



October 6, 2017

Flexion Therapeutics Announces FDA Approval of Zilretta™ (triamcinolone acetonide extended-release injectable suspension) for Osteoarthritis (OA) Knee Pain

- | *Innovative, non-opioid, intra-articular therapy, proven to deliver meaningful analgesia over 12 weeks in patients with moderate to severe OA knee pain*
- | *Product label also includes positive data from type 2 diabetes study*
- | *Commercial supply expected to be available by late October following recent completion of manufacturing process validation*
- | *Conference call scheduled for Monday, October 9, 2017, at 8:00 a.m. ET*

BURLINGTON, Mass., Oct. 06, 2017 (GLOBE NEWSWIRE) -- Flexion Therapeutics, Inc. (Nasdaq:FLXN) today announced that the U.S. Food and Drug Administration (FDA) approved Zilretta™ (triamcinolone acetonide extended-release injectable suspension), the first and only extended-release, intra-articular injection for osteoarthritis knee pain. Zilretta is a non-opioid medicine that employs Flexion's proprietary microsphere technology to provide proven pain relief over 12 weeks.

View the Multimedia News Release:

<https://www.multivu.com/players/English/8186951-flexion-therapeutics-zilretta-fda-approval/>

"The approval of Zilretta marks a major advancement in the treatment landscape for managing OA knee pain," said Michael Clayman, M.D., President and Chief Executive Officer of Flexion. "It comes at a time when our society is in urgent need of non-addictive therapies to help the millions of Americans who suffer from this condition." Dr. Clayman added, "We believe that Zilretta has the potential to be a transformative medicine for the more than five million patients who receive an intra-articular injection for OA knee pain each year."

The FDA approval of Zilretta is based upon data from Flexion's pivotal Phase 3 clinical trial. The randomized, double-blind study enrolled 484 patients at 37 centers worldwide.

Commenting on the approval, Andrew Spitzer, M.D., Co-Director, Joint Replacement Program, Cedars-Sinai Orthopaedic Center, said, "OA knee pain presents a host of challenges for patients and clinicians alike, and there has been very little innovation in this area in recent years. Zilretta is a groundbreaking new therapy, providing clinically meaningful pain relief with a safety profile that is similar to saline."

Sometimes called degenerative joint disease or "wear and tear" arthritis, OA is a progressive and incurable condition and the most common form of arthritis. Its effects may range from intermittent discomfort to the loss of function and severe chronic pain associated with irreversible structural damage.

"As OA progresses, many patients experience intractable joint pain, which can ultimately lead to the need for a total joint replacement," said John Richmond, M.D., Medical Director for Network Development, New England Baptist Hospital. "As a result, healthcare providers are eager for new, non-opioid therapies that may help patients manage their OA pain for extended periods of time. Zilretta gives us an important new non-surgical intervention."

Zilretta's label also includes the results from a double-blind, randomized, parallel-group trial, which examined blood glucose concentrations in patients with type 2 diabetes.

Steven Russell, M.D., Ph.D., Assistant Professor of Medicine, Massachusetts General Hospital Diabetes Research Center, commented, "Our trial demonstrated that Zilretta may avoid the disruptive blood glucose spikes that can be seen with corticosteroid use in patients coping with both knee OA and type 2 diabetes. As a practicing diabetologist, I believe the availability of Zilretta will make intra-articular injection of glucocorticoid an attractive option for these patients."

The pain from OA of the knee can have a profound impact on the people it afflicts, often resulting in a cascade of consequences, which patient advocates warn is only expected to grow.

According to Seth Ginsberg, President and Co-Founder of CreakyJoints[®], a national patient advocacy organization for people with all forms of arthritis, "Despite common misperceptions, OA is not a disease that is limited to the elderly. In fact, the average age of knee OA diagnosis has decreased while the number of people diagnosed with OA of the knee has been steadily rising. That's why our community advocates for and welcomes new therapeutic options for people to consider in consultation with their doctor."

Flexion expects Zilretta will be available in the U.S. by the end of October. For more information, visit www.Zilretta.com or call 1-844-FLEXION.

Conference Call Details

Flexion's management will host a conference call Monday, October 9, 2017, at 8:00 a.m. ET. The dial-in number for the conference call is 855-770-0022 for domestic participants and 908-982-4677 for international participants, with Conference ID # 92539488. A live webcast of the conference call can also be accessed through the "[Investors](#)" tab on the Flexion Therapeutics website, and a replay will be available online after the call.

About Zilretta

Zilretta is the first and only FDA-approved extended-release intra-articular therapy for patients confronting osteoarthritis-related knee pain. Zilretta employs proprietary microsphere technology combining triamcinolone acetonide — a commonly administered, short-acting corticosteroid — with a poly lactic-co-glycolic acid (PLGA) matrix to provide extended pain relief over 12 weeks.

Indication and Important Safety Information

Indication: ZILRETTA[™] (triamcinolone acetonide extended-release injectable suspension) is indicated as an intra-articular injection for the management of osteoarthritis pain of the knee.

Limitations of Use: ZILRETTA is not intended for repeat administration.*

Contraindication: ZILRETTA is contraindicated in patients who are hypersensitive to triamcinolone acetonide, corticosteroids or any components of the product.

Warnings and Precautions

- | **Intra-articular Use Only:** ZILRETTA has not been evaluated and should not be administered by epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal or subcutaneous routes. Serious events have been reported with epidural and intrathecal administration of corticosteroids and none are approved for this use. ZILRETTA should not be considered safe for epidural or intrathecal administration.
- | **Hypersensitivity Reactions:** Rare instances of anaphylaxis, including serious cases, have occurred in patients with hypersensitivity to corticosteroids.
- | **Joint Infection and Damage:** A marked increase in pain accompanied by local swelling, restriction of joint motion, fever and malaise are suggestive of septic arthritis. Examine joint fluid to exclude a septic process. If diagnosis is confirmed, institute appropriate antimicrobial therapy. Avoid injecting corticosteroids into a previously infected or unstable joint. Intra-articular administration may result in damage to joint tissues.
- | **Increased Risk of Infections:** Infection with any pathogen in any location of the body may be associated with corticosteroid use. Corticosteroids may increase the susceptibility to new infection and decrease resistance and the ability to localize infection.
- | **Alterations in Endocrine Function:** Corticosteroids can produce reversible hypothalamic-pituitary-adrenal axis suppression, with potential for adrenal insufficiency after withdrawal of treatment, which may persist for months. In situations of stress during that period, institute corticosteroid replacement therapy.
- | **Cardiovascular and Renal Effects:** Corticosteroids can cause blood pressure elevation, salt and water retention and increased potassium excretion. Monitor patients with congestive heart failure, hypertension and renal insufficiency for edema, weight gain and electrolyte imbalance. Dietary salt restriction and potassium supplementation may be needed.
- | **Increased Intraocular Pressure:** Corticosteroid use may be associated with increased intraocular pressure. Monitor patients with elevated intraocular pressure for potential treatment adjustment.
- | **Gastrointestinal Perforation:** Corticosteroid administration may increase risk of gastrointestinal perforation in patients with certain GI disorders and fresh intestinal anastomoses. Avoid corticosteroids in these patients.
- | **Alterations in Bone Density:** Corticosteroids decrease bone formation and increase bone resorption. Special

consideration should be given to patients with or at increased risk of osteoporosis prior to treatment.

- 1 **Behavior and Mood Disturbances:** Corticosteroids may cause adverse psychiatric reactions. Prior to treatment, special consideration should be given to patients with previous or current emotional instability or psychiatric illness. Advise patients to immediately report any behavior or mood disturbances.

Adverse Reactions: The most commonly reported adverse reactions (incidence $\geq 1\%$) in clinical studies included sinusitis, cough and contusions.

Please see the **full Prescribing Information** at www.ZILRETTAlabel.com.

* The efficacy and safety of repeat administration of ZILRETTA have not been evaluated.

About Osteoarthritis (OA) of the Knee

OA, also known as degenerative joint disease, affects more than 30 million Americans and accounts for more than \$185 billion in annual expenditures. In 2016, more than 15 million Americans were diagnosed with OA of the knee and the average age of physician-diagnosed knee OA has fallen by 16 years, from 72 in the 1990s to 56 in the 2010s. The prevalence of OA is expected to continue to increase as a result of aging, obesity and sports injuries. Each year, more than 15 million Americans are treated for OA-related knee pain, and approximately five million OA patients receive either an immediate-release corticosteroid or hyaluronic acid intra-articular injection to manage their knee pain.

About Flexion Therapeutics

Flexion Therapeutics (Nasdaq:FLXN) is a specialty pharmaceutical company focused on the development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with OA, a type of degenerative arthritis. 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.

Forward-Looking Statements

Statements in this press release regarding matters that are not historical facts, including, but not limited to, statements relating to the future of Flexion; timing for the expected commercial availability of Zilretta; our plans to commercialize Zilretta and its market potential; expected increases in the rate of individuals with OA of the knee; and the potential therapeutic and other benefits of Zilretta, are forward-looking statements. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release and are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those expressed or implied by such statements. These risks and uncertainties include, without limitation, risks associated with the process of launching a new pharmaceutical product in the United States; the risk that we may not be able to maintain and enforce our intellectual property, including intellectual property related to Zilretta; competition from alternative therapies; the risk that we may not be able to successfully hire, train and maintain an effective sales force to commercialize Zilretta; the risk that Zilretta may not be successfully commercialized, including as a result of limitations in Zilretta's label and package insert information; risks regarding our ability to obtain adequate reimbursement from payors for Zilretta; risks related to the manufacture and distribution of Zilretta, including our reliance on sole sources of supply and distribution; risks related to key employees, markets, economic conditions, health care reform, prices and reimbursement rates; and other risks and uncertainties described in our filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in our most recent Annual Report on Form 10-K and subsequent filings with the SEC. The forward-looking statements in this press release speak only as of the date of this press release, and we undertake no obligation to update or revise any of the statements. We caution investors not to place considerable reliance on the forward-looking statements contained in this press release.

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