILRETTA in clinical development in additional indications, may adversely impact the commercial results and potential of ZILRETTA. Thus, significant uncertainty remains regarding the commercial potential of ZILRETTA.

If the commercialization of ZILRETTA is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product and our company could be harmed.

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

Immediate-release TA and other injectable immediate-release steroids, which are the current intra-articular, or IA, standard of care for OA pain, are available in generic form and are therefore relatively inexpensive compared to the pricing for ZILRETTA. These generic steroids also have well-established market positions and familiarity with physicians, healthcare payers and patients. Although we believe the proven and extended pain relief evidenced in our clinical trial demonstrate that ZILRETTA represents a clinically meaningful and highly efficacious option for patients and physicians, it is possible that as we receive data from additional clinical trials or in a post-marketing setting from physician and patient experiences with the commercial product that does not continue to support such interpretations. It is also possible that the FDA, physicians and healthcare payers will not agree with our interpretation of our existing and future clinical trial data. If we are unable to demonstrate the value of ZILRETTA based on our data, our opportunity for ZILRETTA to maintain premium pricing and be commercialized successfully would be adversely affected. For example, although ZILRETTA showed numeric improvements through week 12 in validated, OA specific pain, stiffness, function and quality of life exploratory measures and showed numeric improvements in average daily pain, it did not achieve statistical significance at the week 12 timepoint compared to immediate-release TA. As a result, it is possible that healthcare payers will not agree with our assessment that ZILRETTA's proven pain relief supports premium pricing. In addition, these OA specific data are not included in the ZILRETTA label, which limits our ability to discuss these important results with physicians and healthcare payers.

In addition to existing generic steroids, such as immediate-release TA, the FDA or other applicable regulatory authorities may approve generic products that could compete with ZILRETTA, if we cannot adequately protect it with our patent portfolio. Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. The FDCA, FDA regulations and other applicable regulations and

policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration, conditions of use, or labeling as our product candidate and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent as ZILRETTA. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our product candidates would materially adversely impact our ability to successfully commercialize our product candidates, including ZILRETTA.

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

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

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staffs and experienced commercial and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis drug products or drug delivery technologies that are more effective or less costly than ZILRETTA or any other product candidate that we are currently developing or that we may develop.

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

- the efficacy and safety of our product candidates, including as relative to marketed products and product candidates in development by third parties;
- the ability to distinguish safety and efficacy from existing, less expensive generic alternative therapies;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- the ability to maintain a good relationship with regulatory authorities;
- the ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect intellectual property rights related to our product candidates;

- the ability to manufacture on a cost-effective basis and sell commercial quantities of any of our product candidates that receive regulatory approval; and
- acceptance of any of our product candidates that receive regulatory approval by physicians and other healthcare providers.

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

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

Our strategy is to commercialize ZILRETTA in the United States with a targeted sales and marketing organization. While we have established our commercial team and our sales force, we do not have prior experience commercializing pharmaceutical products as an organization. In order to successfully market ZILRETTA, we must continue to build and maintain our sales, marketing, managerial, compliance and related capabilities or make arrangements with third parties to perform these services. These efforts will continue to be expensive and time-consuming, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. If we are unable to maintain adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to appropriately commercialize ZILRETTA and may not become profitable.

Additionally, our strategy in the United States includes distributing ZILRETTA solely through a limited network of third-party specialty distributors and one specialty pharmacy. While we have entered into agreements with a specialty pharmacy and specialty distributors to distribute ZILRETTA in the United States, they may not perform as agreed or they may terminate their agreements with us. For example, we currently rely on a single specialty pharmacy, which we estimate represents approximately 10% of the ZILRETTA distribution channel, and the loss of that specialty pharmacy or its failure to distribute effectively would adversely affect ZILRETTA's distribution. Also, we may need to enter into agreements with additional specialty distributors or specialty pharmacies, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. In the event that our specialty distributors or specialty pharmacy do not fulfill their contractual obligations to us, or the agreements are terminated without adequate notice, or we are unable to expand our network, shipments of ZILRETTA through, and associated revenues from, these sales channels would be adversely affected. In addition, we expect that it would take a significant amount of time if we were required to change our specialty distributors or specialty pharmacy.

To date, we have not entered into any strategic collaborations for ZILRETTA or any of our product candidates. We face significant competition in seeking appropriate strategic partners, and these strategic collaborations can be intricate and time consuming to negotiate and finalize. We may not be able to negotiate strategic collaborations 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 collaboration outside of the United States because of the numerous risks and uncertainties associated with establishing strategic collaborations. To the extent that we enter into strategic collaborations, our future collaborators 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 ZILRETTA or our other product candidates in territories outside of the United States, or if our potential future collaborators do not successfully commercialize our product candidates in these territories, our ability to generate revenue from product sales will be adversely affected.

We and any future collaborators 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 ZILRETTA or any

other approved products will be limited. In addition, if we are unable to effectively develop and maintain our commercial team, including our U.S. sales force, or maintain and, if needed, expand, our network of specialty distributors and specialty pharmacies, our ability to effectively commercialize ZILRETTA and generate product revenues would be limited.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize ZILRETTA will be harmed.

ZILRETTA is a newly-marketed drug and, therefore, the members of our sales force do not have significant experience promoting ZILRETTA. As a result, we are required to expend significant time and resources to train our sales force to be credible, persuasive and compliant with applicable laws in marketing ZILRETTA for the treatment of patients with OA of the knee. In addition, we must train our sales force to ensure that an appropriate and compliant message about ZILRETTA is being delivered. If we are unable to maintain an effectively trained sales force and equip them with compliant and effective materials, including medical and sales literature to help them appropriately inform and educate regarding the potential benefits and safety of ZILRETTA and its proper administration, our efforts to successfully commercialize ZILRETTA could be put in jeopardy, which would negatively impact our ability to generate product revenues.

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

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

Payers may require documented proof that patients meet certain eligibility criteria in order to be reimbursed for ZILRETTA, for example requiring that a patient first try and fail treatment with an injection of generic corticosteroid. Payers may even require that pre-approval, or prior-authorization, be obtained from the payer for reimbursement of ZILRETTA. Patients are unlikely to use ZILRETTA and, if approved, any other products, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. For example, ZILRETTA is sold to physicians on a “buy and bill” basis. Buy and bill products must be purchased by healthcare providers before they can be administered to patients. Healthcare providers subsequently must seek reimbursement for the product from the applicable third party payer, such as Medicare or a health insurance company. Healthcare providers may be reluctant to administer ZILRETTA because they would have to fund the purchase of the product and then seek reimbursement, which may be different from their purchase price, or because they do not want the additional administrative burden required to obtain reimbursement for the product.

Further, the status of reimbursement codes for ZILRETTA could also affect reimbursement. J-Codes and Q-Codes are reimbursement codes maintained by the Centers for Medicare and Medicaid Services, or CMS that are a component of the Healthcare Common Procedure Coding System (HCPCS) and are typically used to report injectable drugs that ordinarily cannot be self-administered. We do not currently have a specific J-Code or Q-Code for ZILRETTA. Until we can obtain a specific reimbursement code for ZILRETTA, we will need to use a non-specific miscellaneous J-Code for ZILRETTA, which is a temporary code to facilitate reimbursement for physician-administered ZILRETTA. Since miscellaneous J-Codes may be used for a wide variety of products, health plans may have more difficulty determining the actual product used and billed for the patient. As a result, these claims must often be submitted with additional information and manually processed, which can create delays in claims processing times as well as increasing the likelihood for claim errors.

In addition, the market for ZILRETTA and any of our other product candidates may depend significantly on access to third-party payers' medical policies, drug formularies, or lists of medications for which third-party payers provide coverage and reimbursement. The industry competition to be included in such policies or formularies often leads to downward pricing pressures on pharmaceutical companies, and we may be required to offer discounted rates to certain government and other payers to ensure coverage of our drugs. Also, third-party payers may refuse to include a particular branded drug in their policies or formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage and adequate reimbursement will be obtained.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third party coverage and reimbursement for ZILRETTA or, if approved, any of our other product candidates, may not be available or adequate in either the United States or international markets, or may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sales and distribution costs. If coverage and reimbursement are not available or only available at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval, including ZILRETTA, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Guidelines and recommendations published by various organizations can reduce the use of ZILRETTA and any other products we may commercialize.

Government agencies promulgate regulations and guidelines directly applicable to us and to our products and 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 that do not recognize ZILRETTA or our other product candidates, suggest the reduced use of ZILRETTA or our other product candidates, or suggest 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 ZILRETTA or any future products.

ZILRETTA is available to a much larger number of patients and in broader populations through our commercialization efforts as compared to the patients in the clinical studies. We do not know whether the results of ZILRETTA's use in such larger number of patients and broader populations will be consistent with the results from our clinical studies.

While the FDA granted approval of ZILRETTA based on the data included in the NDA, including data from our completed pivotal Phase 3 clinical trial, we do not know whether the results when a large number of patients and broader populations are exposed to ZILRETTA, including results related to safety and efficacy, will be consistent with the results from earlier clinical studies of ZILRETTA that served as the basis for the approval of ZILRETTA. New data relating to ZILRETTA, including from adverse event reports, our on-going repeat-dose safety study, or our studies of ZILRETTA in hip and shoulder OA and bilateral knee OA, may result in changes to the product label and may adversely affect sales, or result in withdrawal of ZILRETTA from the market. The FDA and regulatory authorities in other jurisdictions may also consider any new data in connection with further marketing approval applications. If ZILRETTA or any additional 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 promoted or 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 maintaining market acceptance of the affected product and could substantially increase the costs of commercializing ZILRETTA or any additional products.

Recently enacted and future legislation, including health care reform measures, may increase the difficulty and cost for us to commercialize ZILRETTA and any future products and may affect the prices we may obtain.

The United States and some foreign jurisdictions are considering, or have enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell ZILRETTA, and if approved for sale, our other potential products, profitably. Among policy makers and third-party payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been, and may continue to be, significantly affected by major legislative, congressional and enforcement initiatives. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is already subject to government control.

In March 2010, PPACA was enacted, which was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms. Among the PPACA provisions of importance to the pharmaceutical industry are the following:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program, created under Section 6002 of PPACA, and its implementing regulations that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to "payments or other transfers of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and that applicable manufacturers and applicable group purchasing organizations report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members, with data collection and reporting to CMS currently required by March 31st, of each calendar year;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for non-compliance;
- an FDA-approval framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of PPACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the Health Care Reform Law or otherwise circumvent some of the requirements for health insurance mandated by PPACA. Further, The Tax Cuts and Jobs Act of 2017, signed into law on December 22, 2017, removed the individual mandate starting in 2019 that required individuals to have insurance or face a penalty. Additionally, on January 23, 2018, President Trump signed a continuing resolution on appropriation for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees. Congress may consider additional legislation to replace or repeal other elements of PPACA.

We expect that PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, as well as additional downward pressure on the price that we receive for any approved product, including ZILRETTA. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices, including at the federal level several recent U.S. Congressional inquiries and proposed bills designed to, among other things, increase drug pricing transparency, reduce the cost of drugs under Medicare, review relationships between pricing and manufacturer patient assistance programs, and reform government program drug reimbursement methodologies. Any reduction in reimbursement from Medicare, Medicaid or other government-funded programs may result in a similar reduction in payments from private payers. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing

cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize ZILRETTA and any future products for which we receive regulatory approval. Additionally, we are currently unable to predict what additional legislation or regulation, if any, relating to the healthcare industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business.

Risks Related to Product Development and Regulatory Compliance

We may never obtain regulatory approval of ZILRETTA for additional indications or any approval of our other product candidates in the United States, or we may never obtain approval for or commercialize ZILRETTA or our other product candidates outside of the United States, which would limit our ability to realize their full market potential.

While ZILRETTA has been approved by the FDA for the treatment of patients with OA of the knee, it has not been approved by the FDA for any other indications, and it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market ZILRETTA for other indications or in other jurisdictions, or in order to market any of our other product candidates, we must obtain regulatory approval for each indication and in each applicable jurisdiction, and we may never be able to get such approval for ZILRETTA or our other product candidates. In particular, FX101 and FX201 are at early stages of development and may never reach IND submission or human clinical trials, in which case we may never recover our investment in these product candidates.

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 potential future products in those countries. Other than ZILRETTA in the United States, we do not have any products approved for sale in any jurisdiction, and we do not have experience in obtaining regulatory approval in international markets. If we do not receive marketing approval for ZILRETTA for any other indication or from any regulatory agency other than the FDA, we will never be able to commercialize ZILRETTA for any other indication in the United States or for any indication in any other jurisdiction. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals for our other product candidates, or if regulatory approval in international markets is delayed, our potential market will be reduced and our ability to realize the full market potential of ZILRETTA or our other product candidates will be harmed. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those opportunities.

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.

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 results generated in our completed ZILRETTA pivotal Phase 3 clinical trial do not ensure that any ongoing or future ZILRETTA clinical trial, including our ongoing repeat dose safety clinical trial or our clinical trials of ZILRETTA in hip and shoulder OA and bilateral knee OA, will be successful or consistent with the results generated in the Phase 3 trial.

We have conducted preclinical toxicology studies in healthy dogs with single and repeat doses of ZILRETTA, blank microspheres and immediate-release TA. The immediate-release TA and ZILRETTA groups produced similar findings in these studies. In the single-dose study, local cartilage findings of reduced extracellular matrix were completely reversed by the end of the nine-month recovery period in both the ZILRETTA and immediate-release TA study arms. With repeat administrations of ZILRETTA and immediate-release TA, a larger reduction in extracellular matrix in cartilage partially recovered by six months following the last dose; however, structural

changes in cartilage were observed with repeat administrations of both ZILRETTA and immediate-release TA. Repeat administration of immediate-release TA has a long history of safe clinical use in patients with OA, and in a randomized, double-blind clinical trial conducted in 2003 by Raynauld et al, administration of immediate-release TA or saline every three months for up to two years in 68 OA patients was well-tolerated and demonstrated no deleterious effects in the knee joint when assessed by clinical exam and X-ray evaluation. Using a more sensitive MRI imaging technology in 2015, Driban et al again demonstrated that cartilage structure changes between OA patients treated with immediate-release TA and saline in patients were similar. In 2017, the same authors reporting on the same data set concluded that there was a relative loss of cartilage in the immediate-release TA group. We are studying ZILRETTA in a repeat dose safety clinical trial and if the data from the repeat dose trial are supportive, we intend to seek inclusion of these data in the label for ZILRETTA through submission of a supplemental NDA. It is possible that we could observe detrimental effects on joint structure with repeated doses of ZILRETTA, which would limit ZILRETTA's commercial potential and could harm our ability to maintain regulatory approval or obtain approval to market ZILRETTA in additional indications or additional jurisdictions.

Product candidates 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 trials 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. 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. In any event, our future clinical trials may not be successful.

If ZILRETTA or any other product candidate is found to be unsafe or lack efficacy in particular indications, we will not be able to obtain regulatory approval for the indication and our business could be materially harmed.

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 for our product candidates.

We may experience delays in clinical trials of our products and product candidates. 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 ZILRETTA IND was placed on clinical hold at two points during product development, which delayed completion of our trials and resulted in additional expense. We cannot guarantee that any existing or future IND we submit will not be subject to similar holds.

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 our product candidates could be materially harmed, which could have a material adverse effect on our business.

The regulatory approval process of the FDA is lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates or for ZILRETTA in additional indications, our business will be 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. Although we received regulatory approval of ZILRETTA for the treatment of patients with OA of the knee, it is possible that none of our other product candidates will ever obtain regulatory approval or that we will not be able to obtain regulatory approval for ZILRETTA in additional indications.

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;
- 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.

The lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market ZILRETTA in additional indications or to market our other product candidates at all, which would harm our business, results of operations and prospects.

In addition, even if we were to obtain approval for other product candidates or for ZILRETTA in other indications, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, 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, ZILRETTA has initially been approved for single-dose administration and is not intended for repeat administration, which may limit the extent to which payers reimburse ZILRETTA and physicians prescribe ZILRETTA to their patients. We are conducting a repeat dose clinical trial and intend to use the resulting data to inform our clinical and regulatory perspectives and to create a basis for further interactions with the FDA. However, if we are unable to expand the label for ZILRETTA to include repeat dosing, our ability to fully market ZILRETTA may be limited.

Our product candidates may not receive regulatory approval despite success in clinical trials. 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 granted marketing approval of ZILRETTA for the treatment of patients with OA pain of the knee, and we could face liability if a regulatory authority determines that we are promoting ZILRETTA for any off-label uses.

A company may not promote "off-label" uses for its drug products. An off-label use is the use of a product for an indication that is not described in the product's FDA-approved label in the United States or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from pharmaceutical companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. We intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of ZILRETTA and any future products, but we cannot be sure that the FDA or other regulatory agencies will agree that we have not violated their restrictions. For example, as part of our promotion strategy for ZILRETTA we communicate certain results from our Phase 3 clinical trial and other clinical data that are consistent with, but not directly included in, the product label. While we believe our communication of this data is in accordance with FDA guidance and applicable laws, we cannot be certain that the FDA or other regulatory agencies will agree with our use of this data or our sales force may use such data in a way that is inconsistent with our policies. As a result, we may be subject to criminal and civil liability. In addition, our management's attention could be diverted to handle any such alleged violations. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Federal Food, Drug, and Cosmetic Act, or the FDCA, the federal False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Even though the FDA has granted approval of ZILRETTA for the treatment of patients with OA pain of the knee, the terms of the approval may limit its commercial potential. Additionally, ZILRETTA is still subject to substantial, ongoing regulatory requirements, and our other product candidates may face future development and regulatory difficulties.

Even though the FDA has granted approval of ZILRETTA, the scope and terms of the approval may limit our ability to commercialize ZILRETTA effectively and, therefore, our ability to generate substantial sales revenues. The FDA has approved ZILRETTA only for the treatment of patients with OA of the knee. If any other ongoing clinical studies of ZILRETTA are negative, the FDA could decide to withdraw approval, add warnings or narrow the approved indication in the product label.

ZILRETTA and, if approved, our other product candidates, 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 adverse events, or 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.

We rely on third party collaborators to assist us in meeting our reporting and related obligations. While we work closely with these third parties, we do not control all of their activities. If our third party collaborators do not meet the relevant commitments, we may fail to meet our applicable regulatory requirements.

If we fail to comply with applicable regulatory requirements for ZILRETTA or for any other approved 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.

Any relationships with healthcare professionals, principal investigators, consultants, actual and potential customers, and third-party payers in connection with our current and future business activities are and will continue to be subject, directly or indirectly, to federal and state healthcare laws. If we are unable to comply, or have not fully complied, with such laws, we could face criminal sanctions, civil penalties, administrative penalties, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Our operations are directly or indirectly subject to various federal and state healthcare laws, including without limitation, 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. Our potential exposure under such laws increased significantly with the commercialization of ZILRETTA in the United States through our dedicated sales force. 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, promotion, manufacturing, distribution, pricing, discounting, customer, incentive programs, education programs and other business arrangements and activities. 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, individuals and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in

cash or in kind, to induce or reward, or in return for, either the referral of an individual, or the purchase, order 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 penalties laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government claims for payment 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 imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or 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 PPACA, and its implementing regulations, which 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 CMS 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 CMS 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 and regulations, 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 payer, 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 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, and often are not preempted by HIPAA, 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);
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- 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, rebates 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).

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 and enforcement authorities will conclude that our business practices, including activities undertaken by third parties on our behalf, 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, disgorgement, imprisonment, possible exclusion from participation in Medicare, Medicaid and other government healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations. Moreover, while we do not bill third-party payers directly and our customers make the ultimate decision on how to submit claims, from time-to-time we may provide reimbursement guidance to patients and healthcare providers. If a government authority were to conclude that we provided improper advice and/or encouraged the submission of a false claim for reimbursement, we could face action against us by government authorities. If any of the physicians or other providers or entities with whom we do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occurs, it could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside of the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we fail to develop, acquire or in-license other potential future 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 potential future product candidates in addition to ZILRETTA. Our primary means of expanding our pipeline of product candidates is to select and acquire or in-license product candidates for the treatment of therapeutic indications that complement or augment our current pipeline, or that otherwise fit into our development or strategic plans on terms that are acceptable to us, and/or develop improved formulations and delivery methods for existing FDA-approved products. Developing new formulations or delivery methods of existing or potential future product candidates or identifying, selecting and acquiring or in-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 in-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 completely on third parties to manufacture our commercial supplies of ZILRETTA and our preclinical and clinical drug supplies for our other product candidates.

If we were to experience an unexpected loss of supply of ZILRETTA or our other product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience disruptions in commercial supply of ZILRETTA or delays, suspensions or terminations of clinical trials or regulatory submissions. 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 products and product candidates, including Patheon with respect to supplies of ZILRETTA, must obtain and maintain approval by the FDA. While we work closely with our third party manufacturers on the manufacturing process for our products and 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, or withdraws approval for, these facilities for the manufacture of our products and product candidates, we may need to find alternative manufacturing facilities, which would significantly impact our ability to commercialize, develop, or obtain or maintain regulatory approval for our products and product candidates.

We are particularly reliant on Patheon with respect to maintaining ZILRETTA manufacturing suites. These Patheon facilities required approval from the FDA as a condition of regulatory approval for ZILRETTA, as we rely exclusively on Patheon for commercial supplies of ZILRETTA. In addition, because Patheon manufactures ZILRETTA in the United Kingdom, or U.K., it needs to maintain and update its facility license with the applicable U.K. regulatory agencies and any delay or inability to do so would delay or prevent Patheon from being able to produce commercial supplies of ZILRETTA. Furthermore, the manufacturing process for ZILRETTA is unique and involves specialized equipment and proprietary processes, which subjects us to heightened risks that Patheon will experience delays in the manufacturing process.

We also rely on our manufacturers to purchase from third party suppliers the materials necessary to produce ZILRETTA and our other product candidates for our clinical trials and commercial sales. There are a limited number of suppliers for raw materials that we use to manufacture our products and product candidates and we may 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 ZILRETTA 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 for ZILRETTA or for any other approved products, there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our products, including ZILRETTA.

We expect to continue to depend on contract manufacturers or other third party manufacturers for the foreseeable future. We have entered into long-term commercial supply agreements with our current contract manufacturers in order to maintain adequate supplies to manufacture finished ZILRETTA drug product. We may, however, be unable to enter into such agreements or do so on commercially reasonable terms for potential future product candidates, which could have a material adverse impact upon our business.

We rely on certain sole sources of supply for our products and product candidates and any disruption in the chain of supply may disrupt commercialization of ZILRETTA or cause delay in developing, obtaining approval for, and commercializing our products and product candidates.

Currently, we use the following sole sources of supply for manufacturing ZILRETTA: Farmabios SpA for TA, Evonik Corporation for PLGA, and Patheon for finished microspheres drug product. Because of the unique equipment and process for loading TA onto PLGA microspheres, transferring finished drug product manufacturing activities for ZILRETTA 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 ZILRETTA finished drug suppliers may involve substantial cost and could result in a failure to maintain adequate supplies of ZILRETTA. We expect that for the foreseeable future Patheon will be the only manufacturer qualified as a commercial supplier of ZILRETTA with the FDA. As a result, if supply from Patheon 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 ZILRETTA supplier is relied upon for commercial production.

Our other product candidates, including FX201, also rely on sole sources of supply for the pre-clinical and clinical supply of materials. The manufacturing processes for FX201 and our other product candidates are complex and it may difficult or impossible to finalize appropriate processes for the scaled manufacture of the product candidates.

These factors could cause the disruption of the commercialization of ZILRETTA; delay clinical trials, regulatory submissions, required approvals or commercialization of any of our other product or product candidates; cause us to incur higher costs; or prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required clinical or 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 in the event of a product stockout for ZILRETTA or any of our other product candidate that is approved and launched.

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

As we scale up manufacturing of our products and product candidates, 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 or maintain regulatory approval for commercial marketing. In the future, we may identify impurities or other product related issues, which could result in increased scrutiny by regulatory authorities, suspensions of commercial activities or product recalls, delays in our clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our products or product candidates.

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 Council 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 be certain 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 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 may not be successful in establishing development and commercialization collaborations, which could adversely affect, and potentially prohibit, our ability to fully commercialize ZILRETTA or 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 ZILRETTA's development and commercialization outside of the United States. If we are unable to obtain a partner for ZILRETTA, we may be unable to advance the development of ZILRETTA in territories outside of the United States, which may limit its market potential. 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, in addition to ZILRETTA, receives marketing approval, we may enter into sales and marketing arrangements with third parties with respect to otherwise unlicensed or 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, or at all, we may be unable to successfully develop and seek regulatory approval for our product candidates and/or effectively market and sell ZILRETTA and any other future approved products, if any, in all of the territories outside of the United States where it may otherwise be valuable to do so.

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 products or product candidates or may otherwise fail in development or commercialization efforts, which could adversely affect our ability to develop or commercialize certain of our products or 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 or product candidate or research program under 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 may become 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 division of development or commercialization responsibilities or expenses, 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 products or 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.

Risks Related to Our Business Operations and Industry

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

We are highly dependent on the principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in the commercialization of ZILRETTA or clinical studies of our product candidates may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive or key employee might impede the progress of our development and commercialization objectives.

We have recently undergone a significant expansion of our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2017, we had 251 full-time employees, with approximately 100 of these employees being MBMs hired following approval of ZILRETTA in the United States. In addition, as our company matures, we expect to further expand our employee base to increase our managerial, scientific and engineering, operational, sales, marketing, financial and other resources and to hire more consultants and contractors. This growth will impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our existing or future product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to successfully commercialize ZILRETTA and, if approved, our other product candidates, and compete effectively will depend, in part, on our ability to effectively manage our recent and future growth.

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

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

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

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

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.

We plan to enter into agreements with third parties to market ZILRETTA, and if approved, our other product candidates, outside of the United States. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters, including earthquakes, typhoons, floods and fires.

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

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

Business interruptions could delay us in the process of developing or commercializing our products and product candidates.

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

Risks Related to Our Intellectual Property

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

We rely upon a combination of patents, trade secret protection, confidentiality agreements and proprietary know how, and intend to seek marketing exclusivity for any approved product, including ZILRETTA, in order to protect the intellectual property related to our products and product candidates, and to date we have three issued patents covering ZILRETTA in the United States.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights and our current or future licensors' or collaborators' patent rights are highly uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our products or product candidates in the United States or in other foreign countries. Even for our issued patents and if other patents do successfully issue, third parties may challenge their inventorship, ownership, validity, enforceability or scope in the courts or patent offices in the United States and abroad. This may result in such patents being narrowed or invalidated, which could limit our ability to stop others from using or commercializing similar or identical technologies or products, or limit the duration of the patent protection for our technologies and products. If this were to occur, early generic competition could be expected against ZILRETTA and potentially reduce the value of our product candidates in development. Also, a third party may challenge our rights to patents and patent applications that we license from third parties. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims.

If our patent applications with respect to ZILRETTA or our other product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop ZILRETTA or our other product candidates and threaten our ability to commercialize any resulting products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will not be found invalid and unenforceable or will go unthreatened by third parties. Further, if we encounter delays in regulatory approvals for additional indications or in additional jurisdictions, the period of time during which we could market ZILRETTA or any product candidate under patent protection could be reduced. See "Business—Patents and Patent Applications" in this Annual Report on Form 10-K for additional information regarding our material patents and patent applications.

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

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

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

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

Parties making claims against us may request and/or obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our products or product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products or manufacturing processes, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research, manufacture clinical trial supplies or allow commercialization of our product candidates. We

may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our products or product candidates, which could harm our business significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

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

Competitors may infringe our issued patents, licensed patents or our other intellectual property. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult. Accordingly, for such undetectable infringement or misappropriation our ability to recover damages will be negligible, and we could be at a market disadvantage because we may lack the resources of some of our competitors to monitor for and detect infringement. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in any patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in litigation proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

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

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

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from infringing on our intellectual property rights in all countries outside the United States, and competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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

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

Our owned or licensed patents directed to our product candidates may expire or have limited commercial life before the product candidate is approved for marketing in a relevant jurisdiction.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after our product candidates obtain regulatory approval, which may subject us to increased competition and reduce or eliminate our ability to recover our development costs. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Although we may be able to seek extensions of patent terms where available, including in the United States under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent, we cannot be certain that an extension will be granted, or if granted, what the applicable time period or the scope of patent protection afforded during any extended period will be. The applicable authorities, including the EMA, FDA, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be the case.

We have in-licensed or acquired a portion of our intellectual property necessary to develop our product candidates, and if we fail to comply with our obligations under any of these arrangements, we could lose such intellectual property rights.

We are a party to and rely on several arrangements with third parties, which give us rights to intellectual property that is necessary for the manufacture of ZILRETTA and the development of FX201. In addition, we may enter into similar arrangements in the future. Our current arrangements impose various development, royalty and other obligations on us. If we materially breach these obligations or if our counterparts fail to adequately perform their respective obligations, these exclusive arrangements could be terminated, which would result in our inability to develop, manufacture and sell products that are covered by such intellectual property.

Risks Related to Ownership of Our Common Stock

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

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

- the success or perceived success of the commercialization of ZILRETTA;
- failure to successfully develop and commercialize additional product candidates;
- adverse results or delays in clinical trials;
- inability to obtain additional funding;
- changes in laws or regulations applicable to our products or product candidates;

- inability to obtain adequate product supply for our products or product candidates, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products or technologies by our competitors;
- failure to meet or exceed product development or financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent, product liability or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

The trading price of our common stock may also be dependent upon the valuations and recommendations of the analysts who cover our company. If our results do not meet these analysts' forecasts, the expectations of our investors or any financial guidance or expectations we provide to investors in any period, the market price of our common stock could decline. Our ability to meet analysts' forecasts (including revenue and profitability), investors' expectations and our own guidance or financial expectations is substantially dependent on our ability to increase sales of ZILRETTA and to successfully commercialize ZILRETTA in the United States. Because we are in the early stages of the ZILRETTA launch, we and the analysts who cover our company have limited ability to accurately predict future sales results, and actual results may differ materially from our expectations or those of such analysts.

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

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

As of December 31, 2017, our executive officers, directors and stockholders affiliated with our officers and directors beneficially owned approximately 13.8% of our voting stock. Therefore, these stockholders may have the ability to influence us through this ownership position. These stockholders may be able to determine or significantly influence all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control or significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startup Act, or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenue of at least $1 billion, (b) December 31, 2019, (c) the date on which we are deemed to be a large accelerated filer, which would occur at the beginning of a year if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (d) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements including exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

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

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

We completed our initial public offering on February 18, 2014. As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. For example, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, which require, among other things, that we file with the SEC annually, quarterly and current reports with respect to our business and financial condition. We have incurred and will continue to incur costs associated with the preparation and filing of these reports. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC, and the Nasdaq Global Market have imposed various other requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Stockholder activism, the current political

environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact (in ways we cannot currently anticipate) the manner in which we operate our business. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

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

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

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

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

Pursuant to our 2013 equity incentive plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2013 plan will automatically increase each year by 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2013 plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

We are at risk of securities class action litigation.

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

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

Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, contains rules that limit the ability of a company that undergoes an ownership change to utilize its net operating losses, or NOLs, and tax credits existing as of the date of such ownership change. Under the rules, such an ownership change is generally any change in ownership of more than 50% of a company's stock within a rolling three-year period. The rules generally operate by focusing on changes in ownership among stockholders considered by the rules as owning, directly or indirectly, 5% or more of the stock of a company and any change in ownership arising from new issuances of stock by the company. During the quarter ended June 30, 2014, we completed a Section 382 study through February 11, 2014. The results of this study showed that as of February 11, 2014, one historical ownership change within the meaning

of Section 382 had occurred in 2009. As a result of this Section 382 limitation, approximately $0.3 million of NOLs will expire unutilized. Through the quarter ending December 31, 2017, the Company has completed periodic updates to its Section 382 study through October 31, 2017, which have indicated ownership changes within the meaning of Section 382 have occurred in December 2014 and June 2016, however, it is not anticipated that a portion of the Company's NOLs will expire unutilized as a result of the Section 382 limitations arising from these ownership changes. Subsequent ownership changes as defined by Section 382 may further limit the amount of NOL carryforwards that could be utilized annually to offset future taxable income.

Under the newly enacted federal income tax law, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

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

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

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

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

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;

- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our offices are located in Burlington, Massachusetts at a leased facility used primarily for corporate functions. Due to increased headcount and future growth plans, during 2017, the Company amended the original lease to expand the facility to approximately 30,000 square feet, with another approximately 6,450 square feet of space commencing in April 2018. The lease for the office space expires in October 2023. In addition, the Company has laboratory space in Woburn, Massachusetts of approximately 5,300 square feet at a leased facility which lease expires in 2022.

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is listed on the Nasdaq Global Market and trades under the symbol "FLXN". The following table sets forth the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market for the periods indicated.

Year Ended December 31, 2017	High	Low
First Quarter	$ 29.41	$ 17.91
Second Quarter	$ 29.00	$ 16.51
Third Quarter	$ 26.71	$ 20.15
Fourth Quarter	$ 32.25	$ 19.06

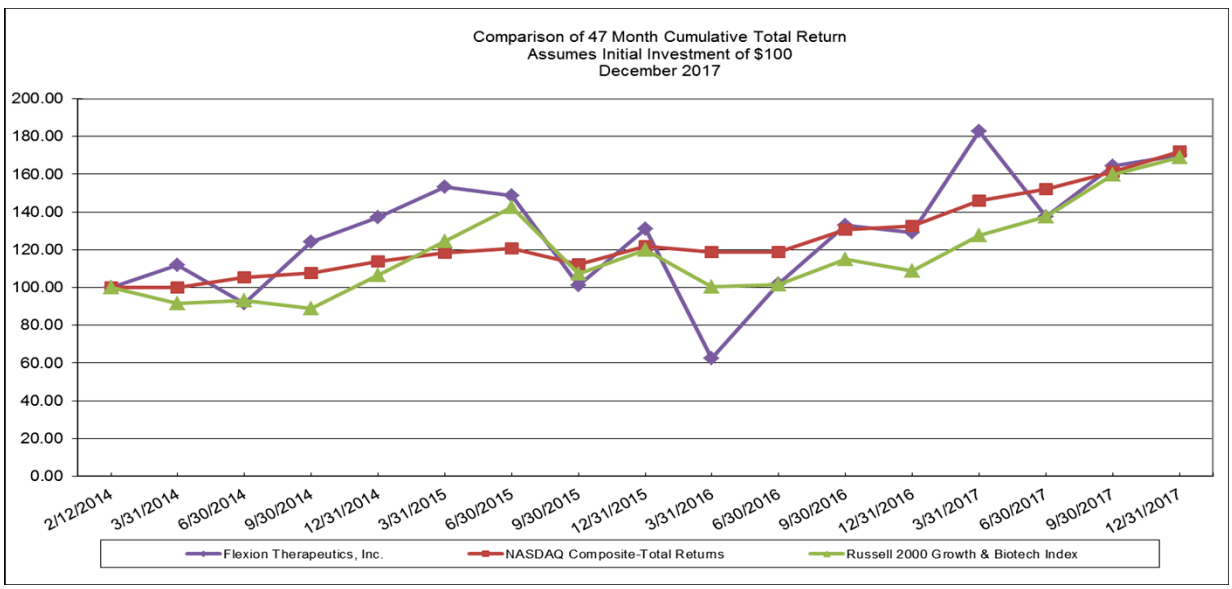
Year Ended December 31, 2016	High	Low
First Quarter	$ 19.42	$ 7.56
Second Quarter	$ 17.87	$ 8.16
Third Quarter	$ 19.63	$ 14.78
Fourth Quarter	$ 23.57	$ 15.93

On March 1, 2018, the last reported sale price of our common stock was $25.16.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph shows a comparison from February 12, 2014 (the date our common stock commenced trading on The NASDAQ Global Market) through December 31, 2017 of the cumulative total return for our common stock, the Russell 2000 Growth and Biotech index and the NASDAQ Composite Index (CCMP). The graph assumes an initial investment of $100 on February 12, 2014. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.



Holders of Record

As of March 1, 2018, there were approximately 15 stockholders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number.

Dividend Policy

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

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Item 6. Selected Financial Data

The following selected financial data should be read together with "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this Annual Report. The selected consolidated financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

We have derived the consolidated statements of operations data for the years ended December 31, 2017, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017 and December 31, 2016 from our audited consolidated financial statements appearing elsewhere in this Annual Report. The selected consolidated statement of operations data for the years ended December 31, 2014 and 2013 and the selected consolidated balance sheet data as of December 31, 2015, 2014 and 2013 are derived from our audited consolidated financial statements not included in this document. The selected consolidated financial data for all periods presented reflects the 1-for-8.13 reverse stock split we effected on January 27, 2014.

	Year Ended December 31,				
	2017	2016	2015	2014	2013
			(in thousands)		
Consolidated Statement of Operations Data:					
Revenues:					
Product revenue, net	$ 355	$ —	$ —	$ —	$ —
Operating expenses:					
Cost of sales	4	—	—	—	—
Research and development	51,231	41,314	32,691	17,923	11,061
Selling, general and administrative	78,801	28,466	13,372	9,064	6,704
Total operating expenses	130,036	69,780	46,063	26,987	17,765
Loss from operations	(129,681)	(69,780)	(46,063)	(26,987)	(17,765)
Other income (expense):					
Interest income	3,718	1,521	1,246	479	234
Interest expense	(11,268)	(1,748)	(571)	(401)	(449)
Other expense	(250)	(1,887)	(927)	(404)	(207)
Total other income (expense)	(7,800)	(2,114)	(252)	(326)	(422)
Net loss	(137,481)	$ (71,894)	$ (46,315)	$ (27,313)	$ (18,187)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (4.16)	$ (2.84)	$ (2.15)	$ (1.97)	$ (23.02)
Weighted average common shares outstanding, basic and diluted[1]	33,027	25,297	21,497	13,894	790

	2017	2016	2015	2014	2013
Consolidated Balance Sheet Data:					
Cash, cash equivalents, marketable securities, and long-term investments	$ 423,916	$ 210,329	$ 118,604	$ 151,625	$ 16,438
Working capital[2]	367,418	191,853	104,044	145,328	11,583
Total assets	441,317	226,262	127,139	153,348	18,731
Total debt[3]	160,010	30,533	15,002	3,564	5,002
Convertible preferred stock	—	—	—	—	74,806
Total stockholders' equity (deficit)	260,274	187,032	103,986	144,942	(64,704)

(1) See Note 3 to our consolidated financial statements appearing elsewhere in this Annual Report for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

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

(3) Total debt includes the current and long-term portion of our term loan, net of debt issuance costs and the 2024 convertible notes, net of the portion of the proceeds allocated to the conversion option and net of debt issuance costs.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of financial condition and results of operations should be read in conjunction with "Item 6. Selected Financial Data" and our consolidated financial statements and related notes appearing elsewhere in this Annual Report. This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Item 1A. Risk Factors". You should carefully read the "Risk Factors" section of this Annual Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, or OA, a type of degenerative arthritis. On October 6, 2017, the U.S. Food and Drug Administration, or FDA, approved ZILRETTA® (triamcinolone acetonide extended-release injectable suspension), as the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA pain of the knee. ZILRETTA is a non-opioid therapy that employs our proprietary microsphere technology to provide pain relief over 12 weeks. We established a full field sales force of Musculoskeletal Business Managers (MBMs) following ZILRETTA's approval. The MBMs were trained, certified and deployed in the field as of November 20, 2017, when they began the process of informing and educating prescribing clinicians about ZILRETTA.

We were incorporated in Delaware in November 2007, and to date we have devoted substantially all of our resources to developing our product candidates, including conducting clinical trials with our product candidates, preparing for the commercialization of ZILRETTA, providing general and administrative support for these operations and protecting our intellectual property. From our inception through December 31, 2017, we have raised approximately $756 million and funded our operations primarily through the sale of our common stock, convertible preferred stock, follow-on public offerings, convertible debt, and debt financing. Until such time, if ever, we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt or other financings, government or third-party funding, and licensing or collaboration arrangements.

We have incurred net losses in each year since our inception in 2007. Our net losses were $137.5 million, $71.9 million, and $46.3 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $349.2 million. Substantially all of our net losses resulted from costs incurred in connection with our development programs and from general and administrative expenses associated with our operations.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially in connection with our ongoing activities, as we:

- continue the development and commercialization of our lead product, ZILRETTA, including our on-going and future clinical trials;
- continue to scale-up manufacturing activities including the supply of clinical trial materials and registration and commercial batches;
- maintain a sales and marketing infrastructure for the commercialization of ZILRETTA;
- expand our development activities and advance additional product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts and operations as a public company.

As part of the commercialization of ZILRETTA, we are closely monitoring the launch, and focus on a number of quantitative metrics. During the fourth quarter, following our launch on November 20th, our MBMs called on approximately 3,600 physicians out of the approximately 9,500 physicians in around 3,500 accounts in our target list. In addition, during this period, our MBMs and Field Access Managers conducted in-depth discussions around reimbursement or product preparation training at approximately 350 accounts and 390 accounts gained experience with ZILRETTA through either purchases or samples. Of the accounts that purchased ZILRETTA, around 20% placed a reorder for additional product within the fourth quarter. On the payer front, we engaged about 20 key commercial insurers that represent roughly 141 million covered lives and greater than 95% of the benefits verifications processed through our FlexForward service resulted in coverage of ZILRETTA.

We may need to raise additional capital for the commercialization of ZILRETTA and completing clinical development of any of our other product candidates. Until such time that we can generate substantial revenue from product sales, we expect to finance our operating activities through a combination of equity offerings, debt or other financings, including convertible debt financings, government or other third-party funding and collaborations, and licensing arrangements. However, we may be unable to raise additional funds or enter into such arrangements when needed on favorable terms, or at all, which would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our development programs or commercialization efforts or grant to others, rights to develop or market product candidates that we would otherwise prefer to develop and market ourselves. Failure to receive additional funding could cause us to cease operations, in part or in full.

Financial Overview

Revenue

Net product sales consist of sales of ZILRETTA, which was approved by the FDA on October 6, 2017 and launched in the United States in October 2017. We had not generated any revenue prior to the launch of ZILRETTA.

Cost of Product Sales

Cost of product sales consists of third-party manufacturing costs, freight and indirect overhead costs associated with sales of ZILRETTA. Cost of product sales also includes period costs related to certain inventory manufacturing services, inventory adjustment charges, and unabsorbed manufacturing and overhead costs. Based on our policy to expense costs associated with the manufacture of our products prior to regulatory approval, the vast majority of the costs of ZILRETTA recognized as revenue during the year ended December 31, 2017 were expensed prior to the October 2017 FDA approval and, therefore, are not included in cost of sales during the period. We expect cost of sales to increase in relation to product revenues as we deplete these inventories.

Operating Expenses

The majority of our operating expenses to date have been related to the development activities of ZILRETTA, and to a lesser extent portfolio expansion efforts.

Research and Development Expenses.

Since our inception, we have focused our resources on our development activities, including: preclinical studies, clinical trials and chemistry manufacturing and controls, or CMC. Our development expenses consist primarily of:

- expenses incurred under agreements with consultants, contract research organizations, or CROs, and investigative sites that conduct our preclinical studies and clinical trials;
- costs of acquiring, developing and manufacturing clinical trial materials;
- personnel costs, including salaries, benefits, stock-based compensation and travel expenses for employees engaged in scientific research and development functions;
- costs related to compliance with regulatory requirements;

- manufacturing costs for ZILRETTA;
- expenses related to the in-license of certain technologies from pharmaceutical companies; and
- allocated expenses for rent and maintenance of facilities, insurance and other general overhead.

We expense research and development costs as incurred. Our direct research and development expenses consist primarily of external-based costs, such as fees paid to investigators, consultants, investigative sites, CROs and companies that manufacture our clinical trial materials and commercial supplies, and are tracked on a program-by-program basis. We do not allocate personnel costs, facilities or other indirect expenses to specific research and development programs. These indirect expenses are included within the amounts designated as "Personnel and other costs" in the table below. Inventory acquired prior to receipt of the marketing approval of ZILRETTA was recorded as research and development expense as incurred. We began capitalizing the costs associated with the production of ZILRETTA after the FDA approval on October 6, 2017.

The following table summarizes our research and development expenses for the periods presented:

	Year Ended December 31,		
(In thousands)	**2017**	**2016**	**2015**
Direct research and development expenses by program:			
Zilretta	$ 20,040	$ 24,609	$ 22,046
FX007	47	349	669
FX005	—	13	247
FX101	655		
Portfolio expansion	4,341	234	—
Other	1,080	620	—
Total direct research and development expenses	26,163	25,825	22,962
Personnel and other costs	25,068	15,489	9,729
Total research and development expenses	$ 51,231	$ 41,314	$ 32,691

Our research and development expenses are expected to increase in the foreseeable future. Specifically, our costs associated with ZILRETTA will increase as we conduct additional clinical trials in an effort to expand ZILRETTA's label to include additional indications and broaden its scope of administration. The ZILRETTA related research and development costs incurred in 2017 were comprised of $15.9 million related to OA knee pain, $3.4 million related to OA knee pain repeat administration, $0.3 million related to shoulder and hip OA pain, and $0.4 million related to bilateral knee OA pain. The primary increase in the portfolio expansion costs in 2017 was due to the December 2017 acquisition of the global rights to FX201 from GeneQuine Biotherapeutics GmbH, or GeneQuine, which required an upfront payment to GeneQuine of $2 million. Evonik Corporation, or Evonik, our supplier of PLGA for ZILRETTA, had previously manufactured finished drug product for our ZILRETTA clinical trial materials; however, in early 2016 we decided to use Patheon UK Limited (part of Thermo Fisher Scientific), or Patheon, as our sole supplier of ZILRETTA finished drug product for clinical trials and commercial supply. We impaired approximately $2,265,000 in manufacturing equipment located at the Evonik facility, resulting in a loss of $2,180,000 which was recorded in research and development expenses during the year ended December 31, 2016.

We cannot determine with certainty the duration of and completion costs associated with ongoing and future clinical trials or the regulatory approval process associated with post-marketing development of ZILRETTA or development of any product candidates in our pipeline. The duration, costs and timing associated with the further development of ZILRETTA or the development of other product candidates will depend on a variety of factors, including uncertainties associated with the results of our clinical trials. As a result of these uncertainties, we are currently unable to estimate with any precision our future research and development expenses for expanded indications for ZILRETTA or any product candidates in our pipeline, or when we may generate sufficient revenue to achieve a positive cash flow position.

We previously performed research and development for the U.S. Department of Defense under a cost reimbursable grant for a Phase 2 clinical trial investigating ZILRETTA in active military and medically retired veterans with post-traumatic knee OA. Reimbursements were recorded as an offset to research and development expenses when invoices for allowable costs were prepared and submitted to the U.S. Department of Defense. We discontinued this Phase 2 trial and terminated the grant as of July 31, 2016. Payments under cost reimbursable grants with agencies of the U.S. government were approximately $757,000.

Selling, General and Administrative Expenses.

Selling, general and administrative expenses consist primarily of personnel costs, including salaries, related benefits, travel expenses and stock-based compensation of our executive, finance, business development, commercial, information technology, legal and human resources functions. Other general and administrative expenses include an allocation of facility-related costs, patent filing expenses, and professional fees for legal, consulting, auditing and tax services.

We anticipate that our general and administrative expenses will increase in the future as we continue to build our corporate and commercial infrastructure to support the continued development and launch of ZILRETTA or any other product candidates. In particular, since ZILRETTA was approved by the FDA on October 6, 2017, we expect to incur material and ongoing increases in general and administrative expenses related to our hiring of a field sales force to market ZILRETTA in the United States. Additionally, we anticipate increased expenses related to the audit, legal and compliance, regulatory, investor relations and tax-related services associated with maintaining compliance with the Securities and Exchange Commission and Nasdaq requirements and healthcare laws and compliance requirements, director and officer insurance premiums and other costs associated with operating as a publicly-traded company.

Other Income (Expense)

Interest income. Interest income consists of interest earned on our cash, cash equivalents, marketable securities, and long-term investments balances. The primary objective of our investment policy is capital preservation.

Interest expense. In April 2017, we issued approximately $201.3 million in principle amount of convertible notes, or the 2024 Convertible Notes, which accrue interest at a rate of 3.375% per annum, payable semi-annually. We expect to pay interest through the maturity of the 2024 Convertible Notes on May 1, 2024. We have also borrowed $30.0 million under our 2015 term loan facility, and we incur interest related to this borrowing at a fixed rate of 6.25% per annum. We expect to incur future interest expense related to this borrowing until February 1, 2020.

Foreign currency gain (loss). We maintain a bank account denominated in British Pounds. All foreign currency payables and cash balances are measured at the applicable exchange rate at the end of the reporting period. All associated gains and losses from foreign currency transactions are reflected in the consolidated statements of operations, within other income and expense.

Other expense. Other expense consists of the net amortization and accretion of premiums and discounts related to our marketable securities, and our realized gains (losses) on redemptions of our marketable securities. We will continue to incur expenses related to net amortization of premiums on marketable securities for as long as we hold these investments.

Income Taxes

As of December 31, 2017, we had $190.9 million and $147.8 million of federal and state net operating loss carryforwards, respectively, and $5.4 million and $2.9 million of federal and state research and development tax credit carryforwards, respectively, available to offset our future taxable income, if any. These federal net operating loss carryforwards and research and development tax credit carryforwards expire at various dates beginning in 2029, if not utilized and are subject to review and possible adjustment by the Internal Revenue Service. The state net

operating loss carryforwards and research and development tax credit carryforwards expire at various dates beginning in 2030 and 2025, respectively, if not utilized and are subject to review and possible adjustment by the state tax authorities. At December 31, 2017, a full valuation allowance was recorded against our net operating loss carryforwards and our research and development tax credit carryforwards.

If we experience a greater than 50% aggregate change in ownership of certain stockholders over a three-year period, utilization of our then-existing net operating loss carryforwards and research and development tax credit carryforwards will be subject to an annual limitation.

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are more fully described in Note 3 to our consolidated financial statements appearing elsewhere in this Form 10-K, we believe that the estimates and assumptions involved in the following accounting policies may have the greatest potential impact on our financial statements and, therefore, consider these to be critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

On October 6, 2017, the FDA approved ZILRETTA. We entered into a limited number of arrangements with customers that are specialty distributors and a specialty pharmacy in the U.S. to distribute ZILRETTA. These arrangements are our initial contracts with customers and, as a result we adopted Accounting Standards Codification ("ASC") Topic 606 - *Revenue from Contracts with Customers* ("Topic 606") as of January 1, 2017. The transition to Topic 606 had no impact on our financial statements because we had no historical revenue prior to the launch of ZILRETTA. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to arrangements that meet the definition of a contract with a customer under Topic 606, including when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and we then assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product revenue, see *Product Revenue, Net* (below).

Product Revenue, Net— We sell ZILRETTA to a limited number of specialty distributors and a specialty pharmacy in the U.S. These customers subsequently resell ZILRETTA to physicians, clinics and certain medical centers or hospitals. In addition to distribution agreements with our customers, we enter into arrangements with government payers that provide for government mandated rebates and chargebacks with respect to the purchase of ZILRETTA

We recognize revenue on product sales when the customer obtains control of ZILRETTA, which occurs at a point in time (upon delivery to the customer). We have determined that the delivery of ZILRETTA to our customers constitutes a single performance obligation. There are no other promises to deliver goods or services beyond what is specified in each accepted customer order. Management has assessed the existence of a significant financing component in the agreements with our customers. The trade payment terms with our customers do not exceed one year and therefore management has elected to apply the practical expedient and no amount of consideration has been allocated as a financing component. Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee for service amounts that are detailed within our contracts with our customers relating to the sale of ZILRETTA. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Our analyses also contemplate application of the constraint in accordance with the guidance, under which it determined a material reversal of revenue would not occur in a future period for the estimates detailed in our financial statements as of December 31, 2017 and, therefore, the transaction price was not reduced further during the year ended December 31, 2017. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our original estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances—We compensate (through trade discounts and allowances) our customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the customers and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss through December 31, 2017, as well as a reduction to trade receivables, net on the condensed consolidated balance sheets.

Product Returns— Consistent with industry practice, we generally offers our customers a limited right of return for product that has been purchased from us based on the product's expiration date. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, net on the condensed consolidated balance sheets. We currently estimate product return liabilities using available industry data and our own sales information, including our visibility into the inventory remaining in the distribution channel. We have not received any returns to date and we believe that returns of our products will be minimal.

Government Chargebacks, Discounts and Rebates— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified VA hospitals and 340b entities at prices lower than the list prices charged to customers who directly purchase the product from us. The 340b Drug Discount Program is a US federal government program created in 1992 that requires drug manufacturers to provide outpatient drugs to eligible health care organizations and covered entities at significantly reduced prices. Customers charge us for the difference between what they pay for the product and the statutory selling price to the qualified government entity. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and trade receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by customers, and we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period-end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which we have not yet issued a credit.

Government Rebates— We are subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the condensed consolidated balance sheets. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. We anticipate our exposure to utilization from the Medicare Part D coverage gap discount program to be immaterial. For Medicaid programs, we estimate the portion of sales attributed to Medicaid patients and record a liability for the rebates to be paid to the respective state Medicaid programs. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Other Incentives— Other incentives which we offer include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the condensed consolidated balance sheets.

To date, our only source of product revenue has been from the U.S. sales of ZILRETTA, which we began shipping to customers in October 2017.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the year ended December 31, 2017:

(In thousands)	Trade Discounts, Allowances and Government chargebacks	Government rebates and other incentives	Returns	Total
Beginning Balance	$ —	$ —	$ —	$ —
Provision related to sales in the current year	100	15	2	117
Credit and payments made	(40)	0	0	(40)
Ending Balance	$ 60	$ 15	$ 2	$ 77

Product Revenue Reserves and Allowances – Chargebacks and fees are recorded as reductions of trade receivables, net on the condensed consolidated balance sheets. Government and other rebates and returns are recorded as a component of accrued expenses and other current liabilities on the condensed consolidated balance sheets.

Inventory—We value our inventories at the lower of cost or estimated net realizable value. We determine the cost of our inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. We perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of product revenues. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of product sales in the consolidated statements of operations and comprehensive loss.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired prior to receipt of marketing approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign. Inventory produced that will be used in promotional marketing campaigns is expensed to selling, general and administrative expense when it is selected for use in a marketing program.

Shipping and handling costs for product shipments are recorded as incurred in cost of product revenues along with costs associated with manufacturing the product, and any inventory write-downs.

Research and Development Costs

As part of the process of preparing our financial statements, we are required to estimate our accrued and third-party prepaid research and development expenses. We base our accrued expenses related to clinical trials on estimates of patient enrollment and related expenses at clinical investigator sites, as well as estimates for services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. We review new and open contracts and communicate with applicable internal and vendor personnel to identify services that have been performed on our behalf and estimate the level of service performed and the associated costs incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost for accrued expenses. The majority of our service providers invoice us monthly in arrears for services performed; however, some require advanced payments. For any services that require such advanced payments, we perform a review, with applicable internal and vendor personnel, to estimate the level of services that have been performed and the associated costs that have been incurred at each reporting period. We accrue expenses related to clinical trials based on contractual amounts applied to the level of patient enrollment and activity according to the protocol. We make estimates of our accrued and prepaid expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis. If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not adjusted our estimates at any particular balance sheet date in any material amount.

Stock-Based Compensation

We measure stock-based awards granted to employees and directors at fair value on the date of the grant and recognize the corresponding compensation expense for those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award, using the straight-line method. We measure stock-based awards granted to non-employees for services received based on the fair value of the equity

instrument issued. The measurement date of the fair value of the equity instrument issued to non-employees is the earlier of the date on which the counterparty's performance is complete or the date on which there is a commitment to perform.

The fair value of each stock-based award granted is estimated using the Black-Scholes option-pricing model. Until February 11, 2014, we were a private company and we lacked company-specific historical and implied volatility information. Therefore, we estimated our expected stock volatility based on the historical volatility of our publicly-traded peer companies for periods that are commensurate with the expected term (in years) of our stock-based awards, and we expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. The expected term of our stock options has been determined utilizing the "simplified" method for awards that qualify as "plain vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future. The assumptions used to determine the fair value of stock-based awards using the Black-Scholes option-pricing model were as follows:

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate	1.97%-2.29%	0.74-1.75%	1.49-1.92%
Dividend yield	0.00%	0.00%	0.00%
Expected term (in years)	6.0	5.6	6.0
Expected volatility	69.9%-72.8%	67.3-99.9%	76.4-83.9%

We recognize compensation expense only for the portion of awards that are expected to vest. On January 1, 2017, we began accounting for forfeitures as they occur rather than estimating future forfeitures. As such, any previously recognized compensation expense for an award will be reversed in the period that the award is forfeited.

RESULTS OF OPERATIONS

Year Ended December 31, 2017 Compared to Year Ended December 31, 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016:

	Year Ended December 31,			
(In thousands)	2017	2016	Change	% Increase/ (Decrease)
Revenues:				
Product revenue, net	$ 355	$ —	$ 355	—
Operating expenses:				
Cost of sales	4	—	4	100.0%
Research and development	51,231	41,314	9,917	24.0%
Selling, general and administrative	78,801	28,466	50,335	176.8%
Total operating expenses	130,036	69,780	60,256	86.4%
Loss from operations	(129,681)	(69,780)	(59,901)	85.8%
Other income (expense):				
Interest income	3,718	1,521	2,197	144.4%
Interest expense	(11,268)	(1,748)	(9,520)	544.6%
Other expense	(250)	(1,887)	1,637	(86.8)%
Total other income (expense)	(7,800)	(2,114)	(5,686)	269.0%
Net loss	(137,481)	(71,894)	$ (65,587)	91.2%

Product Revenue

We began commercially selling ZILRETTA within the United States in October, 2017, following FDA approval on October 6, 2017. For the year ended December 31, 2017, we recorded $0.4 million of net product revenue. For further discussion regarding our revenue recognition policy, see Note 3 to our consolidated financial statements appearing elsewhere in this Form 10-K.

Cost of Sales

Cost of sales was approximately $4 thousand for the year ended December 31, 2017. Based on our policy to expense costs associated with the manufacture of our products prior to regulatory approval, the vast majority of the costs of ZILRETTA recognized as revenue during the year ended December 31, 2017 were expenses prior to the October 2017 FDA approval of ZILRETTA and, therefore, are not included in cost of sales during the period. We expect cost of sales to increase in relation to product revenues as we deplete these inventories.

Research and Development Expenses

	Year Ended December 31,			
(In thousands)	2017	2016	Change	% Increase/ (Decrease)
Direct research and development expenses by program:				
Zilretta	$ 20,040	$ 24,609	$ (4,569)	(18.6)%
FX007	47	349	(302)	(86.5)%
FX005	—	13	(13)	(100.0)%
FX101	655	—	655	100.0%
Portfolio expansion	4,341	234	4,107	1755.1%
Other	1,080	620	460	74.2%
Total direct research and development expenses	26,163	25,825	338	1.3%
Personnel and other costs	25,068	15,489	9,579	61.8%
Total research and development expenses	$ 51,231	$ 41,314	$ 9,917	24.0%

Research and development expenses were $51.2 million and $41.3 million for the years ended December 31, 2017 and 2016, respectively. The increase in research and development expenses year over year of $9.9 million was primarily due to a $5.2 million increase in preclinical expenses related to our portfolio expansion, other program costs, FX101 and a $9.6 million increase in personnel and other employee-related costs for additional headcount and stock compensation expense. This was offset by a $4.9 million decrease in development expenses for ZILRETTA, including CMC and clinical trial costs. The primary increase in the portfolio expansion costs in 2017 is due to the December 2017 acquisition of the global rights to FX201 from GeneQuine which required an upfront payment of $2 million.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $78.8 million and $28.5 million for the years ended December 31, 2017 and 2016, respectively for a year over year increase of $50.3 million. Selling expenses were $45.9 million and $11.1 million for the years ended December 31, 2017 and 2016. The increase in selling expenses year over year of $34.8 million was primarily due to salary and related costs associated with additional headcount (an increase of 138 employees) and costs related to the creation of commercial marketing and sales capabilities.

General and administrative expenses were $32.9 million and $17.4 million for the years ended December 31, 2017 and 2016. The increase in general and administrative expenses year over year of $15.5 million was primarily due to salary and related costs associated with additional headcount and increased stock compensation expense.

Other Income (Expense)

Interest income was $3.7 million and $1.5 million for the years ended December 31, 2017 and 2016, respectively. The increase in interest income was primarily due to a larger average investment balance during 2017.

Interest expense was $11.3 million and $1.7 million for the years ended December 31, 2017 and 2016, respectively. The increase in interest expense was primarily due to interest incurred on the 2024 Convertible Notes.

Other expense was $0.3 million and $1.9 million for the years ended December 31, 2017 and 2016, respectively. Other expense decreased primarily due to foreign currency related gains realized during the year ended December 31, 2017 versus foreign currency losses incurred during the year ended December 31, 2016.

Year Ended December 31, 2016 Compared to Year Ended December 31, 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015 (certain items may not foot due to rounding):

	Year Ended December 31,			
(In thousands)	2016	2015	Change	% Increase/ (Decrease)
Revenues:				
Product revenues, net	$ —	$ —	$ —	—
Operating expenses:				
Cost of sales	—	—	—	—
Research and development	41,314	32,691	8,623	26.4%
Selling, general and administrative	28,466	13,372	15,094	112.9%
Total operating expenses	69,780	46,063	23,717	51.5%
Loss from operations	(69,780)	(46,063)	(23,717)	51.5%
Other income (expense):				
Interest income	1,521	1,246	275	22.1%
Interest expense	(1,748)	(571)	(1,177)	206.1%
Other expense	(1,887)	(927)	(960)	103.6%
Total other income (expense)	(2,114)	(252)	(1,862)	738.9%
Net loss	$ (71,894)	$ (46,315)	$ (25,579)	55.2%

Research and Development Expenses

	Year Ended December 31,			
(In thousands)	2016	2015	Change	% Increase/ (Decrease)
Direct research and development expenses by program:				
Zilretta	$ 24,609	$ 22,046	$ 2,563	11.6%
FX007	$ 349	$ 669	(320)	(47.8)%
FX005	$ 13	$ 247	(234)	(94.7)%
Portfolio expansion	$ 234	$ —	234	100.0%
Other	$ 620	$ —	620	100.0%
Total direct research and development expenses	25,825	22,962	2,863	12.5%
Personnel and other costs	15,489	9,729	5,760	59.2%
Total research and development expenses	$ 41,314	$ 32,691	$ 8,623	26.4%

Research and development expenses were $41.3 million and $32.7 million for the years ended December 31, 2016 and 2015, respectively. The increase in research and development expenses year over year of $8.6 million was primarily due to $2.6 million in ZILRETTA program expenses related to the previously completed pivotal Phase 2b clinical trial, the conduct of the recently completed Phase 3 clinical trial, and manufacturing expenses related to

clinical trial and potential commercial supplies. In addition, $6.0 million in personnel and other employee-related costs for additional headcount, stock compensation expense, and consulting costs contributed to the increase.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $28.5 million and $13.4 million for the years ended December 31, 2016 and 2015, respectively. The increase in general and administrative expenses of $15.1 million was primarily due to salary and related costs associated with additional headcount, costs related to the creation of commercial marketing and sales capabilities and stock compensation expense.

Other Income (Expense)

Interest income was $1.5 million and $1.2 million for the years ended December 31, 2016 and 2015, respectively. The increase in interest income was primarily due to a larger average investment balance during 2016.

Interest expense was $1.7 million and $0.6 million for the years ended December 31, 2016 and 2015, respectively. The increase in interest expense was primarily due to interest incurred on the $30.0 million borrowed under our credit facility with MidCap Financial Funding XIII Trust and Silicon Valley Bank, which we entered into on August 4, 2015.

Other expense was $1.9 million and $0.9 million for the years ended December 31, 2016 and 2015, respectively. Other expense increased due to a net amortization of premiums on larger average marketable securities and long-term investments balances.

Liquidity and Capital Resources

As of December 31, 2017, we have generated $0.4 million in revenue and have incurred losses since our inception in 2007. As of December 31, 2017, we had an accumulated deficit of $349.2 million. We anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development and selling, general and administrative expenses will continue to increase and, as a result, we may need additional capital to fund our operations, which we may seek to obtain through one or more equity offerings, debt and convertible debt financings, government or other third-party funding, and licensing or collaboration arrangements.

Since our inception through December 31, 2017, we have funded our operations primarily through the sale of our common stock and convertible preferred stock, convertible debt, and venture debt financing. From our inception through December 31, 2017, we had raised approximately $756 million from such transactions, including amounts from our initial and follow-on public offerings during 2014, 2016 and 2017 as well as our 2024 Convertible Notes issuance in 2017. As of December 31, 2017, we had cash and cash equivalents of $127.8 million and marketable securities of $264.6 million, and long-term investments of $31.5 million. Based on our current operating plan we anticipate that our existing cash, cash equivalents and marketable securities will fund our operations for at least the next twelve months from the date of issuance of the financial statements included in this report. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to capital preservation.

The following table shows a summary of our cash flows for each of the years ended December 31, 2017, 2016 and 2015:

	Year Ended December 31,		
(In thousands)	**2017**	**2016**	**2015**
Cash flows used in operating activities	$ (107,831)	$ (62,472)	$ (38,949)
Cash flows used in investing activities	(118,792)	(132,754)	(13,245)
Cash flows provided by financing activities	323,497	163,197	12,040
Net increase (decrease) in cash and cash equivalents	$ 96,874	$ (32,029)	$ (40,154)

Net Cash Used in Operating Activities

Operating activities used $107.8 million of cash in the year ended December 31, 2017. The cash used in operating activities in the year ended December 31, 2017 resulted primarily from our 2017 net loss of $136.8 million offset by changes in our operating assets and liabilities of $11.9 million and non-cash charges of $18.0 million. Changes in our operating assets and liabilities consisted primarily of a $2.2 million increase in accounts receivable and inventory and $0.4 million increase in prepaid expenses, offset by an increase of $10.2 million in accrued expenses and other current liabilities and an increase of $3.5 million in accounts payable. The increase in accrued expenses and other current liabilities was primarily attributable to increased expenses related to payroll and other employee related expenses, professional services fees and interest expense on loans. Non-cash charges consisted primarily of $10.8 million of stock-based compensation expense, $2.0 million in depreciation expense, $4.8 million related to the amortization of the debt discount and debt issuance costs related to the 2024 Convertible Notes, and $0.3 amortization and accretion related to our investments.

Operating activities used $62.5 million of cash in the year ended December 31, 2016. The cash used in operating activities in the year ended December 31, 2016 resulted primarily from our 2016 net loss of $71.9 million offset by changes in our operating assets and liabilities of $1.0 million and non-cash charges of $11.0 million. Changes in our operating assets and liabilities consisted primarily of a $2.9 million increase in prepaid expenses, offset by an increase of $2.8 million in accrued expenses and other current liabilities and a decrease of $1.0 million in accounts payable. The increase in accrued expenses and other current liabilities was primarily attributable to increased expenses related to clinical research and contract manufacturing services, and the costs associated with the creation of commercial marketing and sales capabilities. These changes were partially offset by an increase in other assets of $0.5 million. Non-cash charges consisted primarily of $6.8 million of stock-based compensation expense $1.2 million in depreciation expense, a $2.3 million loss on disposal of property and equipment and $0.7 amortization and accretion related to our investments.

Operating activities used $38.9 million of cash in the year ended December 31, 2015. The cash used in operating activities in the year ended December 31, 2015 resulted primarily from our 2015 net loss of $46.3 million offset by changes in our operating assets and liabilities of $1.5 million and non-cash charges of $5.9 million. Changes in our operating assets and liabilities consisted primarily of a $1.6 million increase in our accounts payable, and an increase of $0.4 million in accrued expenses. The increase in accounts payable, accrued expenses and other current liabilities was primarily attributable to increased expenses related to clinical research and contract manufacturing services. These changes were partially offset by an increase in other assets of $0.5 million. Non-cash charges consisted primarily of $4.6 million of stock-based compensation expense and $0.4 million in depreciation expense and loss on disposal of property and equipment and $0.9 amortization and accretion related to our investments.

Net Cash Used in Investing Activities

Net cash used in investing activities was $118.8 million in the year ended December 31, 2017. Net cash used in investing activities consisted primarily of cash used to purchase marketable securities of $356.7 million, partially offset by cash received from the redemption and sale of marketable securities of $240.2 million. In addition, $2.1 million of cash was used to purchase property and equipment, primarily computer equipment relating to the creation of commercial sales capabilities and further developing our manufacturing capabilities at our contract manufacturer, Patheon U.K. Limited.

Net cash used in investing activities was $132.8 million in the year ended December 31, 2016. Net cash used in investing activities consisted primarily of cash used to purchase marketable securities of $196.1 million, partially offset by cash received from the redemption and sale of marketable securities of $72.1 million. In addition, $8.4 million of cash was used to purchase property and equipment, primarily to further develop our manufacturing capabilities at our contract manufacturer, Patheon U.K. Limited.

Net cash used in investing activities was $13.2 million in the year ended December 31, 2015. Net cash used in investing activities in the year ended December 31, 2015 consisted primarily of cash used to purchase marketable securities of $145.8 million, partially offset by cash received from the redemption and sale of marketable securities of $137.7 million. In addition, $5.2 million of cash was used to purchase property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $323.4 million, $163.2 million and $12.0 million in the years ended December 31, 2017, 2016 and 2015, respectively. Net cash provided by financing activities in the year ended December 31, 2017 consisted primarily of $194.8 million of proceeds received from the issuance of the 2024 Convertible Notes, $132.7 million in proceeds from the follow-on offerings of our common stock, and $4.9 million in proceeds from the exercise of stock options and the issuance of common stock related to our employee stock purchase plan that was partially offset by $0.6 million in financing costs associated with our follow-on financing in 2017.

Net cash provided by financing activities in the year ended December 31, 2016 consisted of $15.0 million borrowed under our credit facility with MidCap Financial Funding XIII Trust and Silicon Valley Bank in July 2016, $147.9 million in proceeds from follow-on offerings of our common stock, as well as, $0.6 million in proceeds from the exercise of stock options and the issuance of common stock related to our employee stock purchase plan that was partially offset by $0.3 million in financing costs associated with our follow-on financing in 2016.

Net cash provided by financing activities in the year ended December 31, 2015 consisted of $15.0 million borrowed under our credit facility with MidCap Funding XIII Trust and Silicon Valley Bank in August 2015, offset by $3.5 million paid to satisfy our 2013 loan obligation. In addition, we received $0.9 million in proceeds from the exercise of stock options and the issuance of common stock related to our employee stock purchase plan that was partially offset by $0.2 million in financing costs associated with our follow-on financing in late 2014 and $0.1 million in issuance costs associated with our long-term loan obligation.

Contractual Obligations

The following table discloses aggregate information about our contractual obligations and the periods in which payments are due as of December 31, 2017:

	Payments Due By Period				
	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
			(in thousands)		
Long-term debt obligation (including interest)[1]	$ 25,913	$ 11,082	$ 14,831	$ —	$ —
Operating lease obligations[2]	8,587	1,338	3,024	3,022	1,203
Monthly base fee to Patheon[3]	63,646	6,891	16,216	16,216	24,323
2024 Convertible notes obligations[4]	244,832	6,792	13,584	13,584	210,872
Supply agreement with Evonik[5]	3,894	694	3,200	—	—
Total	$ 346,872	$ 26,797	$ 50,855	$ 32,822	$ 236,398

(1) Represents the contractually required principal and interest payments on our credit facility in accordance with the required payment schedule and the 9% final payment to the lender on February 1, 2020. Amounts associated with future interest payments to be made were calculated using the fixed interest rate of 6.25% per annum.

(2) Represents the contractually required payments under our operating lease obligations in existence as of December 31, 2017 in accordance with the required payment schedule. No assumptions were made with respect to renewing the lease terms at the expiration date of their initial terms.

(3) Represents the contractually required monthly base fee to Patheon for the operation of the manufacturing suite.

(4) Represents the contractually required interest payments in accordance with the required payment schedule and the final principal payment of $201.3 million due on May 1, 2024.

(5) Represents contractually required purchases of PLGA for clinical and commercial supply of ZILRETTA. The required purchases are based upon a binding 24 month rolling forecast of 100% of our total volume requirements for the PLGA product. Beginning in December, 2020, the required purchases reduce to 50% of our total volume requirements for the PLGA product. Since the current required 24 month rolling forecast does not go beyond December 2019, any potential minimum purchases in the year 2020 and beyond are not fixed or determinable and therefore no amounts are presented in the table above.

The table above reflects only payment obligations that are fixed or determinable. We enter into contracts in the normal course of business with CROs for clinical trials, with contract manufacturers for clinical and commercial supply manufacturing, and with vendors for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

In July 2015, we amended the lease for our primary office space which increased the size of our leased premises and extended the lease term through October 31, 2019. In September 2015, we exercised an option to lease an additional 5,400 square feet under this amended lease. The total cash obligation for the base rent from inception through the lease termination date for the office space committed to under the lease, as amended, is approximately $2,900,000.

On September 21, 2016, we entered into a second amendment to our existing lease for approximately 6,748 additional square feet of rented space located in Burlington, Massachusetts. The lease began October 1, 2016 and expired on October 31, 2017. During October 2016, the Company lease payment for this additional space was $18,275.83 in incremental rent. Beginning in November 2016 through October 2017, our lease payments for the additional space increased to $18,838.17 per month in incremental rental cash outflow.

On April 7, 2017, we further amended the Lease to extend the term to October 31, 2023 on the then-existing office space, including the temporary space, consisting of approximately 28,600 square feet of office space in Burlington, Massachusetts. From November 2016 through October 2017, our lease payment for this space was approximately $80,000 per month. Also, as part of this amendment to the Lease, we leased an additional 1,471 square feet of office space beginning in 2018. The lease payment for the 1,471 square feet of office space is approximately $4,100 per month.

On October 6, 2017, we exercised our option for an additional 6,450 square feet of space, with the term expected to commence on or about April 1, 2018. After April 2018, we will have approximately 36,500 square feet of office space in Burlington, Massachusetts under a lease term expiring on October 31, 2023. In addition to the base rent for the office space, which increases over the term of the amended Lease, we are responsible for its share of operating expenses and real estate taxes.

In February 2017, we entered into a five-year lease for laboratory space located in Woburn, Massachusetts with a monthly lease payment of approximately $15,000, which increases over the term of the lease, plus a share of operating expenses. The total cash obligations for the term of the lease are approximately $0.9 million.

Also in July 2015, we and Patheon U.K. Limited, or Patheon, entered into a Manufacturing and Supply Agreement, or the Manufacturing Agreement and Technical Transfer and Service Agreement, or the Technical Transfer Agreement, for the manufacture of clinical and commercial supplies of ZILRETTA.

Under the terms of the Technical Transfer Agreement, Patheon has agreed to undertake certain technical transfer activities and construction services needed to prepare its United Kingdom facility for the manufacture of ZILRETTA in dedicated manufacturing suites. This agreement will remain in effect unless and until it expires or is terminated. Upon termination of this agreement (other than termination by us in the event that Patheon does not meet the construction and manufacturing milestones or for a breach by Patheon), we will pay for the wind down costs related to the removal of our manufacturing equipment and for Patheon's termination costs up to a capped amount.

Under the terms of the Manufacturing Agreement, following the FDA approval date of the suites, we have agreed to purchase finished, packaged or unpackaged product from Patheon. In addition, we will pay a monthly base fee to Patheon for the operation of the manufacturing suites, and will reimburse Patheon for purchases of raw materials and equipment made on its behalf, certain nominal expenses and additional services. We estimate that the aggregate monthly base fees and reimbursement costs for equipment will be approximately 100 million GBP over the entire term of the Manufacturing Agreement. Unless earlier terminated, this agreement will expire on the 10th anniversary of the FDA approval date for the initial manufacturing suite. Future expenditures associated with the purchase of finished ZILRETTA product from Patheon are primarily driven by the potential commercial requirements and demand for our products which cannot be fully determined at this time.

In December 2017, we entered into a definitive agreement with GeneQuine to acquire the global rights to FX201. As part of the asset purchase transaction with GeneQuine, we made an upfront payment of $2 million. We may also be required to make additional milestone payments during the development of FX201, including up to $8.7 million through Phase 2 proof of concept (PoC) and, following successful PoC, up to an additional $54 million in development and global regulatory approval milestone payments. The transaction was accounted for as an asset acquisition, as it did not qualify as a business combination. The upfront fee was attributed to the intellectual property acquired, and recognized as research and development expense in December 2017 as the FX201 rights had not been commercially approved, and have no alternative future use. Future milestone payments earned prior to regulatory approval of FX201 would be recognized as research and development expense in the period when the milestone events become probable of being achieved. Future milestones earned upon regulatory approval would be recognized as an intangible asset and amortized to expense over its estimated life. As of December 31, 2017 none of the future milestone payments owed under the arrangement was probable of being achieved. As part of the transaction, we became the direct licensee of certain underlying Baylor College of Medicine (Baylor) patents and other proprietary rights related to FX201 for human applications. The Baylor license agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patent and other proprietary rights directly related to FX201, with a similar non-exclusive license to certain Baylor intellectual property rights that are not specific to FX201. The license agreement with Baylor includes a low single-digit royalty on net sales of FX201 and requires us to use reasonable efforts to develop FX201 according to timelines set out in the license agreement. In December 2017, we also entered into a Master Production Services Agreement with SAFC Carlsbad, Inc., a part of MilliporeSigma, for the manufacturing of pre-clinical and initial clinical supplies of FX201.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements that are reasonably likely to have a current or future material effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

Recent Accounting Pronouncements

A discussion of recent accounting pronouncements is included in Note 3 to the consolidated financial statements in this Annual Report on Form 10-K.

JOBS Act

On April 5, 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are relying on other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company," we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act, and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. As of December 31, 2017 we had not met any of these criteria.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by a sudden change in market interest rates on our investment portfolio.

- Our term loan carries a fixed interest rate and, thus, we are not subject to interest rate risk.
- We have borrowed $30.0 million under our credit facility. Amounts outstanding under the credit facility bear interest at a fixed rate equal to 6.25% per annum. As of December 31, 2017, the carrying value of the term loan was $22.9 million.
- Our 2024 Convertible Notes carry a fixed interest rate and, thus we are not subject to interest rate risk.
- We have borrowed $201.3 million under the 2024 Convertible Notes. Amounts outstanding bear interest at a fixed rate of 3.375% per annum. As of December 31, 2017, the carrying value of the 2024 Convertible Notes, net of the portion of the proceeds allocated to the conversion option and net of debt issuance costs was $137.1 million.

We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash and cash equivalents and certificates of deposit do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Most of our transactions are conducted in U.S. dollars. We do have certain material agreements with vendors located outside the United States, which have transactions conducted primarily in British Pounds and Euros. As of December 31, 2017 we had approximately $0.3 million in payables to vendors denominated in British pounds. As of December, 2017, we also had approximately $1.4 million in cash denominated in British pounds. A hypothetical 10% change in foreign exchange rates would result in either a $0.1 million increase, in the event the U.S. dollar strengthens relative to the British pound, or a $0.1 million decrease, in the event the U.S. dollar weakens relative to the British pound, of cash denominated in British pounds.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
of Flexion Therapeutics, Inc.:

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Flexion Therapeutics, Inc. and its subsidiary as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 8, 2018

We have served as the Company's auditor since 2010.

Flexion Therapeutics, Inc.

Consolidated Balance Sheets

(In thousands, except share amounts)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 127,789	$ 30,915
Marketable securities	264,589	174,688
Accounts receivable, net	410	—
Inventories	1,799	—
Prepaid expenses and other current assets	3,403	3,790
Total current assets	397,990	209,393
Property and equipment, net	11,189	11,664
Long-term investments	31,538	4,725
Restricted cash	600	480
Total assets	$ 441,317	$ 226,262
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 6,222	$ 2,161
Accrued expenses and other current liabilities	14,383	6,245
Current portion of long-term debt	9,967	9,134
Total current liabilities	30,572	17,540
Long-term debt, net	12,936	21,399
2024 convertible notes, net	137,107	—
Other long-term liabilities	428	291
Total liabilities	181,043	39,230
Commitments and contingencies		
Preferred Stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2017 and December 31, 2016 and 0 shares issued and outstanding at December 31, 2017 and December 31, 2016	—	—
Stockholders' equity:		
Common stock, $0.001 par value; 100,000,000 shares authorized; 37,610,897 and 31,667,469 shares issued and outstanding, at December 31, 2017 and December 31, 2016, respectively	38	32
Additional paid-in capital	609,810	398,757
Accumulated other comprehensive loss	(407)	(71)
Accumulated deficit	(349,167)	(211,686)
Total stockholders' equity	260,274	187,032
Total liabilities and stockholders' equity	$ 441,317	$ 226,262

The accompanying notes are an integral part of these consolidated financial statements.

Flexion Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except per share amounts)

	Year Ended December 31,		
	2017	2016	2015
Revenues:			
Product revenue, net	$ 355	$ —	$ —
Operating expenses:			
Cost of sales	4	—	—
Research and development	51,231	41,314	32,691
Selling, general and administrative	78,801	28,466	13,372
Total operating expenses	130,036	69,780	46,063
Loss from operations	(129,681)	(69,780)	(46,063)
Other income (expense):			
Interest income	3,718	1,521	1,246
Interest expense	(11,268)	(1,748)	(571)
Other expense	(250)	(1,887)	(927)
Total other income (expense)	(7,800)	(2,114)	(252)
Net loss	$ (137,481)	$ (71,894)	$ (46,315)
Net loss per common share, basic and diluted	$ (4.16)	$ (2.84)	$ (2.15)
Weighted average common shares outstanding, basic and diluted	33,027	25,297	21,497
Other comprehensive income (loss) :			
Unrealized gains (losses) from available-for-sale securities, net of tax of $0	(336)	26	(92)
Total other comprehensive income (loss)	(336)	26	(92)
Comprehensive loss	$ (137,817)	$ (71,868)	$ (46,407)

The accompanying notes are an integral part of these consolidated financial statements.

Flexion Therapeutics, Inc.

Consolidated Statements of Changes in Stockholders' Equity

(In thousands)

	Common Stock					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2014	21,440	$ 21	$ 238,402	$ (5)	$ (93,477)	$ 144,941
Issuance of common stock for equity awards	109	1	592	—	—	593
Employee Stock Purchase Plan	21	—	276			276
Stock-based compensation expense	—	—	4,583	—	—	4,583
Net loss	—	—	—	—	(46,315)	(46,315)
Other comprehensive loss	—	—	—	(92)	—	(92)
Balance at December 31, 2015	21,570	$ 22	$ 243,853	$ (97)	$ (139,792)	$ 103,986
Issuance of common stock net of issuance costs	10,040	10	147,491			147,501
Issuance of common stock for equity awards	30	—	167			167
Employee Stock Purchase Plan	27	—	476			476
Stock-based compensation expense			6,770			6,770
Net loss	—	—	—	—	(71,894)	(71,894)
Other comprehensive income	—	—	—	26		26
Balance at December 31, 2016	31,667	$ 32	$ 398,757	$ (71)	$ (211,686)	$ 187,032
Issuance of common stock net of issuance costs	5,520	6	132,171			132,177
Issuance of common stock for equity awards	334	—	3,858			3,858
Employee Stock Purchase Plan	90	—	1,016			1,016
Stock-based compensation expense	—	—	11,542			11,542
Portion of convertible debt proceeds allocated to equity component			62,466			62,466
Net loss	—	—	—	—	(137,481)	(137,481)
Other comprehensive loss	—	—	—	(336)		(336)
Balance at December 31, 2017	37,611	$ 38	$ 609,810	$ (407)	$ (349,167)	$ 260,274

The accompanying notes are an integral part of these consolidated financial statements.

Flexion Therapeutics, Inc.

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Cash flows from operating activities			
Net loss	$ (137,481)	$ (71,894)	$ (46,315)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	2,008	1,151	238
Stock-based compensation expense	11,542	6,770	4,583
Other non-cash charges	—	37	40
Amortization of premium (discount) on marketable	333	729	871
Loss on disposal of fixed assets	—	2,283	150
Amortization of convertible debt discount and debt issuance costs	4,826		
Premium paid on securities purchased	(857)	(543)	—
Changes in operating assets and liabilities:			
Accounts receivable	(410)	95	—
Inventory	(1,799)	—	—
Prepaid expenses, other current and long-term assets	387	(2,873)	(526)
Accounts payable	4,188	(993)	1,581
Accrued expenses and other current and long-term liabilities	9,432	2,766	429
Net cash used in operating activities	(107,831)	(62,472)	(38,949)
Cash flows from investing activities			
Purchases of property and equipment	(2,146)	(8,440)	(5,197)
Change in restricted cash	(120)	(400)	48
Purchases of marketable securities	(356,754)	(196,061)	(145,798)
Sale and redemption of marketable securities	240,228	72,147	137,702
Net cash used in investing activities	(118,792)	(132,754)	(13,245)
Cash flows from financing activities			
Proceeds from the issuance of 2024 convertible notes	201,250	—	-
Payment of debt issuance costs	(6,470)	(42)	(108)
Proceeds from the offering of common stock	132,666	147,889	—
Payments on notes payable	(8,333)	—	(3,500)
Proceeds from issuance of notes payable	—	15,000	15,004
Payments of public offering costs	(490)	(293)	(225)
Proceeds from the exercise of stock options	3,858	167	593
Proceeds from Employee Stock Purchase Plan	1,016	476	276
Net cash provided by financing activities	323,497	163,197	12,040
Net increase (decrease) in cash and cash equivalents	96,874	(32,029)	(40,154)
Cash and cash equivalents at beginning of period	30,915	62,944	103,098
Cash and cash equivalents at end of period	$ 127,789	$ 30,915	$ 62,944
Supplemental disclosures of cash flow information:			
Cash paid for interest	$ 5,080	$ 1,297	$ 572
Supplemental disclosures of non-cash financing activities:			
Public offering costs included in accounts payable or accrued	$ —	$ 95	$ —
Portion of debt proceeds allocated to equity component	$ 62,466	$ —	$ —
Purchases of property and equipment in accounts payable and accrued expenses	$ 9	$ 622	$ 1,576

The accompanying notes are an integral part of these consolidated financial statements.

Flexion Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of the Business

Flexion Therapeutics, Inc. ("Flexion" or the "Company") was incorporated under the laws of the state of Delaware on November 5, 2007. Flexion is a biopharmaceutical company focused on the development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis ("OA"), a type of degenerative arthritis. On October 6, 2017, the U.S. Food and Drug Administration, or FDA, approved ZILRETTA®, as the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA related knee pain. ZILRETTA is a non-opioid therapy that employs Flexion's proprietary microsphere technology to provide pain relief over 12 weeks.

The Company is subject to risks and uncertainties common to companies in the biopharmaceutical industry, including, but not limited to, new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, and the ability to secure additional capital to fund operations. Successfully commercializing ZILRETTA will require significant sales and marketing efforts and the Company's pipeline programs may require significant additional research and development efforts, including extensive preclinical and clinical testing. These activities will in turn require significant amounts of capital, adequate personnel infrastructure and extensive compliance reporting capabilities. There can be no assurance when, if ever, the Company will realize significant revenue from the sales of ZILRETTA or if the development efforts supporting the Company's pipeline, including future clinical trials, will be successful.

The accompanying consolidated financial statements have been prepared on a basis which assumes that the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the normal course of business. The Company has incurred recurring losses and negative cash flows from operations. As of December 31, 2017, the Company had cash, cash equivalents, marketable securities, and long-term investments of $423.9 million. Management believes that current cash, cash equivalents and marketable securities on hand at December 31, 2017 should be sufficient to fund operations for at least the next twelve months beyond the date of issuance of these financial statements. The future viability of the Company is dependent on its ability to raise additional capital to finance its operations and to fund increased research and development costs in order to seek approval for commercialization of its product candidates. This capital is necessary for the Company to support the commercialization of ZILRETTA and to perform the research and development activities required to develop the Company's product candidates in order to generate future revenue streams. The Company may not be able to obtain financing on acceptable terms, or at all. If the Company is unable to obtain funding on a timely basis the Company may need to curtail its operations including research and development which could adversely affect its prospects.

2. Financing Transactions

On June 8, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,900,000 shares of the Company's common stock at a price to the public of $14.00 per share including shares sold pursuant to the partial exercise of the underwriters' option to purchase additional shares. The Company received net proceeds from the follow-on financing of $77.4 million after deducting underwriting discounts, commissions, and offering costs paid by the Company.

On November 15, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 4,140,000 shares of the Company's common stock at a price to the public of $18.00 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares. The Company received net proceeds from the follow-on financing of $70.1 million after deducting underwriting discounts, commissions, and offering costs paid by the Company.

On May 2, 2017 the Company issued an aggregate of $201.3 million principal amount of the 2024 Convertible Notes. The 2024 Convertible Notes have a maturity date of May 1, 2024 are unsecured and accrue interest at a rate of 3.375% per annum, payable semi-annually on May 1 and November 1 of each year, beginning November 1, 2017. The Company received $194.8 million for the sale of the 2024 Convertible Notes, after deducting fees and expenses of $6.5 million.

On October 16, 2017, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,520,000 shares of the Company's common stock at a price to the public of $25.50 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares. The Company received net proceeds from the follow-on financing of $132.2 million after deducting underwriting discounts, commissions, and offering costs paid by the Company.

The Company's total issued common stock as of December 31, 2017 was 37,610,897 shares.

3. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC") and Generally Accepted Accounting Principles ("GAAP") for financial information, including the accounts of the Company and its wholly owned subsidiary after elimination of all significant intercompany accounts and transactions.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and judgments that may affect the reported amounts of assets and liabilities, expenses and related disclosures. The Company bases estimates and judgments on historical experience and on various other factors that it believes to be reasonable under the circumstances. The most significant estimates in these consolidated financial statements include useful lives with respect to long-lived assets, such as property and equipment and leasehold improvements, accounting for stock-based compensation, and accrued expenses, including clinical research costs. The Company's actual results may differ from these estimates under different assumptions or conditions. The Company evaluates its estimates on an ongoing basis. Changes in estimates are reflected in reported results in the period in which they become known by the Company's management.

Revenue Recognition

On October 6, 2017, the FDA approved ZILRETTA. The Company entered into a limited number of arrangements with specialty distributors and a specialty pharmacy in the U.S. (collectively, its "Customers") to distribute ZILRETTA. These arrangements are the Company's initial contracts with customers and, as a result the Company adopted Accounting Standards Codification ("ASC") Topic 606 - *Revenue from Contracts with Customers* ("Topic 606") as of January 1, 2017. There is no impact for the transition to Topic 606 because the Company had no historical revenue prior to the launch of ZILRETTA. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract with a customer under Topic 606, including when it is probable that the entity will collect the consideration it is

entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product revenue, see *Product Revenue, Net* (below).

Product Revenue, Net— The Company sells ZILRETTA to its customers who then subsequently resell the Company's products to physicians, clinics and certain medical centers or hospitals. In addition to distribution agreements with customers, the Company enters into arrangements with government payers that provide for government mandated rebates and chargebacks with respect to the purchase of the Company's products.

The Company recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time (upon delivery to the customer). We have determined that the delivery of ZILRETTA to our customers constitutes a single performance obligation. There are no other promises to deliver goods or services beyond what is specified in each accepted customer order. Management has assessed the existence of a significant financing component in the agreements with our customers. The trade payment terms with our customers do not exceed one year and therefore management has elected to apply the practical expedient and no amount of consideration has been allocated as a financing component. Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee for service amounts that are detailed within contracts between the Company and its customers relating to the Company's sale of its products. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. The Company's analyses also contemplated application of the constraint in accordance with the guidance, under which it determined a material reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2017 and, therefore, the transaction price was not reduced further during the year ended December 31, 2017. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's original estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances—The Company compensates (through trade discounts and allowances) its customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss through December 31, 2017, as well as a reduction to trade receivables, net on the condensed consolidated balance sheets.

Product Returns— Consistent with industry practice, the Company generally offers customers a limited right of return for product that has been purchased from the Company based on the product's expiration date. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, net on the condensed consolidated balance sheets. The Company currently estimates product return liabilities using available industry data and its own sales information, including its visibility into the inventory remaining in the distribution channel. The Company has not received any returns to date and believes that returns of its products will be minimal.

Government Chargebacks, Discounts and Rebates— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified VA hospitals and 340b entities at prices lower than the list prices charged to customers who directly purchase the product from the Company. The 340b Drug Discount Program is a US federal government program created in 1992 that requires drug manufacturers to provide outpatient drugs to eligible health care organizations and covered entities at significantly reduced prices. Customers charge the Company for the difference between what they pay for the product and the statutory selling price to the qualified government entity. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and trade receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the Customer's notification to the Company of the resale. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at each reporting period-end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

Government Rebates— The Company is subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the condensed consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. We anticipate the Company's exposure to utilization from the Medicare Part D coverage gap discount program to be immaterial. For Medicaid programs, the Company estimates the portion of sales attributed to Medicaid patients and records a liability for the rebates to be paid to the respective state Medicaid programs. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Other Incentives— Other incentives which the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the condensed consolidated balance sheets.

To date, the Company's only source of product revenue has been from the U.S. sales of ZILRETTA, which it began shipping to customers in October 2017.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the year ended December 31, 2017:

(In thousands)	Trade Discounts, Allowances and Government chargebacks	Government rebates and other incentives	Returns	Total
Beginning Balance	$ —	$ —	$ —	$ —
Provision related to sales in the current year	100	15	2	117
Credit and payments made	(40)	0	0	(40)
Ending Balance	$ 60	$ 15	$ 2	$ 77

Product Revenue Reserves and Allowances – Chargebacks and fees are recorded as reductions of trade receivables, net on the condensed consolidated balance sheets. Government and other rebates and returns are recorded as a component of accrued expenses and other current liabilities on the condensed consolidated balance sheets.

Inventory—The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of product revenues. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of product sales in the consolidated statements of operations and comprehensive loss.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired prior to receipt of marketing approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign. Inventory produced that will be used in promotional marketing campaigns is expensed to selling, general and administrative expense when it is selected for use in a marketing program.

Shipping and handling costs for product shipments are recorded as incurred in cost of product revenues along with costs associated with manufacturing the product, and any inventory write-downs.

Consolidation

The accompanying consolidated financial statements include the Company and its wholly-owned subsidiary, Flexion Securities Corporation, Inc. The Company has eliminated all intercompany transactions. In addition, Flexion Therapeutics, Inc. is registered to do business in the United Kingdom through its branch office located in Swindon, United Kingdom.

U.S. Government Grant

In 2015, the Company performed research and development for a U.S. Government agency under a cost reimbursable grant for clinical development of ZILRETTA. The related costs incurred under the grant are included in research and development expense in the statement of operations. Reimbursements were recorded as an offset to R&D expense when invoices for allowable costs were prepared and submitted to the Department of Defense. Due to challenges of enrolling military personnel with post-traumatic knee OA, we discontinued the Phase 2 trial and terminated the grant as of July 31, 2016. Payments under cost reimbursable grants with agencies of the U.S. Government are provisional payments subject to adjustment upon audit by the U.S. government.

Accounts Receivable

Accounts receivable are recorded net of customer allowances for distribution fees and chargebacks, and doubtful accounts. Allowances for distribution fees and chargebacks are based on contractual terms. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers and individual customer circumstances. At December 31, 2017, the Company determined that an allowance for doubtful accounts was not required. No accounts were written off during the year ended December 31, 2017.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The Company currently invests available cash in money market funds of a major financial institution, corporate bonds, government obligations and commercial paper.

Marketable Securities

Marketable securities consist of investments with original maturities greater than ninety days and less than one year from the balance sheet date. Long-term investments consist of investments with maturities of greater than one year. The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Realized gains and losses are determined on a specific identification basis and are included in other income (loss). Amortization and accretion of discounts and premiums is recorded in other income.

Restricted Cash

The balance at December 31, 2017 consists of $600,000 in an account at a commercial bank to collateralize a credit card account, which is classified as long-term restricted cash.

The balance at December 31, 2016 consists of a $30,000 certificate of deposit to collateralize a credit card account with a commercial bank with an additional $400,000 to further collateralize the credit card account, and classified as long-term restricted cash. In addition, the Company held a letter of credit to the lessor of the Company's Burlington facility of $50,000 as a security deposit pursuant to the lease agreement and classified as long-term restricted cash. In 2017, the certificate of deposit and the letter of credit were closed and reclassified out of restricted cash.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation and amortization expense is recognized using the straight-line method over the following estimated useful lives:

	Estimated Useful Life (Years)
Computers, office equipment, and minor computer software	3
Computer software	7
Manufacturing equipment	7-10
Furniture and fixtures	5

Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Costs of major additions and betterments are capitalized and depreciated on a straight-line basis over their useful lives. Repairs and maintenance costs are expensed as incurred. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to income. Property and equipment includes construction-in-progress, which is not yet in service, and is estimated to have a useful life of 7 years once placed into service.

Foreign Currencies

The Company maintains a bank account designated in British Pounds. All foreign currency payables and cash balances are measured at the applicable exchange rate at the end of the reporting period. All associated gains and losses from foreign currency transactions are reflected in the consolidated statements of operations within other income and expenses.

Impairment of Long-Lived Assets

The Company reviews its long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows.

Debt Issuance Costs, net

As of December 31, 2017 and 2016, the carrying value of debt issuance costs was $4,111,729 and $100,760, respectively, presented as a direct deduction from the carrying amounts of long-term debt. In addition, $356,852, $36,607 and $41,103 respectively, of debt issuance costs were amortized and recognized as interest expense in the statement of operations for the years ended December 31, 2017, 2016 and 2015.

Research and Development

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, depreciation, clinical trial and related clinical manufacturing costs, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock based-awards granted to employees at the fair value at the date of grant using the Black-Scholes option-pricing model. The fair value of the awards is recognized as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is re-measured using the then current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies stock-based compensation expense in the consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified, or in the case of a non-employee, in the same manner as the award recipient's service costs are classified.

The Company recognizes compensation expense only for the portion of awards that are expected to vest. The Company accounts for forfeitures as they occur and does not estimate future forfeitures. As such, previously recognized compensation expense for an award shall be reversed in the period that the award is forfeited.

Concentration of Credit Risk and Significant Suppliers

Financial instruments that potentially expose the Company to concentration of credit risk consist primarily of commercial paper and corporate bonds. The Company generally invests its cash in money market funds, government and corporate bonds, and commercial paper at one financial institution. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is completely dependent on third-party manufacturers and product suppliers for research and commercial activities. In particular, the Company relies on a limited number of manufacturers and relies on them to purchase from third-party suppliers the materials necessary to produce its product candidates for its clinical trials and for commercial supply. These programs would be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients.

For the year-ended December 31, 2017, two individual customers accounted for 94% of the Company's total revenue and accounts receivable. No other customer accounted for more than 10% of net product revenue or accounts receivable for the year-ended December 31, 2017.

Comprehensive Loss

Comprehensive income (loss) includes net loss as well as other changes in stockholders' deficit that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) in all periods presented was unrealized gains (losses) on available-for-sale securities.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the differences between financial statement carrying amounts of existing assets and liabilities and their respective tax basis. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Fair Value Measurements

Fair value is defined as the exchange price that would be received to sell an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. Valuation techniques used to measure fair value must

maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted market prices in active markets for identical assets or liabilities. Level 1 consists primarily of financial instruments whose value is based on quoted market prices, such as exchange-traded instruments and listed equities.
- Level 2 — Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's financial instruments consist of cash equivalents, marketable securities, restricted cash, accounts payable and accrued expenses, its term loan and 2024 Convertible Notes (Note 10). The estimated fair value of the Company's financial instruments, with the exception of the 2024 Convertible Notes, approximates their carrying values.

The fair value of the 2024 Convertible Notes, which differs from their carrying value, is influenced by interest rates, stock price and stock price volatility and is determined by prices for the 2024 Convertible Notes observed in market trading. The market for trading of the 2024 Convertible Notes is not considered to be an active market and therefore the estimate of fair value is based on Level 2 inputs. The estimated fair value of the 2024 Convertible Notes, face value of $201.3 million, was $248.9 million at December 31, 2017.

Net Loss Per Share

The Company follows the two-class method when computing net loss per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based on their respective rights to receive dividends as if all income for the period had been distributed.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net loss attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities, including the assumed conversion of our 2024 Convertible Notes, outstanding stock options and unvested restricted common stock, except where the result would be anti-dilutive. Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of the conversion of the 2024 Convertible Notes, the exercise of outstanding stock options and the vesting unvested restricted common stock. In the diluted net loss per share calculation, net loss would also be adjusted for the elimination of interest expense on the 2024 Convertible Notes, if the impact was not anti-dilutive. For periods in which the Company has reported net losses, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Potential common shares will always be anti-dilutive for periods in which the Company has reported a net loss. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for the years ended December 31, 2017, 2016 and 2015.

Segment Data

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company is a biopharmaceutical company focused on the development and commercialization of novel, local therapies. All revenues for the year ended December 31, 2017 were generated in the United States.

Recently Issued and Adopted Accounting Pronouncements

In May 2014, the FASB issued guidance which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. In August 2015, the FASB issued Accounting Standards Update 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date. This latest standard defers the effective date of revenue standard ASU 2014-09 by one year and permits early adoption on a limited basis. Since the Company has not generated revenue to date, this guidance will only impact future periods, if any, when revenue is earned. This update will replace existing revenue recognition guidance under GAAP when it becomes effective for the Company beginning January 1, 2018, with early adoption permitted in the first quarter of 2017. The updated standard will permit the use of either the retrospective or cumulative effect transition method. The Company adopted this guidance as of January 1, 2017. As the Company had not recognized any revenue under the prior revenue recognition guidance, there was no impact from the adoption of the new revenue recognition guidance.

In July 2015, the FASB issued ASU No. 2015-11, *Inventory (Topic 330): Simplifying the Measurement of Inventory* ("ASU 2015-11"). The new standard applies only to inventory for which cost is determined by methods other than last-in, first-out and the retail inventory method, which includes inventory that is measured using first-in, first-out or average cost. Inventory within the scope of ASU 2015-11 is required to be measured at the lower of cost and net realizable value. Net realizable value is the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation. ASU 2015-11 was effective for us on January 1, 2017. The adoption of ASU 2015-11 did not have a material impact on our results of operations, cash flows or financial position.

In November 2015, the FASB issued ASU 2015-17, *Income Taxes* (Topic 740), to simplify the presentation of deferred income taxes. Under the new standard, both deferred tax liabilities and assets are required to be classified as noncurrent in a classified balance sheet. ASU 2015-17 became effective for the Company on January 1, 2017. Given the Company has a full valuation against its deferred tax assets and liabilities, adopting this guidance did not have a material impact to the Company's financial statements.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities* ("ASU 2016-01"). This new standard amends certain aspects of accounting and disclosure requirements of financial instruments, including the requirement that equity investments with readily determinable fair values be measured at fair value with changes in fair value recognized in our results of operations. This new standard does not apply to investments accounted for under the equity method of accounting or those that result in consolidation of the investee. Equity investments that do not have readily determinable fair values may be measured at fair value or at cost minus impairment adjusted for changes in observable prices. A financial liability that is measured at fair value in accordance with the fair value option is required to be presented separately in other comprehensive income for the portion of the total change in the fair value resulting from change in the instrument-specific credit risk. In addition, a valuation allowance should be evaluated on deferred tax assets related to available-for-sale debt securities in combination with other deferred tax assets. ASU 2016-01 will be effective for us on January 1, 2018. The adoption of ASU 2016-01 is not expected to have a material impact on our financial position or results of operations.

In February 2016, the FASB issued ASU 2016-02, *Leases* ("ASU 2016-02"), to increase transparency and comparability among organizations by recognizing lease assets and liabilities, including for operating leases, on the balance sheet and disclosing key information about leasing arrangements. ASU 2016-02 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018. The Company is currently evaluating the impact that the adoption of this guidance may have on the Company's financial statements. We currently expect that most of our operating lease commitments will be subject to the new standard and recognized as operating lease liabilities and right-of-use assets upon our adoption of ASU 2016-02.

In March 2016, the FASB released ASU 2016-09, which amends ASC Topic 718, Compensation-Stock Compensation, to require changes to several areas of employee share-based payment accounting in an effort to simplify share-based reporting. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, forfeitures, and intrinsic value accounting for private entities. ASU 2016-09 became effective for the Company on January 1, 2017. Upon adoption, the Company no longer records stock compensation expense net of forfeitures and the impact of adopting the guidance was not material to the consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). The new standard requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. ASU 2016-13 will be effective for us for fiscal years beginning on or after January 1, 2020, including interim periods within those annual reporting periods and early adoption is permitted. We are currently evaluating the impact of our adoption of ASU 2016-13 in our consolidated financial statements.

In August 2016, the FASB issued ASU 2016-15, Statement of cash flows (Topic 230), to increase the consistency of presentation in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. ASU 2016-15 will become effective for fiscal years, and the interim periods within those years, beginning after December 15, 2017. The Company is currently evaluating the potential impact that the adoption of this guidance may have on the Company's financial statements.

In November, 2016, the FASB issued ASU 2016-18, *Statement of cash flows* (Topic 230): Restricted Cash, to provide specific guidance on the cash flow classification and presentation of changes in restricted cash and restricted cash equivalents. The amendments in ASU 2016-18 require that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 will become effective for fiscal years, and the interim periods within those years, beginning after December 15, 2017. Early adoption is permitted, including adoption in an interim period. The Company is currently evaluating the impact of this accounting standard on its condensed consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU 2017-01"). This new standard clarifies the definition of a business and provides a screen to determine when an integrated set of assets and activities is not a business. The screen requires that when substantially all of the fair value of the gross assets acquired (or disposed of) is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. ASU 2017-01 will be effective for us on January 1, 2018. However, we have adopted ASU 2017-01 as of January 1, 2017, with prospective application to any business development transaction.

4. Fair Value of Financial Assets

The following tables present information about the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2017 and 2016 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2017 Units:			
(In thousands)	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ —	$ 109,196	$ —	$ 109,196
Marketable securities	—	296,127	—	296,127
	$ —	$ 405,323	$ —	$ 405,323

(In thousands)	Fair Value Measurements as of December 31, 2016 Units: Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ —	$ 9,830	$ —	$ 9,830
Marketable securities	—	179,414	—	179,414
	$ —	$ 189,244	$ —	$ 189,244

As of December 31, 2017 and 2016, the Company's cash equivalents that are invested in money market funds are valued based on Level 2 inputs. The Company measures the fair value of marketable securities using Level 2 inputs and primarily relies on quoted prices in active markets for similar marketable securities. During the years ended December 31, 2017 and 2016, there were no transfers between Level 1, Level 2 and Level 3. Amortization and accretion of discounts and premiums are recorded in other income.

The Company has a term loan outstanding under its 2015 credit facility with MidCap Financial Funding XIII Trust and Silicon Valley Bank (the "2015 term loan"). The amount outstanding on its 2015 term loan is reported at its carrying value in the accompanying balance sheet. The Company determined the fair value of the 2015 term loan using an income approach that utilizes a discounted cash flow analysis based on current market interest rates for debt issuances with similar remaining years to maturity, adjusted for credit risk. The 2015 term loan was valued using Level 2 inputs as of December 31, 2017 and December 31, 2016. The result of the calculation yielded a fair value that approximates its carrying value.

On May 2, 2017 the Company issued 3.375% convertible senior notes due 2024 (the "2024 Convertible Notes") with embedded conversion features. The Company estimated the fair value of the 2024 Convertible Notes using a discounted cash flow approach to derive the value of a debt instrument using the expected cash flows and the estimated yield related to the convertible notes. The significant assumptions used in estimating the expected cash flows were: the estimated market yield based on an implied yield and credit quality analysis of a term loan with similar attributes, and the average implied volatility of the Company's traded and quoted options available as of May 2, 2017. The Company recorded approximately $136.7 million as the fair value of the liability on May 2, 2017, with a corresponding amount recorded as a discount on the initial issuance of the 2024 Convertible Notes of approximately $64.5 million. The debt discount was recorded to equity and is being amortized to the debt liability over the life of the 2024 Convertible Notes using the effective interest method.

The fair value of the 2024 Convertible Notes, which differs from their carrying value, is influenced by interest rates, stock price and stock price volatility and is determined by prices for the 2024 Convertible Notes observed in market trading. The market for trading of the 2024 Convertible Notes is not considered to be an active market and therefore the estimate of fair value is based on Level 2 inputs. The estimated fair value of the 2024 Convertible Notes, face value of $201.3 million, was $248.9 million at December 31, 2017.

5. Marketable Securities

As of December 31, 2017 and 2016, the fair value of available-for-sale marketable securities by type of security was as follows:

(In thousands)	December 31, 2017 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial Paper	$ 22,436		$ —	$ 22,436
U.S.Government obligations	$ 121,470	$ —	$ (136)	$ 121,334
Corporate Bonds	$ 152,630	$ —	$ (273)	$ 152,357
	$ 296,536	$ —	$ (409)	$ 296,127

	December 31, 2016			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial Paper	$ 7,769	$ —	$ —	$ 7,769
U.S.Government obligations	$ 75,524	$ 5	$ (12)	$ 75,517
Corporate Bonds	$ 96,193	$ 1	$ (66)	$ 96,128
	$ 179,486	$ 6	$ (78)	$ 179,414

At December 31, 2017, marketable securities consisted of $264.6 million of investments that mature within twelve months and $31.5 million of investments that mature within fifteen months. At December 31, 2016, marketable securities consisted of $174.7 million of investments that mature within twelve months and $4.7 million of investments that mature within fifteen months.

6. Prepaid Expenses, Other Current Assets, and Other Assets

Prepaid expenses and other current assets and other assets consisted of the following as of December 31, 2017 and 2016:

	December 31,	
(in thousands)	2017	2016
Prepaid expenses	$ 2,359	$ 1,086
Deposits	66	2,099
Interest receivable on marketable securities	978	605
Total prepaid expenses and other current assets	$ 3,403	$ 3,790

On December 1, 2016, Flexion paid a refundable NDA fee in the amount of $2.0 million to the FDA. The Company evaluated each of the published criteria to qualify for a waiver and concluded all criteria were met and thus, obtaining a refund of the fee was probable. As of December 31, 2016 the NDA fee was classified as a deposit in other current assets. On May 16, 2017, Flexion received the full refund of this NDA fee.

7. Inventory

Inventory consisted of the following as of December 31, 2017:

	December 31,	
(In thousands)	2017	2016
Raw Materials	$ 928	$ -
Work in process	746	-
Finished goods	125	-
Total inventories	$ 1,799	$ -

Inventory acquired prior to receipt of the marketing approval for ZILRETTA was expensed as research and development expense as incurred. The Company began to capitalize the costs associated with the production of ZILRETTA upon receipt of FDA approval of ZILRETTA on October 6, 2017. The Company reduces its inventory to net realizable value for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders, as well as product shelf life. At December 31, 2017, the Company determined that no write-downs to inventory for potentially excess, dated or obsolete inventory were required.

8. Property and Equipment, Net

Property and equipment, net, as of December 31, 2017 and 2016 consisted of the following:

	December 31,	
(In thousands)	2017	2016
Computer and office equipment	$ 1,124	$ 573
Manufacturing equipment	11,780	10,099
Furniture and fixtures	456	402
Software	434	434
Leasehold improvements	474	278
Construction—in progress	305	1,254
	14,573	13,040
Less: Accumulated depreciation	(3,384)	(1,376)
Total property and equipment, net	$ 11,189	$ 11,664

Depreciation expense for the years ended December 31, 2017, 2016 and 2015, was $2.0 million , $1.2 million, and $0.2 million, respectively. During the years ended December 31, 2017, 2016, and 2015, $0, $2.7 million, and $0.2 million of property and equipment was disposed of, resulting in a loss of $0, $2.3 million, and $0.1 million, respectively.

9. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities at December 31, 2017 and 2016 consisted of the following:

	December 31,	
(In thousands)	2017	2016
Research and Development	$ 1,023	$ 1,605
Payroll and other employee-related expenses	9,309	3,393
Professional services fees	2,591	927
Interest expense	1,249	161
Other	211	159
Total accrued expenses and other current liabilities	$ 14,383	$ 6,245

10. Debt

Term Loan

On August 4, 2015, the Company entered into a credit and security agreement with MidCap Financial Trust, as agent, and MidCap Financial Funding XIII Trust and Silicon Valley Bank, as lenders, (the "Lenders"), to borrow up to $30,000,000 in term loans. The Company concurrently borrowed an initial term loan of $15,000,000 under the facility. The Company granted the Lenders a security interest in substantially all of its personal property, rights and assets, other than intellectual property, to secure the payment of all amounts owed under the credit facility. The Company agreed not to encumber any of its intellectual property without the Lenders' prior written consent. The Company also agreed to maintain a balance in cash or cash equivalents at Silicon Valley Bank equal to the principal balance of the loan plus 5% for so long as the Company maintains any cash or cash equivalents in non-secured bank accounts.

On July 22, 2016, the Company borrowed the remaining $15,000,000 under the credit and security agreement, in the form of a second term loan. The second term loan is subject to the same credit terms as the initial term loan under the facility.

The credit and security agreement also contains certain representations, warranties, and covenants of the Company as well as a material adverse event clause. As of December 31, 2017, the Company was compliant with financial covenants.

Borrowings under the credit facility accrue interest monthly at a fixed interest rate of 6.25% per annum. Following an interest-only period of 19 months, principal will be due in 36 equal monthly installments commencing March 1, 2017 and ending February 1, 2020 (the "maturity date"). Upon the maturity date, the Company will be obligated to pay a final payment equal to 9% of the total principal amounts borrowed under the facility. The final payment amount is being accreted to the carrying value of the debt using the straight line method, which approximates the effective interest method. As of December 31, 2017, the carrying value of the term loan was approximately $22.9 million, of which $10.0 million was due within 12 months and $12.9 million was due in greater than 12 months.

In connection with the credit and security agreement, the Company incurred debt issuance costs totaling approximately $150,000. These costs are being amortized over the estimated term of the debt using the straight-line method which approximates the effective interest method. The Company deducted the debt issuance costs from the carrying amount of the debt as of December 31, 2017 and December 31, 2016.

As of December 31, 2017, annual principal and interest payments due under the 2015 term loan are as follows:

Year	Aggregate Minimum Payments
2018	11,082
2019	10,449
2020	4,383
Total	$ 25,914
Less interest	(311)
Less final payment	(2,700)
Total	$ 22,903

2024 Convertible Notes

On May 2, 2017 the Company issued an aggregate of $201.3 million principal amount of the 2024 Convertible Notes. The 2024 Convertible Notes have a maturity date of May 1, 2024 are unsecured and accrue interest at a rate of 3.375% per annum, payable semi-annually on May 1 and November 1 of each year, beginning November 1, 2017. The Company received $194.8 million in proceeds for the sale of the 2024 Convertible Notes, after deducting fees and expenses of $6.5 million.

Upon conversion of the 2024 Convertible Notes, at the election of each holder of a 2024 Convertible Note (the Holder), the note will be convertible into cash, shares of the Company's common stock, or a combination thereof, at the Company's election (subject to certain limitations in the 2015 term loan), at a conversion rate of approximately 37.3413 shares of common stock per $1,000 principal amount of the 2024 Convertible Notes, which corresponds to an initial conversion price of approximately $26.78 per share of the Company's common stock.

The conversion rate is subject to adjustment from time to time upon the occurrence of certain events, including, but not limited to, fundamental change events and certain corporate events that occur prior to the maturity date of the notes. In addition, if the Company delivers a notice of redemption, the Company will increase, in certain circumstances, the conversion rate for a holder who elects to convert its notes in connection with such a corporate event or notice of redemption, as the case may be. At any time prior to the close of business on the business day immediately preceding February 1, 2024, Holders may convert all, or any portion, of the 2024 Convertible Notes at their option only under the following circumstances:

(1) during any calendar quarter commencing after the calendar quarter ending on June 30, 2017 (and only during such calendar quarter), if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

(2) during the five business day period after any ten consecutive trading day period (the "measurement period") in which the trading price per $1,000 principal amount of notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;

(3) if the Company calls any or all of the notes for redemption, at any time prior to the close of business on the business day immediately preceding the redemption date; and

(4) upon the occurrence of specified corporate events.

On or after February 1, 2024, until the close of business on the business day immediately preceding the maturity date, holders may convert their notes at any time, regardless of the foregoing circumstances. The Company may redeem, for cash, all or any portion of the 2024 Convertible Notes, at its option, on or after May 6, 2020 if the last reported sale price of the Company's common stock has been at least 130% of the conversion price for at least 20 trading days during any 30 consecutive day trading period, at a redemption price equal to 100% of the principal amount of the 2024 Convertible Notes to be redeemed, plus accrued and unpaid interest.

The 2024 Convertible Notes are considered convertible debt with a cash conversion feature. Per ASC 470-20, Debt with Conversion and Other Options, the Company has separated the convertible debt into liability and equity components based on the fair value of a similar debt instrument excluding the embedded conversion option. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature. The allocation was performed in a manner that reflected our non-convertible debt borrowing rate for similar debt. The equity component of the 2024 Convertible Notes was recognized as a debt discount and represents the difference between the proceeds from the issuance of the 2024 Convertible Notes and the fair value of the liability of the 2024 Convertible Notes on their respective dates of issuance. The excess of the principal amount of the liability component over its carrying amount ("debt discount") is amortized to interest expense using the effective interest method over seven years. The equity component is not re-measured as long as it continues to meet the conditions for equity classification. The liability component of $136.7 million was recorded as long-term debt at May 2, 2017 with the remaining equity component of $64.5 million recorded as additional paid-in capital.

In connection with the issuance of the 2024 Convertible Notes, the Company incurred approximately $6.5 million of debt issuance costs, which primarily consisted of underwriting, legal and other professional fees, and allocated these costs to the liability and equity components based on the allocation of the proceeds. Of the total debt issuance costs, $4.4 million were allocated to the liability component and are recorded as a reduction of the 2024 Convertible Notes in our consolidated balance sheets. The remaining $2.1 million was allocated to the equity component and is recorded as a reduction to additional paid-in capital.

Debt discount and issuance costs of $68.9 million are being amortized to interest expense over the life of the 2024 Convertible Notes using the effective interest rate method. As of December 31, 2017, the stated interest rate was 3.375%, and the effective interest rate was 9.71%. Interest expense related to the 2024 Convertible Notes for the year ended December 31, 2017 was $9.0 million, including $4.4 million related to amortization of the debt discount.

The table below summarizes the carrying value of the 2024 Convertible Notes as of December 31, 2017:

	(*in thousands*)
Gross proceeds	$ 201,250
Portion of proceeds allocated to equity component (additional paid-in capital)	(64,541)
Debt issuance costs	(6,470)
Portion of issuance costs allocated to equity component (additional paid-in capital)	2,075
Amortization of debt discount and debt issuance costs	4,793
Carrying value 2024 Convertible Notes	$ 137,107

11. Preferred Stock

On February 17, 2014, the Company filed an amended and restated Certificate of Incorporation (the "Restated Certificate") in connection with the closing of the Company's initial public offering. As of December 31, 2017, under the Restated Certificate, the Company is authorized to issue 10,000,000 shares of preferred stock with a par value of $0.001 per share.

12. Common Stock

On June 7, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,900,000 shares of the Company's common stock at a price to the public of $14.00 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On November 15, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 4,140,000 shares of the Company's common stock at a price to the public of $18.00 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On October 16, 2017, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,520,000 shares of the Company's common stock at a price to the public of $25.50 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of any holders of Preferred Stock. As of December 31, 2017, no dividends have been declared.

13. Commitments and Contingencies

Operating Leases

Burlington Lease

In May 2013, the Company entered into a lease for office space in Burlington, Massachusetts (the "Lease"). The term of the Lease was for 42-months with minimum monthly lease payments beginning at $17,588 per month and escalating over the lease term. In July 2015, the Company amended the Lease to add approximately 4,700 square feet of additional office space, with the option to lease and additional 5,400 square feet in the same building in Burlington, Massachusetts. In addition, at the time, the Company leased approximately 6,700 square feet of temporary space for use prior to delivery of the additional space. This amendment also extended the term of the Lease through October 31, 2019. On September 30, 2015, the Company exercised its option for the additional 5,400 square feet of office space. On September 21, 2016, the Company entered into another amendment to extend the Lease for the 6,700 square feet of temporary space until October 31, 2017.

On April 7, 2017, the Company further amended the Lease to extend the term to October 31, 2023 on the then-existing office space, including the temporary space, consisting of approximately 28,600 square feet of office space in Burlington, Massachusetts. From November 2016 through October 2017, the Company's lease payment for this space was approximately $80,000 per month. Also, as part of this amendment to the Lease, the Company leased an additional 1,471 square feet of office space beginning in 2018. The lease payment for the 1,471 square feet of office space is approximately $4,100 per month

On October 6, 2017, the Company exercised its option for an additional 6,450 square feet of space, with the term expected to commence on or about April 1, 2018. After April 2018, the Company will have approximately 36,500 square feet of office space in Burlington, Massachusetts under a lease term expiring on October 31, 2023. In addition to the base rent for the office space, which increases over the term of the amended Lease, the Company is responsible for its share of operating expenses and real estate taxes.

Woburn Lease

In February 2017, the Company entered into a five-year lease for laboratory space located in Woburn, Massachusetts with a monthly lease payment of approximately $15,000, which increases over the term of the lease, plus a share of operating expenses. The total cash obligations for the term of the lease are approximately $0.9 million.

The Company incurred rent expense of $998,108, $668,350, and $373,202 for the years ended December 31, 2017, 2016 and 2015, respectively.

Future minimum lease payments under the Company's lease obligations are as follows:

Year	Aggregate Minimum Payments (in thousands)
2018	1,338
2019	1,491
2020	1,533
2021	1,576
2022	1,447
2023	1,203
Total	$ 8,588

Manufacturing and Supply Agreement with Patheon U.K. Limited

In July 2015, the Company and Patheon U.K. Limited ("Patheon") entered into a Manufacturing and Supply Agreement (the "Manufacturing Agreement") and Technical Transfer and Service Agreement (the "Technical Transfer Agreement") for the manufacture of ZILRETTA, the Company's lead program, which is an intra-articular (IA), extended-release steroid for the treatment of osteoarthritis.

Patheon agreed in the Technical Transfer Agreement to undertake certain transfer activities and construction services needed to prepare Patheon's United Kingdom facility for the commercial manufacture of ZILRETTA in dedicated manufacturing suites. The Company provided Patheon with certain equipment and materials necessary to manufacture ZILRETTA and pays Patheon a monthly fee for such activities and reimburse Patheon for certain material, equipment and miscellaneous expenses and additional services.

The initial term of the Manufacturing Agreement is 10 years from approval by the U.S. Food and Drug Administration, or FDA, of the Patheon manufacturing suites for ZILRETTA. The Company pays a monthly base fee to Patheon for the operation of the manufacturing suites and a per product fee for each vial based upon a forecast of commercial demand. The Company also reimburses Patheon for purchases of materials and equipment made on its behalf, certain nominal expenses and additional services. The Manufacturing Agreement will remain in full effect

unless and until it expires or is terminated. Upon termination of the Manufacturing Agreement (other than termination by Flexion in the event that Patheon does not meet the construction and manufacturing milestones or for a breach by Patheon), Flexion will be obligated to pay for the costs incurred by Patheon associated with the removal of our manufacturing equipment and for Patheon's termination costs up to a capped amount.

Future minimum payments under the Company's agreed obligations are as follows:

Year Ending December 31,	
2018	6,891
2019	8,108
2020	8,108
2021	8,108
2022	8,108
2023 and thereafter	24,323
Total	$ 63,646

Evonik Supply Agreement

In November 2016, the Company entered into a Supply Agreement with Evonik Corporation ("Evonik") for the purchase of PLGA which is used in the manufacturing of potential clinical and commercial supply of ZILRETTA. Pursuant to the Supply Agreement, Flexion is obligated to submit rolling monthly forecasts to Evonik for PLGA supply, a portion of which will constitute binding orders. In addition, Flexion agreed to certain minimum purchase requirements, which decrease over time, and which do not apply (i) during periods in which Evonik is in material breach of the Supply Agreement or is unable to perform its obligations due to a force majeure event, (ii) with respect to orders that Evonik is unable to supply in excess of binding orders, (iii) for orders Evonik is unable to timely deliver or does not deliver conforming product and provides a credit for such order, or (iv) during an uncured material quality failure by Evonik. Flexion agreed to purchase PLGA batches at a specified price per gram in U.S. dollars, subject to adjustment from time to time, including due to changes in price indices and in the event the initial term of the Supply Agreement is extended. The total term of the agreement is five years. Upon termination of the Supply Agreement (other than termination due to the bankruptcy of either Evonik or Flexion) Flexion is obligated to pay the costs associated with the binding supply forecast provided to Evonik. The Supply Agreement will renew for two successive two year terms upon mutual written consent by both parties.

Southwest Research Institute License Agreement

On July 25, 2014, the Company entered into an exclusive worldwide license agreement with Southwest Research Institute ("SwRI") with respect to the use of SwRI's proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including ZILRETTA. Under the agreement, the Company paid an upfront fee of $120,000 to SwRI. In February 2017, Flexion executed an agreement with SwRI to transfer manufacturing equipment to SwRI in consideration for SwRI deeming the additional milestone payment to have been fully paid by Flexion.

FX201 Related Agreement

In December 2017, we entered into a definitive agreement with GeneQuine Biotherapeutics GmbH ("GeneQuine") to acquire the global rights to FX201. As part of the asset purchase transaction with GeneQuine, we made an upfront payment to GeneQuine of $2 million. We may also be required to make additional milestone payments during the development of FX201, including up to $8.7 million through Phase 2 proof of concept (PoC) and, following successful PoC, up to an additional $54 million in development and global regulatory approval milestone payments. The transaction was accounted for as an asset acquisition, as it did not qualify as a business combination. The upfront fee was attributed to the intellectual property acquired, and recognized as research and development expense in December 2017 as the FX201 rights had not been commercially approved, and have no alternative future use. Future milestone payments earned prior to regulatory approval of FX201 would be recognized as research and development expense in the period when the milestone events become probable of being achieved. Future milestones earned upon regulatory approval would be recognized as an intangible asset and amortized to

expense over its estimated life. As of December 31, 2017 none of the future milestone payments owed under the arrangement was probable of being achieved. As part of the transaction, we became the direct licensee of certain underlying Baylor College of Medicine (Baylor) patents and other proprietary rights related to FX201 for human applications. The Baylor license agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patent and other proprietary rights directly related to FX201, with a similar non-exclusive license to certain Baylor intellectual property rights that are not specific to FX201. The license agreement with Baylor includes a low single-digit royalty on net sales of FX201 and requires us to use reasonable efforts to develop FX201 according to timelines set out in the license agreement. In December 2017, we also entered into a Master Production Services Agreement with SAFC Carlsbad, Inc., a part of MilliporeSigma, for the manufacturing of pre-clinical and initial clinical supplies of FX201.

14. Stock-Based Compensation

2013 Equity Incentive Plan

On January 27, 2014, the Company's stockholders approved the 2013 Equity Incentive Plan (the "2013 Plan"), which became effective on February 11, 2014, the date of execution of the underwriting agreement pursuant to which the Company's common stock was priced for its initial public offering. Prior to the effective date of the 2013 Plan, the Company granted stock-based awards pursuant to the 2009 Stock Incentive Plan (the "2009 Plan), which had similar features to the 2013 Plan. The 2013 Plan provides for the grant of incentive stock options ("ISOs"), non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation. Initially, the maximum number of shares of the Company's common stock that may be issued pursuant to stock awards under the 2013 Plan was 2,337,616, which is the sum of (i) 1,230,012 shares, plus (ii) the number of shares remaining available for grant under the 2009 Plan, plus (iii) any shares subject to outstanding stock options or other stock awards that would have otherwise returned to the 2009 Plan (such as upon the expiration or termination of a stock award prior to vesting). Additionally, the number of shares of common stock reserved for issuance under the 2013 Plan will automatically increase on January 1 of each year, beginning on January 1, 2015 and continuing through and including January 1, 2023, by 4% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the board of directors. The maximum number of shares that may be issued upon the exercise of ISOs under the 2013 Plan is 4,684,989 shares. As of December 31, 2017, there were 344,296 options outstanding under the 2009 Plan.

On September 11, 2017, the Company's compensation committee approved an amendment to the 2013 Plan to reserve an additional 1,500,000 of the Company's common stock to be used exclusively for grants of inducement awards to individuals who were not previously employees or non-employee directors of the Company (or following a bona fide period of non-employment with the Company).

The Company currently grants stock-based awards pursuant to the 2013 Plan. As of December 31, 2017, 2,313,178 shares were available for future issuance under the 2013 Plan. Stock option vesting typically occurs over four years for employees and directors and is at the discretion of the board of directors. Options granted have a maximum term of up to 10 years. As of December 31, 2017, there were 3,455,669 options outstanding under the 2013 Plan.

Stock Options

During the years ended December 31, 2017, 2016 and 2015, the Company granted stock options for the purchase of 1,448,100, 1,816,575, and 657,250 shares of common stock, respectively, to certain employees and directors. The vesting conditions for most of these awards are time-based, and the awards typically vest 25% after one year and monthly thereafter for the next 36 months, except for annual option grants to non-employee directors of the Company whose initial grants vest 25% after one year and monthly thereafter for the next 24 months and whose annual grants vest in equal monthly installments during the 12-month period following the grant date, pursuant to the Company's Non-Employee Director Compensation Policy. Awards typically expire after 10 years.

Stock Option Valuation

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company was a private company prior to 2014, and lacks company-specific historical information for a sufficient period of time or implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of the Company's common stock since the Company's initial public offering together with the historical volatility of its publicly-traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price for a sufficient period of time. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The relevant data used to determine the value of the stock option grants for the years ended December 31, 2017, 2016 and 2015 is as follows:

	December 31,		
	2017	2016	2015
Risk-free interest rates	1.97%-2.29%	0.74-1.75%	1.49-1.92%
Expected dividend yield	0.00%	0.00%	0.00%
Expected term (in years)	6.0	5.6	6.0
Expected volatility	69.9%-72.8%	67.3-99.9%	76.4-83.9%

The following table summarizes stock option activity for the year ended December 31, 2017:

(In thousands, except per share amounts)	Shares Issuable Under Options	Weighted Average Exercise Price
Outstanding as of December 31, 2016	3,079	$ 14.84
Granted	1,448	22.29
Exercised	(308)	12.25
Cancelled	(419)	22.78
Outstanding as of December 31, 2017	3,800	$ 17.75
Options vested and expected to vest at December 31, 2017	3,800	$ 17.75
Options exercisable at December 31, 2017	1,689	$ 14.99

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock. A total of 308,011, 30,195, and, 109,441 options were exercised during the years ended December 31, 2017, 2016 and 2015, respectively. The aggregate intrinsic value of stock options exercised was $2,947,768, $236,889, and $1,584,657 for the years ended December 31, 2017, 2016 and 2015, respectively.

At December 31, 2017, 2016 and 2015 the Company had options for the purchase of 3,799,965, 3,079,175, and 1,657,225 shares of common stock outstanding, with a weighted average remaining contractual term of 8.0, 7.8, and 7.9 years, respectively, and with a weighted average exercise price of $17.75, $14.84, and $14.28 per share, respectively. At December 31, 2017, 2016 and 2015 there were options for the purchase of 1,688,652, 1,173,671, and 728,621 shares of common stock exercisable under these stock option awards, with a weighted average remaining contractual life of 6.8, 6.7, 6.9 years , respectively, and an aggregate intrinsic value of $16,985,787, $8,745,505, and 7,714,057, respectively.

The weighted average grant date fair value of options granted during the years ended December 31, 2017, 2016 and 2015 was $14.33, $11.50, and $15.08, respectively.

Restricted Stock Units

On January 4, 2016, the Company granted 189,300 RSUs with performance and time-based vesting conditions to certain executives. These RSUs vest, and the underlying shares of common stock become deliverable, beginning when ZILRETTA is approved (the "Milestone"). The number of shares that vest varies based on the timing of achieving the Milestone. As a result of the Milestone being achieved on October 6, 2017, the number of shares of the Company's common stock earned under these awards is 122,800, subject to ongoing employment with the Company for a period of 2 years. The 122,800 shares had an approximate value of $2.2 million as of the original grant date of which $1.6 million was recognized in the fourth quarter of 2017 upon achieving the milestone and the remaining $0.6 million will be recognized over a period of two years.

The following table summarizes the RSU activity for the year ended December 31, 2017:

(In thousands, except per share amounts)	Number of Shares	Weighted Average Grant Date Fair Value
Nonvested as of December 31, 2016	189	$ 15.77
Granted	—	—
Cancelled	(66)	—
Vested/Released	(41)	16.43
Nonvested as of December 31, 2017	82	$ 16.43

Stock-based Compensation

The Company recorded stock-based compensation expense related to stock options, restricted stock and shares purchased under the employee stock purchase plan for the years ended December 31, 2017, 2016 and 2015 as follows:

	Year Ended December 31,		
(In thousands)	2017	2016	2015
Research and development	$ 3,979	$ 2,341	$ 1,412
Selling, general and administrative	7,563	4,429	3,171
	$ 11,542	$ 6,770	$ 4,583

As of December 31, 2017, unrecognized stock-based compensation expense for stock options outstanding was $25.5 million which is expected to be recognized over a weighted average period of 2.8 years. As of December 31, 2017, unrecognized stock-based compensation expense for restricted stock units outstanding was $0.6 million which is expected to be recognized over a period of 2 years.

Employee Stock Purchase Plan

On January 27, 2014, the Company's stockholders approved the Employee Stock Purchase Plan. A total of 209,102 shares of common stock were reserved for issuance under this plan. The Employee Stock Purchase Plan became effective on February 11, 2014, the date of execution of the underwriting agreement pursuant to which the Company's common stock was priced for its initial public offering. During the year ended December 31, 2017 and 2016, 89,704 and 20,896 shares, respectively, were purchased by employees under the plan. Additionally, the number of shares of common stock reserved for issuance under the Employee Stock Purchase Plan will automatically increase on January 1 of each year, beginning on January 1, 2015 and continuing through and including January 1, 2023, by 1% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the board of directors.

15. Net Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the years ended December 31, 2017, 2016 and 2015:

	Year ended December 31,		
(In thousands)	2017	2016	2015
Numerator:			
Net loss	$ (137,481)	$ (71,894)	$ (46,315)
Net loss:	$ (137,481)	$ (71,894)	$ (46,315)
Denominator:			
Weighted average common shares outstanding, basic and diluted	33,027	25,297	21,497
Net loss per share, basic and diluted	$ (4.16)	$ (2.84)	$ (2.15)

The following common stock equivalents were excluded from the calculation of diluted net loss per share as including them would have an anti-dilutive effect:

	Year ended December 31,	
	2017	2016
Shares issuable upon conversion of the 2024 convertible notes	5,017	—
Stock Options	3,602	2,345
Restricted Stock Units	147	188
	8,766	2,533

16. Income Taxes

The Company has generated losses since inception. Accordingly, there is no tax provision or benefit for the years ended December 31, 2017, 2016, and 2015, respectively .

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	3.0	5.0	4.9
Federal and state research and development tax credits	0.9	2.7	4.7
Change in deferred tax asset valuation allowance	(11.6)	(40.0)	(45.4)
Tax law change	(25.1)		
Other	(1.2)	(1.7)	1.8
Effective income tax rate	—%	—%	—%

The Company's net deferred tax assets consisted of the following:

	December 31,	
	2017	2016
Net operating loss carryforwards	$ 48,496	$ 36,880
Research and development tax credit carryforwards	7,725	7,078
Accruals and other temporary differences	3,578	4,897
Debt discount	(14,630)	0
Capitalized research and development expenses, net	29,673	34,579
Total deferred tax assets	74,842	83,434
Valuation allowance	(74,842)	(83,434)
Net deferred tax asset	$ —	$ —

As of December 31, 2017, the Company had federal and state net operating loss carryforwards of approximately $190.1 million and $147.8 million, respectively, which begin to expire in 2029 for federal purposes and in 2030 for state purposes. In addition, the Company had federal and state research and development tax credit carryforwards of approximately $5.4 million and $2.9, respectively, available to reduce future tax liabilities, which begin to expire in 2029 for federal purposes and 2025 for state purposes. Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of net operating loss carryforwards and capitalized research and development expenses. Management has considered the Company's history of cumulative net losses incurred since inception, as well as its lack of commercialization of any products or generation of any revenue from product sales since inception, and determined that it is more likely than not that the Company will not realize the benefits of its deferred tax assets. As a result, a full valuation allowance has been established at December 31, 2017 and 2016.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (the "Act"), a tax reform bill which, among other items, reduces the current corporate federal tax rate to 21% from 35%. The rate reduction is effective January 1, 2018. The Company concluded that the Act will cause our deferred tax assets to be revalued. As changes in tax laws or rates are enacted, deferred tax assets and liabilities are adjusted through income tax expense in the period of enactment. During the fourth quarter, we estimated the reduction in the value of our deferred tax assets to be $34.5 million as a result of the Act, which was offset by a corresponding change in the valuation allowance.

The Securities and Exchange Commission issued Staff Accounting Bulletin No. 118 ("SAB 118") on December 23, 2017. SAB 118 provides a one-year measurement period from a registrant's reporting period that includes the Act's enactment date to allow the registrant sufficient time to obtain, prepare and analyze information to complete the accounting required under ASC 740.

The ultimate impact of the Act on our reported results in 2018 and beyond may differ from the estimates provided herein, possibly materially, due to, among other things, changes in interpretations and assumptions we have made, guidance that may be issued, and other actions we may take as a result of the Act, different from that presently contemplated.

During year ended December 31, 2017, the Company recorded to equity a deferred tax liability relating to the discount on its 2024 Convertible Notes (see Note 10) with an equal and offsetting adjustment to the valuation allowance.

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

Through the quarter ending December 31, 2017, the Company has completed periodic updates to its Section 382 study through October 31, 2017, which have indicated ownership changes within the meaning of Section 382 have occurred in December 2014 and June 2016, however, it is not anticipated that a portion of the Company's NOLs will expire unutilized as a result of the Section 382 limitations arising from these ownership changes. Subsequent ownership changes defined by Section 382 may further limit the amount of NOL carryforwards that could be utilized annually to offset future taxable income.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2017 and 2016 were as follows:

	Year Ended December 31,		
	2017	2016	2015
Valuation allowance as of beginning of year	$ (83,434)	$ (54,773)	$ (33,826)
Decreases recorded as benefit to income tax provision	36,606	4,771	2,858
Decreases recorded as benefit to equity	24,537	—	—
Increases recorded to income tax provision	(52,551)	(33,432)	(23,805)
Valuation allowance as of end of year	$ (74,842)	$ (83,434)	$ (54,773)

In each reporting period, the Company considers whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. No liabilities for unrecognized tax benefits were recorded as of December 31, 2017 and 2016.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax years are still open under statute from 2013 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The resolution of tax matters is not expected to have a material effect on the Company's consolidated financial statements.

17. Quarterly Financial Data (unaudited)

The following information has been derived from unaudited consolidated financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair statement of such information.

	Three Months Ended			
(in thousands, except per share amounts)	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenues	$ 0	$ 0	$ 0	$ 355
Operating expenses	23,782	26,902	31,221	48,132
Net loss	(23,879)	(28,880)	(34,188)	(50,534)
Net loss per common share—basic and diluted	$ (0.75)	$ (0.91)	$ (1.07)	$ (1.38)
Weighted average common shares—basic and diluted	31,704	31,826	31,931	36,644

	Three Months Ended			
(in thousands, except per share amounts)	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Operating expenses	$ 16,673	$ 14,120	$ 17,435	$ 21,552
Net loss	(16,815)	(14,185)	(17,782)	(23,112)
Net loss per common share—basic and diluted	$ (0.78)	$ (0.63)	$ (0.65)	$ (0.79)
Weighted average common shares—basic and diluted	21,570	22,666	27,524	29,347

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We are responsible for maintaining disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Disclosure controls and procedures are controls and other procedures designed to ensure that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Based on our management's evaluation (with the participation of our principal executive officer and our principal financial officer) of our disclosure controls and procedures as required by Rules 13a-15(e) and Rule 15d-15(e) under the Exchange Act, our principal executive officer and our principal financial officer have concluded that our disclosure controls and procedures were effective to achieve their stated purpose as of December 31, 2017, the end of the period covered by this report.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2017, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2017, our internal control over financial reporting was effective based on those criteria. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

This annual report does not include an attestation report of our registered public accounting firm due to a transition period established by the JOBS Act for emerging growth companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item and not set forth below will be set forth in the section headed "Election of Directors" and "Executive Officers" in our Proxy Statement for our 2018 Annual Meeting of Stockholders, or Proxy Statement, to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017, and is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is available on the Corporate Governance section of our website, www.flexiontherapeutics.com. We intend to disclose on our website any amendments to, or waivers from, our code of business conduct and ethics that are required to be disclosed pursuant to SEC rules.

Item 11. Executive Compensation

The information required by this item will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in the section headed "Security Ownership of Certain Beneficial Owners and Management" in our Proxy Statement and is incorporated herein by reference.

The information required by Item 201(d) of Regulation S-K will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be set forth in the section headed "Transactions With Related Persons" in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be set forth in the section headed "Ratification of Selection of Independent Registered Public Accounting Firm" in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this report.

1. Financial Statements

The financial statements of Flexion Therapeutics, Inc. listed below are set forth in Item 8 of this report for the year ended December 31, 2017:

2. Financial Statement Schedules

These schedules have been omitted because the required information is included in the consolidated financial statements or notes thereto or because they are not applicable or not required.

3. Exhibits

Unless otherwise indicated, all references to previously filed Exhibits refer to Flexion's filings with the SEC under File No. 001-36287. The following exhibits are filed as part of, or incorporated by reference, into this report. Each management contract or compensatory plan or arrangement required to be identified by this item is so designated in such list.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of Flexion (Exhibit 3.1, Current Report on Form 8-K filed on February 19, 2014)
3.2	Amended and Restated Bylaws of Flexion (Exhibit 3.2, Current Report on Form 8-K filed on February 19, 2014)
4.1	Form of Common Stock Certificate of Flexion (Exhibit 4.1, Registration Statement on Form S-1 (File No. 333-193233), as amended, filed on January 29, 2014)
4.2	Amended and Restated Investor Rights Agreement, dated December 3, 2012, between Flexion and certain of its stockholders (Exhibit 4.2, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
4.3	Conversion, Amendment and Waiver Agreement, dated January 27, 2014, between Flexion and certain of its stockholders (Exhibit 4.3, Registration Statement on Form S-1 (File No. 333-193233), as amended, filed on January 29, 2014)
4.4	Indenture, dated as of May 2, 2017, by and between Flexion and Wells Fargo Bank, National Association, as trustee (Exhibit 4.1, Current Report on Form 8-K filed on May 2, 2017)
4.5	Form of Note representing Flexion's 3.375% Convertible Senior Notes due 2024 (included as Exhibit A to the Indenture filed as Exhibit 4.1, Current Report on Form 8-K filed on May 2, 2017)
4.6	Consent and Second Amendment to Credit and Security Agreement, dated April 24, 2017, between Flexion and MidCap Financial Trust, as administrative agent (Exhibit 4.3, Current Report on Form 8-K filed on May 2, 2017)
	Management Contracts and Compensatory Plans
10.1	Form of Indemnity Agreement between Flexion and its directors and officers (Exhibit 10.1, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.2	Flexion Therapeutics, Inc. 2009 Equity Incentive Plan and Forms of Stock Option Agreement, Notice of Exercise and Stock Option Grant Notice thereunder (Exhibit 10.2, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.3	Flexion Therapeutics, Inc. 2013 Equity Incentive Plan, as amended, and Forms of Stock Option Agreement, Notice of Exercise and Stock Option Grant Notice thereunder (Exhibit 99.1, Current Report on Form 8-K, filed September 14, 2017)
10.4	Form of Restricted Stock Unit Award Agreement and Restricted Stock Unit Grant Notice under the Flexion Therapeutics, Inc. 2013 Equity Incentive Plan (Exhibit 99.1, Current Report on Form 8-K filed on December 22, 2015)
10.5	Flexion Therapeutics, Inc. 2013 Employee Stock Purchase Plan (Exhibit 10.4, Registration Statement on Form S-1 (File No. 333-193233), as amended, filed on January 29, 2014)
10.6	Flexion Therapeutics, Inc. Non-Employee Director Compensation Policy, as revised
10.7	Amended and Restated Offer Letter between Flexion and Michael D. Clayman, M.D. (Exhibit 10.6, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.8	Amendment to Amended and Restated Offer Letter between Flexion and Michael D. Clayman, M.D. (Exhibit 10.7, Annual Report on Form 10-K filed on March 28, 2014)

Exhibit Number	Description
10.9	Amended and Restated Offer Letter between Flexion and Neil Bodick, M.D., Ph.D. (Exhibit 10.7, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.10	Amendment to Amended and Restated Offer Letter between Flexion and Neil Bodick, M.D., Ph.D. (Exhibit 10.9, Annual Report on Form 10-K filed on March 28, 2014)
10.11	Amended and Restated Offer Letter between Flexion and Scott Kelley
10.12	Amended and Restated Offer Letter between Flexion and Mark Levine
10.13	Amended and Restated Offer Letter between Flexion and Kerry Wentworth
10.14	Flexion Therapeutics, Inc. Change in Control Severance Benefit Plan and Form of Participation Agreement (Exhibit 99.1, Current Report on Form 8-K filed on June 23, 2017)
	Other Agreements
10.15	Lease, dated February 22, 2013, between Flexion and The Trustees of Mall Road Trust (Exhibit 10.14, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.16	First Amendment of Lease, dated July 13, 2015, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (as successor in interest to The Trustees of Mall Road Trust) (Exhibit 10.3, Quarterly Report on Form 10-Q filed on November 9, 2015)
10.17	Second Amendment of Lease, dated December 15, 2015, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.20, Annual Report on Form 10-K filed on March 11, 2016)
10.18*	Exclusive License Agreement, dated July 25, 2014, between Flexion and Southwest Research Institute (Exhibit 10.21, Annual Report on Form 10-K filed on March 11, 2016)
10.19*	Manufacturing and Supply Agreement, dated July 31, 2015, between Flexion and Patheon UK Limited (Exhibit 10.1, Quarterly Report on Form 10-Q filed on November 9, 2015)
10.20*	Technical Transfer and Service Agreement, dated July 31, 2015, between Flexion and Patheon UK Limited (Exhibit 10.2, Quarterly Report on Form 10-Q/A filed on January 26, 2016)
10.21	Credit and Security Agreement, dated August 4, 2015, between Flexion and MidCap Financial Trust, as administrative agent, and the Lenders listed on the Credit Facility Schedule attached thereto (Exhibit 10.4, Quarterly Report on Form 10-Q filed on November 9, 2015)
10.22	Third Amendment of Lease, dated May 8, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on August 3, 2016)
10.23	Fourth Amendment of Lease, dated June 29, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.2, Quarterly Report on Form 10-Q filed August 3, 2016)
10.24	Fifth Amendment of Lease, dated July 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.3, Quarterly Report on Form 10-Q filed August 3, 2016
10.25	Sixth Amendment of Lease, dated September 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on November 7, 2016)
10.26	Seventh Amendment of Lease, dated September 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on August 8, 2017)
10.27	Supply Agreement, dated November 10, 2016, between Flexion and Evonik Corporation (Exhibit 10.29, Annual Report on Form 10-K filed on March 10, 2017)
10.28	Amendment to Exclusive License Agreement, dated February 7, 2017, between Flexion and Southwest Research Institute (Exhibit 10.30, Annual Report on Form 10-K filed on March 10, 2017)
21.1	Subsidiaries of Flexion Therapeutics, Inc.

Exhibit Number	Description
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
24.1	Power of Attorney (reference is made to the signature page thereto)
31.1	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

* Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

Item 16. 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on the 8th day of March, 2018.

FLEXION THERAPEUTICS, INC.

By: /s/ Michael D. Clayman, M.D.
Michael D. Clayman, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael D. Clayman, M.D. and Mark S. Levine, and each of them, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Michael D. Clayman, M.D. Michael D. Clayman, M.D.	President, Chief Executive Officer and Member of the Board of Directors *(Principal Executive Officer and Principal Financial and Accounting Officer)*	March 8, 2018
/s/ Patrick J. Mahaffy Patrick J. Mahaffy	Chairman of the Board of Directors	March 8, 2018
/s/ Scott Canute Scott Canute	Member of the Board of Directors	March 8, 2018
/s/ Samuel D. Colella Samuel D. Colella	Member of the Board of Directors	March 8, 2018
/s/ Heath Lukatch, Ph.D. Heath Lukatch, Ph.D.	Member of the Board of Directors	March 8, 2018
/s/ Sandesh Mahatme Sandesh Mahatme	Member of the Board of Directors	March 8, 2018
/s/ Ann Merrifield Ann Merrifield	Member of the Board of Directors	March 8, 2018
/s/ Alan Milinazzo Alan Milinazzo	Member of the Board of Directors	March 8, 2018
/s/Mark Stejbach Mark Stejbach	Member of the Board of Directors	March 8, 2018

Corporate Headquarters

10 Mall Road, Suite 301
Burlington, MA 01803

Stock Information

The common stock of the company is traded on the Nasdaq Global Market under the symbol FLXN

Annual Meeting

The Annual Meeting of Stockholders will be

Wednesday, June 20, 2018
1:30 p.m., ET

Marriott Hotel
1 Mall Road
Burlington, MA 01803

Legal Counsel

Cooley LLP
San Diego, CA

Independent Auditors

PricewaterhouseCoopers LLP
Boston, MA

Transfer Agent

Computershare Trust Company
Louisville, KY
www.computershare.com/investor

Executive Committee

Mike Clayman, MD
Chief Executive Officer & Co-Founder

Neil Bodick, MD, PhD
Chief Scientific Officer & Co-Founder

Dan Deardorf
Senior Vice President, Commercial

Scott Kelley, MD
Chief Medical Officer

Dan Leblanc, MS
Senior Vice President, CMC Operations

Mark Levine
General Counsel and Corporate Secretary

Adam Muzikant, PhD
Vice President, Business Development

Kerry Wentworth
Chief Regulatory Officer

Christina Willwerth
Senior Vice President, Program Management and Strategy

Board of Directors

Patrick Mahaffy, MA (Chairman of the Board)
President and CEO, Clovis Oncology

Michael Clayman, MD
Chief Executive Officer, Flexion Therapeutics

Scott A. Canute, MBA
Founder and Principal, Magis Consulting

Sam Colella, MBA
Managing Director, Versant Ventures

Heath Lukatch, PhD
Partner, TPG

Sandy Mahatme, LLM
Executive Vice President, CFO and CBO, Sarepta Therapeutics

Ann Merrifield, MBA
Independent, Former CEO of PathoGenetix

Alan W. Milinazzo
Partner, Heidrick & Struggles International

Mark P. Stejbach
Senior Vice President and CCO, Alkermes

We will provide stockholders without charge, upon written request, a copy of our Annual Report on Form 10-K, including the financial statements, schedules and list of exhibits. We will furnish stockholders a copy of any exhibit to such report upon written request and payment of reasonable expenses in furnishing the exhibit. Requests should be sent to Investor Relations at our corporate headquarters. In addition, our Annual Report on Form 10-K, other filings with the Securities and Exchange Commission, and press releases, along with general information about our business, are available through our website at www.flexiontherapeutics.com.

Flexion Therapeutics
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