Flexion Therapeutics Inc
Form 10-K
March 10, 2017

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, 2016

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, or a smaller reporting company.

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

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, 2016 was approximately $341,322,482.

The number of outstanding shares of the registrant's common stock as of March 2, 2017 was 31,731,824.

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 2017 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, 2016.

FLEXION THERAPEUTICS, INC.

FORM 10-K—ANNUAL REPORT

For the Fiscal Year Ended December 31, 2016

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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. The Company has tried to identify forward-looking statements by using words such as "believe," "may," "could," "will," "estimate," "continue," "anticipate," "intend," "seek," "plan," "expect," "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 not generated any revenue from, or received regulatory approval for, any of our product candidates; we are a development stage company and will require additional capital prior to commercializing Zilretta™ (also known as FX006) or any of our other potential future product candidates; we may be unable to successfully complete the development of, obtain regulatory approval for, or commercialize Zilretta or any of our other product candidates; we rely on third parties to manufacture and conduct the clinical trials of our product candidates, which could delay or limit their future development or regulatory approval; we currently do not have the infrastructure to commercialize any of our product candidates if such products receive regulatory approval; 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 Flexion Therapeutics, Inc. and our subsidiary, Flexion Securities Corporation, Inc.

Overview

We are a specialty pharmaceutical 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. In May 2016, the U.S Food and Drug Administration informed us that the safety and efficacy data from the registration program for Zilretta™ (FX006), our lead investigational product candidate, were acceptable to support the submission of a new drug application, or NDA. In December 2016, we submitted the NDA for Zilretta, and in February 2017, we announced that the FDA accepted the Zilretta NDA for filing and has established a user fee goal date under the Prescription Drug User Fee Act (PDUFA) of October 6, 2017. Zilretta, is an injectable, extended-release, intra-articular, or IA, meaning "in the joint," steroid that we are developing as a treatment for patients with moderate to severe OA pain. We specifically designed Zilretta to combine a commonly administered steroid, triamcinolone acetonide, or TA, with poly lactic-co-glycolic acid, referred to as PLGA, with the goal of providing sustained therapeutic concentrations in the joint and persistent analgesic effect. Zilretta is intended to address the limitations of current IA therapies by providing extended, local analgesia while avoiding systemic side effects, which are effects that can occur throughout the body as a result of drug that is released from the site of injection into circulating blood. To date, we have completed seven clinical trials in which nearly 700 patients with OA of the knee have been treated with Zilretta. The overall frequency of treatment-related adverse events in these trials has been similar to those observed with placebo and no drug-related serious adverse events have been reported. Both the magnitude and duration of pain relief provided by Zilretta in clinical trials have been shown to be clinically meaningful with the magnitude of pain relief amongst the largest seen to date in OA clinical trials.

Based on the strength of our pivotal and other clinical trials, we believe that Zilretta has the potential to address a significant unmet medical need for OA pain management by providing safe, effective and extended pain relief. We believe the following attributes uniquely distinguish Zilretta:

- An injectable, IA, extended-release investigational treatment for patients with moderate to severe OA pain that has demonstrated in clinical trials to date the following:
- significant improvements in validated OA specific measures compared to the current injectable standard of care,
- significant pain relief against placebo as measured by the weekly mean of the Average Daily Pain, or ADP, score at weeks 1 through 16 and, on average, an approximately 50 percent reduction in pain from baseline over week 12,
- persistent therapeutic concentrations of drug in the joint and durable efficacy,
- statistically significant ($p<0.05$, 2-sided) reduction in the rise of blood glucose compared to that observed following immediate- release TA injection in Type 2 diabetic patients who also have knee OA,
- highly significant ($p<0.0001$, 2-sided) and clinically meaningful pain relief against placebo as measured by the weekly mean of the ADP score,
- reduced rescue medicine consumption compared with placebo and immediate-release TA, and,
- an acceptable safety profile with limited systemic exposures and the potential for fewer serious side effects compared to oral treatment options for OA pain.
- Amongst the largest analgesic effects seen in OA clinical trials.
- Strong proprietary position through a combination of patents, trade secrets and proprietary know-how, as well as eligibility for marketing exclusivity.

- Well-defined Section 505(b)(2) of the Federal Food Drug and Cosmetic Act, or FDCA, regulatory pathway seeking approval for a novel formulation of an already approved immediate-release steroid used by orthopedists and rheumatologists.
- Familiarity of orthopedists and rheumatologists with IA injections utilizing the same steroid at the same dose.
- Potential for pharmacoeconomic benefits due to improved efficacy and durability that could delay costly and invasive total joint replacement, also referred to as total joint arthroplasty, or TJA.

We have worldwide commercialization rights for Zilretta. 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. If Zilretta is approved, we intend to market our products in the United States through our own sales force targeting specialty physicians, including orthopedists and rheumatologists. While we believe that the United States represents the most attractive market for Zilretta, we will continue to evaluate opportunities to develop and commercialize Zilretta in territories outside the United States.

Zilretta and our PLGA formulation technology is protected through a combination of patents, trade secrets, and proprietary know-how, and we intend to seek marketing exclusivity for any approved products.

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

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

Our projections indicate that by 2030 approximately 23.5 million of the 45 million OA patients will have knee OA. According to IMS Health, each year over 5.5 million large joint OA patients in the United States receive IA steroid injection treatments in the knee, hip, and shoulder, within over 4.2 million of these being knee injections. In 2015, the number of patients that received knee injections of IA steroids increased approximately 12% over 2014. We estimate that an additional 1 million patients received knee injections of IA HA, which the FDA approved for use only in the knee. Despite recent negative guidance related to HA as a treatment for knee OA from specialty societies (e.g. the

American Academy of Orthopedic Surgeons (AAOS) and the Osteoarthritis Research Society International (OARSI)) and given that select payer groups have limited reimbursement for the entire class of HA

products, which collectively may begin to put downward pressure on HA sales, HA sales in the United States were approximately $948 million in 2015, with a cost per treatment ranging from $500 to $1000. We believe the vast majority of these sales were related to knee therapy. Our clinical trials to date evaluated Zilretta in patients with knee OA, which represents the most common joint treated with IA therapies.

Given the limitations of current therapies, we believe Zilretta, if approved, would provide an attractive therapeutic alternative. Clinical trials to date for Zilretta have demonstrated significant improvements in validated OA specific measures compared to the current injectable standard of care, persistent therapeutic concentrations of drug in the joint and durable efficacy, and an attractive safety profile with limited systemic exposures.

Our Strategy

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

- Focus initially on novel product candidates that provide long-lasting analgesia locally while avoiding systemic side effects. We intend to develop anti-inflammatory and analgesic therapies for the treatment of patients with musculoskeletal conditions, beginning with OA. Many OA patients will eventually require IA injection therapies to control their pain as the disease progresses. Currently available IA steroids, none of which are formulated for extended-release, 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 months of pain during that time. While the benefits of HA injections generally last for a longer period of time than steroid injections, they are only marginally more effective than placebo. As a result, we believe there is a significant unmet medical need for persistent, effective and safe OA pain relief that can be addressed by extended-release injection therapies. We have therefore formulated our IA product candidate, Zilretta, with the goal of achieving effective drug concentrations in the joint for months, while avoiding significant plasma concentrations of drug that may have systemic side effects.
- Mitigate development risk and expedite regulatory timeline to product approval. We seek 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. Our extended-release technology employs PLGA delivery systems, which are already used in approved extended-release drug products outside of OA and in approved surgical devices. Because Zilretta incorporates an already approved steroid in PLGA, it qualifies for the Section 505(b)(2) NDA pathway under the FDCA, which can be an expeditious, cost-effective means to seek product approval, as well as to potentially expand indications for this product candidate. Section 505(b)(2) of the FDCA enables the applicant to rely, in part, on published literature or the FDA's findings of safety and efficacy for an existing product in support of its application.
- 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, if approved, we can cost-effectively commercialize Zilretta with our own specialty sales and marketing organization in the United States, and thereby retain more of the commercial value of this product candidate. In prior years, Genzyme Corporation, which was subsequently acquired by Sanofi, supported sales of Synvisc by utilizing a sales force of approximately 110 representatives. We believe we can establish an effective U.S. commercial organization with our own specialty sales force of approximately100 representatives that target orthopedists and rheumatologists. While we believe that the United States represents the most attractive market for Zilretta, we will continue to evaluate opportunities to develop and commercialize Zilretta in territories outside the United States where we believe there is adequate pricing and reimbursement available.

Osteoarthritis

Overview

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

- With the U.S. population between the ages of 45 and 64 having grown 31.5% from 2000 through 2010 and accounting for 26.4% of the total population, we expect changing demographics will likely contribute to a growing number of OA patients.
- Approximately 35% 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 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 patients 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.

There is no cure for OA. As a result, current treatments are intended to address 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 a new therapy which meaningfully and durably relieves pain and improves function could delay TJA.

Current Treatments for OA

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

IA Injection Treatments. When non-pharmacologic therapy and oral pain medications prove inadequate, physicians typically transition patients to IA injections. Steroids are first line IA therapy and when this does not provide sufficiently durable pain relief, patients may progress to IA HA, a significantly more expensive, but currently reimbursable, therapy with only marginally greater effect than placebo. Triamcinolone acetonide, or TA, the corticosteroid used in Zilretta, is amongst the most commonly prescribed IA corticosteroid injections.

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

TJA. 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 the patient may 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 payors would be willing to reimburse additional OA therapies that have the potential to delay the need for TJA.

Limitations of Current Treatments for OA

Current 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 and cardiovascular events, and, importantly, are eventually ineffective at managing OA pain as the disease progresses.

IA therapies, including steroids and HA preparations, are generally well-tolerated but provide pain relief that is insufficient or inadequate in duration. All IA steroid therapies approved for OA are immediate-release suspensions or solutions that leave the joint within hours to days and 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 standards of care dictate that IA steroid suspensions not be administered more frequently than once every three months. Based on internal analysis, we believe approximately 44% of patients receiving IA immediate-release steroids are unsatisfied with the duration of benefit.

Despite U.S. sales of approximately $948 million in 2015 , IA HA therapies, which are approved only for treatment in the knee, produce only marginally more effective pain relief than placebo and may have no discernible effect on a patient's ability to carry out their daily activities. In treatment guidelines for knee OA published in May 2013, the AAOS concluded that current published studies do not show any clinically effective response for HA injections. As a result, the guidelines do not recommend HA treatment for symptomatic knee OA due to lack of efficacy and, most recently, certain insurance carriers are no longer providing policy coverage of HA and this may begin to put downward pressure on HA sales.

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

In sum, current therapies, for OA pain are inadequate and do not address the desire among physicians and healthcare payors to manage pain for longer periods of time, which can delay TJA.

The Flexion Extended Release Technology

Our extended-release technology allows us to incorporate pharmaceuticals in PLGA microspheres. 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 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 therapeutic concentrations of drug in the joint, while minimizing systemic exposure. We believe we are the first company to administer PLGA microspheres into a human joint, and preclinical and clinical data suggest that Zilretta may provide local therapeutic concentrations that could last for at least three months and result in very low systemic concentrations of drug. The pharmacokinetic, or PK, clinical trials of Zilretta provide

direct evidence that following a single injection, therapeutic concentrations of TA are maintained locally (in the joint) for at least 12 weeks, while very low concentrations of TA enter systemic circulation. Furthermore, clinical data from our pivotal efficacy trials of Zilretta suggest that following a single injection, Zilretta can provide durable local pain relief and functional improvement, while producing very low systemic concentrations and attractive systemic safety profiles. Together these data suggest that the persistent local delivery

of Zilretta's active pharmaceutical ingredient from PLGA microspheres has the potential to provide prolonged, local therapeutic effects while reducing the potential for systemic side effects.

Zilretta is our lead, late-stage, intra-articular, extended-release investigational steroid treatment that combines TA with PLGA. Zilretta was specifically designed to provide sustained therapeutic concentrations in the joint and persistent analgesic effect, and is intended to address the limitations of current IA therapies by providing local and long lasting analgesia over a period of months while minimizing systemic exposure and avoiding serious side effects. In our completed Phase 3 clinical trial, Zilretta demonstrated significant and clinically meaningful pain relief compared to placebo through week 16. Zilretta also showed significant and clinically meaningful improvements in validated OA specific secondary outcome measures at each measured time point through 12 weeks in that trial compared to the current injectable standard of care, immediate-release TA. While Zilretta showed numeric improvement versus immediate-release TA at weeks 2 through 12 on the average daily pain rating scale, it did not achieve statistical significance in that measure throughout the duration of the trial.

The frequency of treatment-related side effects was comparable across all treatment arms in the trial.

As previously reported, Flexion discontinued the internal development of FX007 for post-operative pain and FX005 for the treatment of end-stage OA patients.

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. Method of manufacturing and method of use claims have been granted by the U.S PTO, with a patent term in 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.

Zilretta—Late-Stage Candidate for IA Therapy for Patients with Moderate to Severe OA Pain

Development Program

To date, we have completed seven clinical trials in which we have evaluated Zilretta against either immediate-release TA injection or placebo (saline) or both. A total of approximately 1,200 patients were treated in these seven clinical trials, of which nearly 700 patients received Zilretta, 260 patients received immediate-release TA and 262 patients received placebo.

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 intra-articular injection of 40 mg Zilretta or 40 mg immediate-release TA. Blood glucose levels were evaluated for a total of 3 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 Week 6/Day 43. 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