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Flexion Therapeutics Reports Primary Endpoint Met in Pivotal Phase 3 Trial of Zilretta™ in Knee Osteoarthritis

- *Primary endpoint at week 12 against placebo achieved p value of <0.0001; statistically significant and clinically meaningful pain relief demonstrated at weeks 1 through 16*
- *Zilretta also achieved statistical significance on WOMAC® A (pain), WOMAC B (stiffness) and WOMAC C (function) through week 12 against both placebo and immediate-release triamcinolone acetonide*
- *Zilretta patients experienced, on average, a 50 percent reduction in pain from baseline over weeks 1 through 12*
- *Zilretta, an investigational non-opioid/non-NSAID, has received Fast-Track designation by FDA; planned NDA submission on track for second half of 2016*
- *Conference call tomorrow, February 17, at 9:00 a.m. ET*

BURLINGTON, Mass., Feb. 16, 2016 (GLOBE NEWSWIRE) -- Flexion Therapeutics, Inc. (Nasdaq:FLXN) today reported that the Phase 3 clinical trial for its lead drug candidate Zilretta (also known as FX006) met its primary endpoint at week 12, demonstrating highly significant ($p<0.0001$), durable and clinically meaningful pain relief against placebo in patients with moderate to severe osteoarthritis (OA) knee pain. In addition, Zilretta achieved statistically significant analgesia against placebo at weeks 1 through 16 and patients treated with Zilretta experienced, on average, a 50 percent reduction in pain from baseline over weeks 1 through 12. In pre-specified analyses, Zilretta achieved statistical significance against placebo in validated OA and quality of life secondary measures through week 12.

In pre-specified secondary measures, compared to immediate-release triamcinolone acetonide (TCA), the most commonly injected intra-articular (IA) corticosteroid, Zilretta achieved statistical significance through 12 weeks on WOMAC A[1] (pain), WOMAC B (stiffness) and WOMAC C (function) and the validated Knee injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale and was numerically superior at weeks 2 through 12 on the daily pain rating scale, although it did not achieve statistical significance in that measure.

The frequency of treatment-related side effects was comparable across all treatment arms in the trial. 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 are extremely gratified with these Phase 3 data that strongly reinforce Zilretta's previous clinical efficacy results, which are consistent with substantial and durable pain relief," said Flexion Therapeutics President and Chief Executive Officer Michael Clayman, M.D. "We believe that Zilretta has the potential to become an important new non-opioid treatment in a therapeutic area that hasn't seen meaningful innovation in many years. More than 12 million people in the U.S. suffer from the painful and debilitating effects of knee OA and many have not found effective relief with existing therapies. We look forward to working closely with the U.S. Food and Drug Administration (FDA) as we prepare to submit our New Drug Application (NDA) for Zilretta."

Zilretta was designed using proprietary microsphere technology and is intended to provide localized and long-lasting pain relief over a period of months while minimizing systemic exposure and avoiding serious side effects common to oral therapies prescribed for OA pain. Current oral treatment options for OA knee pain include non-steroidal anti-inflammatory drugs (NSAIDS), COX II inhibitors and opioids. All are labeled with black box warnings for serious, sometimes fatal, side effects. IA medicines, such as immediate-release corticosteroids and hyaluronic acid injected into the joint, are generally well-tolerated but fail to produce pain relief of sufficient magnitude or duration.

"There have been no major advances in the treatment of OA for decades and given the limited efficacy and the safety liabilities of available therapies, patients are in need of a new treatment option," said Stan Cohen, M.D., Medical Director, Metroplex Clinical Research Center and Clinical Professor of Internal Medicine, UT Southwestern Medical School, Dallas. "These data suggest that Zilretta has the potential to be a significant advance in pain management for patients with OA of the knee."

About the Phase 3 Trial

The randomized, double-blind Phase 3 placebo-controlled, active-comparator trial enrolled 486 patients at approximately 40 centers worldwide. Patients were randomized to one of three treatment groups (1:1:1) and received either a single IA injection of 40 mg of Zilretta, normal saline (placebo) or 40 mg of immediate-release TCA. Each patient was evaluated for efficacy and safety during seven outpatient visits over 24 weeks after receiving an injection. The primary objective of the study was to assess the magnitude of pain relief of Zilretta at 12 weeks against placebo. The secondary objectives of the study were to assess the magnitude and duration of pain relief and effect of Zilretta against placebo and immediate-release TCA in a variety of additional pre-specified measures.

Flexion plans to present detailed results from the Phase 3 clinical trial at an upcoming scientific meeting.

Conference Call

At 9:00 a.m. ET tomorrow, Flexion's management will host a conference call to discuss the Phase 3 clinical results and provide a general update on the Zilretta program. The dial-in number for the conference call is (855) 770-0022 for U.S. participants and (908) 982-4677 for international participants, with Conference ID # 51030771. A live webcast of the conference call can also be accessed through the "Investors" tab on the Flexion Therapeutics website at www.flexiontherapeutics.com. A webcast replay will be available online after the call.

About Osteoarthritis of the Knee

OA is a common joint disease that affects 27 million Americans, and the prevalence of the disease is expected to significantly grow as a result of aging, obesity and sports injuries. OA is a type of degenerative arthritis that is caused by the progressive breakdown and eventual loss of cartilage in one or more joints. OA is characterized by pain, swelling, stiffness and decreased mobility of the affected joint. While OA is being diagnosed at increasingly younger ages, prevalence rises after age 45, and the knee is one of the most commonly affected joints. In 2014, more than 12 million Americans were diagnosed with OA of the knee. OA has a significant impact on the daily lives of patients, and it commonly affects large weight-bearing joints like the knees and hip but also occurs in the shoulders, hands, feet and spine. As the disease progresses, it becomes increasingly painful and debilitating, culminating, in many cases, in the need for total joint replacement.

Each year, at least five million OA patients in the U.S. receive immediate-release corticosteroid and hyaluronic acid IA injections for knee pain, but these injections generally provide limited relief, and no alternative injectable therapy has been approved in more than a decade. Opioids are another treatment option, and as many as 40 percent of Medicare patients are prescribed opioids for chronic OA pain.

About Zilretta

Zilretta is being investigated as the first IA sustained-release, non-opioid treatment for patients with moderate to severe OA pain. Zilretta employs proprietary microsphere technology combining TCA — a commonly administered, short-acting corticosteroid — with a polymer (PLGA) intended to provide persistent concentrations of drug locally to both amplify the magnitude and prolong the duration of pain relief.

To date, over 600 patients have been treated with Zilretta in clinical trials. No drug-related serious adverse events have been observed in these trials and adverse events have typically been localized, mild and comparable to those observed with immediate-release TCA and placebo. The data from these trials are consistent with Zilretta providing meaningful and durable pain relief.

About Flexion Therapeutics

Flexion 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. The company's lead product candidate, Zilretta, is being investigated for its potential to provide improved analgesic therapy for the millions of U.S. patients who receive IA injections for knee OA annually. The company is also investigating another product candidate, FX007, a locally administered TrkA receptor antagonist for post-operative pain.

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; our ongoing development of Zilretta and our other product candidates; our interpretation of the data and results from our Zilretta clinical trials; our plans for, and the expected timing of, our Zilretta NDA submission

with the FDA; our plans to commercialize Zilretta and its market potential; and the potential therapeutic and other benefits of Zilretta and our other product candidates, 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 discovering, developing, manufacturing and obtaining regulatory approval for drugs that are safe and effective for use as human therapeutics; 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 and our other product candidates, which could delay or limit their future development or regulatory approval; our ability to meet anticipated clinical trial commencement, enrollment and completion dates and regulatory filing dates for Zilretta; the fact that we will require additional capital, including prior to commercializing Zilretta or any of our other product candidates, and may be unable to obtain such additional capital in sufficient amounts or on terms acceptable to us; the risk that we may not be able to maintain and enforce our intellectual property, including intellectual property related to Zilretta and our other product candidates; competition from alternative therapies; regulatory developments and safety issues, including difficulties or delays in obtaining regulatory approvals to market Zilretta or our other product candidates; the risk that the FDA and foreign regulatory authorities may not agree with our interpretation of the data from our clinical trials of Zilretta and may require us to conduct additional clinical trials; Zilretta may not receive regulatory approval or be successfully commercialized, including as a result of the FDA's or other regulatory authorities' decisions regarding labeling and other matters that could affect its availability or commercial potential; 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.

[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.

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