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Flexion Therapeutics Announces Publication of Results from Pivotal Phase 3 Study of ZILRETTA® (triamcinolone acetonide extended-release injectable suspension) in the Journal of Bone and Joint Surgery

BURLINGTON, Mass., April 18, 2018 (GLOBE NEWSWIRE) -- Flexion Therapeutics, Inc. (Nasdaq:FLXN) today announced that the key results from the previously completed pivotal Phase 3 study evaluating ZILRETTA (triamcinolone acetonide extended-release injectable suspension) have been published in the print and online edition of the [Journal of Bone and Joint Surgery](#) (Vol 100 (8) pp 666 — 677). ZILRETTA was approved by the U.S. Food and Drug Administration (FDA) on October 6, 2017, as an intra-articular (IA) injection for the management of pain associated with osteoarthritis (OA) of the knee.

The randomized, double-blind, placebo-controlled, active-comparator Phase 3 trial enrolled 484 patients at 37 centers worldwide. Patients were randomized to one of three treatment groups (1:1:1) and received either a single IA injection of ZILRETTA (32 mg), normal saline-placebo or triamcinolone acetonide in crystalline suspension (TACs) (40 mg). Data from this study served as the foundation for ZILRETTA's New Drug Application and subsequent FDA approval.

"These data demonstrate ZILRETTA's ability to provide rapid, substantial and persistent pain relief in individuals with knee OA," said Michael Clayman, M.D., President and Chief Executive Officer of Flexion. "The publication of these results in the prestigious *Journal of Bone and Joint Surgery* helps advance the dialogue within the medical and scientific communities about the important role ZILRETTA can play in the treatment paradigm of OA knee pain, presenting an important option for the millions of Americans who confront this painful disease."

The primary study objective was to assess the magnitude of pain relief at 12 weeks in patients receiving ZILRETTA compared with saline-placebo as measured by the weekly mean of the average daily pain (ADP) score. Each patient was evaluated for efficacy and safety during seven outpatient visits over 24 weeks after receiving an injection.

Professor Philip Conaghan, M.D., Ph.D., lead study investigator and Chair of Musculoskeletal Medicine at the University of Leeds stated, "OA of the knee is a serious condition that is highly prevalent globally, often leaves people in chronic pain and presents a high economic burden to society. These data reflect the clinical trial rigor necessary to guide the understanding of this novel therapeutic option and represent an important milestone for the OA scientific and clinical communities."

Key findings and conclusions reported by the authors include that ZILRETTA:

- 1 Met its primary endpoint, demonstrating a highly statistically significant ($p < 0.0001$) reduction in ADP versus saline-placebo at week 12, with durable pain relief in patients with moderate to severe OA knee pain;
 - Provided an approximately 50 percent reduction in pain from baseline over weeks 1 through 12, a benefit that extended through week 16.
- 1 Was favored when compared with saline-placebo and TACs at each time point through 12 weeks on exploratory measures — WOMAC A¹ (pain), WOMAC B (stiffness) and WOMAC C (function) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale;
- 1 Demonstrated reduced rescue medicine consumption compared with saline-placebo and TACs (exploratory endpoint);
- 1 Was superior to saline-placebo, but the difference between ZILRETTA and TACs as measured by ADP was not statistically significant;
- 1 Demonstrated an acceptable safety profile, with adverse events being generally mild and occurring at similar frequencies across treatment groups. The most common adverse events for ZILRETTA with an incidence greater than 5 percent were joint pain, headache and back pain. No drug-related serious adverse events were observed and no patients treated with ZILRETTA discontinued the study due to a treatment-related side effect.

"Many patients are prescribed opioids for the pain associated with OA of the knee, which have shown only moderate success and are often eclipsed by significant adverse effects including addiction and withdrawal," said John Richmond, M.D., Medical Director for Network Development, New England Baptist Hospital. "The development of non-opioid alternatives for patients with OA knee pain is crucial for our society, and it is exciting to be able to offer ZILRETTA in my clinical practice

as a new treatment."

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

Indication: ZILRETTA 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:

- 1 **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.
- 1 **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.
- 1 **Hypersensitivity reactions:** Serious reactions have been reported with triamcinolone acetonide injection. Institute appropriate care if an anaphylactic reaction occurs.
- 1 **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 $\geq 1\%$) in clinical studies included sinusitis, cough, and contusions.

Please see ZilrettaLabel.com for full Prescribing Information.

About ZILRETTA

ZILRETTA is the first and only 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. 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 is the most common joint disease, affecting more than 30 million Americans and accounting 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 IOA 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; ZILRETTA's 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 commercializing new pharmaceutical products; the fact that results of past clinical trials may not be predictive of subsequent trials; our reliance on third parties to manufacture and conduct clinical trials of ZILRETTA; 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;

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 Annual Report on Form 10-K for the year ended December 31, 2017 filed with the SEC on March 8, 2018 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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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.