March 6, 2018

# Flexion Therapeutics Presents Clinical Data at AAOS 2018 Annual Meeting and the American Pain Society Annual Scientific Meeting

- Post-hoc analysis demonstrates potential of ZILRETTA® (triamcinolone acetonide extended-release injectable suspension) to provide effective pain relief regardless of prior intra-articular corticosteroid use
- Effects of ZILRETTA show improvement on health-related quality of life in patients with knee osteoarthritis
- Analysis of assay sensitivity identifies differences in clinical instruments used to assess pain

BURLINGTON, Mass., March 06, 2018 (GLOBE NEWSWIRE) -- Flexion Therapeutics, Inc. (Nasdaq:FLXN) will present positive data from three studies of ZILRETTA® (triamcinolone acetonide extended-release injectable suspension), also referred to as TA-ER/FX006, in patients with osteoarthritis (OA) knee pain. Two data presentations will be given at the American Academy of Orthopaedic Surgeons (AAOS) 2018 Annual Meeting, taking place March 6 — 10 in New Orleans, Louisiana. A separate poster presentation was delivered at the American Pain Society (APS) Annual Scientific Meeting held March 4-6 in Anaheim, California.

"These presentations shine light on ZILRETTA's potential to provide effective pain relief in patients who have been previously treated with an immediate-release steroid, and they suggest that treatment with ZILRETTA may lead to improvements in key quality of life measures," said Michael Clayman, M.D., President and Chief Executive Officer of Flexion. "Also of interest is the finding that the Average Daily Pain (ADP) tool appears less sensitive than the OA specific WOMAC[1] instrument. These data are refining our understanding of the assays and will help to guide the design of future trials."

**Presentations at AAOS:**

**Title:** Impact of Prior Intra-Articular Corticosteroid Injections on the Efficacy of TA-ER, an Intra-Articular Extended-Release Formulation of Triamcinolone Acetonide, in Patients with Osteoarthritis of the Knee: Post-Hoc, Pooled Analysis of Three Randomized Controlled Trials
**Conference:** AAOS
**Oral Presentation:** 908
**Location:** Room 353
**Date and Time:** Friday, March 9, 2018: 5:18 PM-5:24 PM (CST)

The post-hoc analysis utilized data from 586 patients with knee OA enrolled in three Phase 2/3 randomized, controlled trials, and compared the duration of the analgesic effects in 159 patients (ZILRETTA n=94; PBO, n=65) who had received prior intra-articular corticosteroid (IACS) treatment and 427 patients (ZILRETTA n=230; PBO, n=197) with no prior IACS history.

The analysis showed that at 12 weeks after intra-articular (IA) treatment, pain reduction with ZILRETTA was statistically significant in the subgroup with no prior IACS compared with saline-placebo (PBO) (p=0.0002) and numerically favored ZILRETTA over placebo in the subgroup with prior IACS (p=0.0530). In patients with no prior IACS, pain relief in the ZILRETTA group was significantly improved compared with PBO through 19 weeks after treatment (p=0.0124). The results suggest ZILRETTA may provide extended analgesic benefit effect when utilized as the initial IA treatment in patients with knee OA.

**Title:** Effects of an Intra-Articular, Extended-Release Corticosteroid (TA-ER) Treatment on Health-Related Quality of Life in Patients with Knee Osteoarthritis: Comparison with General Population Controls
**Conference:** AAOS
**Poster Presentation:** P0906
**Location:** Academy Hall B
**Date and Time:** Presenters will be at their poster March 8-10 from 11:30 AM - 12:30 PM (CST) daily to answer questions from attendees.

The post-hoc analysis utilizing clinical data from three randomized Phase 2/3 trials of ZILRETTA compared Health Utilities Index Mark 3 (HUI-3) values, a validated measure of health-related quality of life (HRQoL), between 255 knee OA patients

(males, n=106; females, n=149) who received ZILRETTA and 393 males and 596 females in the general U.S. population obtained from the Health Utilities Inc. database.[2]

Results show that prior to treatment with ZILRETTA, the mean HUI-3 score for patients ≥53 years of age with knee OA was substantially lower compared with individuals ≥53 years in the general U.S. population (0.415 vs. 0.768, respectively, for women, and 0.472 vs. 0.799 for men). Following treatment with ZILRETTA, HUI-3 scores in women and men with knee OA improved at Week 4, Week 8 and Week 12 (0.657, 0.644 and 0.618, respectively, for women, and 0.692, 0.674 and 0.652 for men). In the exploratory analysis, changes in HUI-3 scores following ZILRETTA treatment in patients with knee OA exceeded minimally important clinical differences and were within 80% of the reference values for the general matched population.

**Poster Presentation at American Pain Society Annual Scientific Meeting:**

**Title:** Assay Sensitivity of Average Daily Pain and Western Ontario and McMaster Osteoarthritis Index A-pain (WOMAC-A) in a Phase 3 Trial of Intra-Articular TA-ER for Osteoarthritis Knee Pain
**Conference:** APS
**Poster Presentation:** 262
**Date:** March 4-6, 2018

The post-hoc study evaluated the sensitivity of the ADP and WOMAC-A instruments used in the Phase 3 trial of ZILRETTA. In the Phase 3 trial, ZILRETTA demonstrated significant improvement compared with PBO but not active comparator as measured by ADP. However, when assessed using the WOMAC-A instrument, ZILRETTA demonstrated significant improvement over both PBO and triamcinolone acetonide crystalline suspension.

Results show that the Standardized Effect Size values for ADP were consistently lower than those for WOMAC-A. The analysis of assay sensitivity suggests that trial and instrument characteristics, including an enriched population using baseline ADP and scale differences between the ADP and WOMAC-A instruments, may produce variability in assessment of pain responses. Study authors recommend considering these observations when evaluating the magnitude of analgesic benefit observed between active therapies and defining the primary end-point in future trials.

**Indication and Select Important Safety Information for ZILRETTA (triamcinolone acetonide extended-release injectable suspension)**

**Indication:** ZILRETTA (triamcinolone acetonide extended-release injectable suspension) is indicated as an intra-articular injection for the management of osteoarthritis pain of the knee. It 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. ZILRETTA should not be considered safe for epidural or intrathecal administration.
- **Serious Neurologic Adverse Reactions with Epidural and Intrathecal Administration:** Serious neurologic events have been reported following epidural or intrathecal corticosteroid administration. Corticosteroids are not approved for this use.
- **Hypersensitivity reactions:** Serious reactions have been reported with triamcinolone acetonide injection. Institute appropriate care if an anaphylactic reaction occurs.
- **Joint infection and damage:** A marked increase in joint pain, joint swelling, restricted motion, fever and malaise may suggest septic arthritis. If this occurs, conduct appropriate evaluation and if confirmed, institute appropriate antimicrobial treatment.

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

**Please see ZilrettaLabel.com for full Prescribing Information.**

**About ZILRETTA**

ZILRETTA is the first and only 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. ZILRETTA received approval from the U.S. Food and Drug Administration on October 6, 2017 and the company initiated the full commercial launch on November 20, 2017.

**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 biopharmaceutical 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 and one of the *Top Places to Work* in Massachusetts by *The Boston Globe*.

**Forward-Looking Statements**

This release contains forward-looking statements that are based on the current expectations and beliefs of Flexion. Statements in this press release regarding matters that are not historical facts, including, but not limited to, statements relating to the future of Flexion; expected increases in the rate of individuals with OA of the knee; expected increases in the prevalence of OA; 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 designing and conducting clinical trials; the fact that results of past clinical trials may not be predictive of ongoing or subsequent trials; competition from alternative therapies; and other risks and uncertainties described in our filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 filed on November 6, 2017 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.

**References**

[1] WOMAC (Western Ontario and McMaster Universities Arthritis Index) is a validated, widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness and physical functioning of the joints.

[2] www.healthutilities.com.

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