April 4, 2016

Flexion Therapeutics Announces Presentation of Results From Pivotal Phase 2b and Phase 3 Clinical Trials for Zilretta™ at Osteoarthritis Research Society International (OARSI) 2016 World Congress

- *Positive data from Zilretta Phase 2b and Phase 3 clinical trials demonstrate consistent efficacy across both studies with substantial and persistent pain relief*
- *In the Phase 3 trial Zilretta, in contrast to immediate-release triamcinolone acetonide (TCA), exceeds American Academy of Orthopedic Surgeons (AAOS) criteria for clinically important effects on pain and function*
- *Safety data from these studies are comparable to placebo and immediate-release TCA*
- ***CONFERENCE CALL TODAY APRIL 4, 2016 AT 9:00 A.M. EDT***

BURLINGTON, Mass., April 04, 2016 (GLOBE NEWSWIRE) -- Results from two Flexion Therapeutics, Inc. (Nasdaq:FLXN) sponsored pivotal clinical trials showed that its lead drug candidate Zilretta (also known as FX006) provided sustained and significant pain relief in patients with moderate to severe osteoarthritis (OA) knee pain. Professor Philip Conaghan, M.B., B.S., Ph.D., F.R.A.C.P., F.R.C.P., Chair of Musculoskeletal Medicine at the University of Leeds, presented the results at the OARSI 2016 World Congress in Amsterdam in a podium presentation that is available at http://flexiontherapeutics.com/programs-pipeline/scientific-publications.

Following the presentation Professor Conaghan said, "Consistent results across two pivotal clinical trials with Zilretta suggest that, at last, we have a long-lasting intra-articular therapy that is highly effective and has the potential to change the treatment paradigm for osteoarthritis."

"We are delighted to be able to now share the detailed data from these studies which clearly demonstrate clinically meaningful and statistically significant pain relief in patients with knee OA. In addition, we are especially gratified by the Phase 3 data that demonstrate clear differentiation of Zilretta from immediate-release TCA," said Michael Clayman, M.D., Flexion Therapeutics' President and CEO. "Based on these data we have scheduled a pre-New Drug Application (NDA) meeting in May with the U.S. Food and Drug Administration (FDA) with the intent to gain the Agency's endorsement to submit an NDA in the second half of 2016."

The Phase 3 trial was a randomized, double-blind, placebo-controlled, active-comparator trial that 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 intra-articular 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 as measured by the weekly mean of the average daily pain (ADP) score. The secondary objectives of the study assessed the magnitude and duration of pain relief and effect of Zilretta against placebo and immediate-release TCA in additional pre-specified measures.

Phase 3 study data from the OARSI podium presentation and from additional company analyses are summarized below and posted to the Flexion website at http://flexiontherapeutics.com/programs-pipeline/scientific-publications.

In the Phase 3 study, Zilretta:

- Met its primary endpoint at week 12, demonstrating highly significant ($p < 0.0001$, 2-sided) and clinically meaningful pain relief against placebo as measured by the weekly mean of the ADP score.
- Achieved statistically significant pain relief against placebo as measured by the weekly mean of the ADP score at weeks 1 through 16 and demonstrated, on average, an approximately 50 percent reduction in pain from baseline over weeks 1 through 12.
- Achieved numerically superior pain relief against immediate-release TCA at weeks 2 through 12 as measured by the weekly mean of the ADP score, but did not achieve statistical significance in that measure.
- Achieved statistical significance against placebo and immediate-release TCA at each time point through 12 weeks on WOMAC A (pain), WOMAC B (stiffness) and WOMAC C (function) and the Knee injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale.

- Demonstrated in a pre-specified subset analysis of patients with unilateral knee pain (35 percent of subjects in the study), substantially magnified effects in the weekly mean of the ADP score, WOMAC A, B and C and KOOS quality of life and significantly enhanced separation from placebo and immediate-release TCA in all of these measures.
- Demonstrated reduced rescue medicine consumption compared with placebo and immediate-release TCA.

The Phase 3 data were also evaluated for clinical relevance by applying established AAOS criteria. In its 2013 publication, "Evidence-Based Guideline: Treatment of Osteoarthritis of the Knee," the AAOS comprehensively reviewed the available literature on existing treatments and determined a minimal relative improvement in WOMAC A, B and C measures that would be meaningful to patients. This is referred to as the Minimal Clinically Important Improvement (MCII). The Phase 3 data show that Zilretta exceeds the MCII in WOMAC A, B and C and thus demonstrates a clinically important effect, whereas immediate-release TCA in this study does not.

The Phase 2b trial enrolled 310 participants in a multi-center, randomized, double-blind study, in which the participants received an injection of either 40 mg or 20 mg of FX006, or a placebo (saline). The 40 mg arm of Zilretta, compared to placebo, demonstrated statistical significance in average pain relief over weeks 1 through 12 ($p = 0.0012$; 2-sided) and over weeks 1 through 24 ($p = 0.0209$; 2-sided). At weekly time points, 40 mg of Zilretta also demonstrated superiority to placebo in pain relief beginning at week 1, continuing to week 11 and also at week 13 ($p < 0.05$ at each time point; 2-sided). The primary endpoint of the trial, superiority in pain relief at 12 weeks, did not reach statistical significance ($p = 0.0821$; 2-sided). A pre-specified, commonly applied sensitivity analysis (Baseline Observation Carried Forward/Last Observation Carried Forward (BOCF/LOCF)) that addresses patient dropouts, however, did demonstrate statistical significance for the primary endpoint at 12-weeks ($p = 0.042$).

Across both the Phase 2b and Phase 3 studies, there were no drug related serious adverse events for Zilretta and the frequency of treatment-related side effects was comparable across all study arms.

Conference Call

Flexion's management will host a conference call today at 9:00 a.m. EDT. 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 # 84943960. A live webcast of the conference call can also be accessed through the "Investors" tab on the Flexion Therapeutics website. 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 intra-articular (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; Zilretta's 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.

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