



Xgene Pharmaceutical Announces Positive Top-Line Results from Phase 1b/2a Trial of Topical Gel XG004 for the Treatment of Osteoarthritis (OA) Pain of the Knee

- *Patients had acceptable safety and good tolerability to all regimens tested*
- *Compared with placebo, 5% and 10% XG004 topical gel BID and TID treatment for one week resulted in substantial pain relief and improvement in physical function and sleep quality*

Cayman Island, April 26, 2023: Xgene Pharmaceutical today announced the results of a multiple dose-escalation Phase 1b/2a study in patients with painful knee osteoarthritis (OA), evaluating the safety and exploratory efficacy of topical administration of XG004, an investigational drug of a patented new chemical entity with dual-action to treat both nociceptive and neuropathic pain (NCT05454020).

The study tested 5% and 10% XG004 topical gel applied once (qd), twice (bid) or thrice (tid) daily for 7 consecutive days, respectively, in 32 OA patients with moderate to severe pain and Kellgren-Lawrence grade of II-IV.

All patients demonstrated good tolerability and acceptable safety profile. There were no serious adverse events, nor discontinuations from the study drug or the study.

All treatment regimens improved the exploratory efficacy measures. On top of the placebo effect, the twice and thrice daily drug applications resulted in symptom relief in Western Ontario and McMaster Universities (WOMAC) pain, physical function, stiffness, total score and daily walking pain with standard effect sizes of 0.639, 0.444, 0.528 0.508, and 0.343 by the end of 7 days treatment, respectively. Furthermore, these treatment regimens improved pain-induced sleep interference with an effect size of 0.752. Numerically greater reduction of rescue medication use was observed in the XG004-treated patients than in placebo-treated patients. Assessed with Patient Global Impression of Change (Minimally worse + No Change + Minimally improved + Much improved + Very much improved), 72.2% patients with XG004 BID and TID treatment reported at least “minimally improved” and 27.8% reported “no change”, while 50% reported at least “minimally improved” and 50% reported “no change” or “minimally worse” in the placebo-treated patients.



Although active comparator was not tested in this study, to better understand the effective size, a previously published study demonstrated that “Topical diclofenac sodium 1% gel (four times a day: qid) demonstrated therapeutic efficacy after 12 weeks topical treatment in knee OA patients with Kellgren-Lawrence grade of I-III (lighter joint damage than the patients enrolled in XG004 study), with standard effect sizes of 0.311, 0.303 and 0.227 in WOMAC pain, function and movement pain, respectively (*Baraf et al. Safety and Efficacy of Topical Diclofenac Sodium 1% Gel in Knee Osteoarthritis: A Randomized Controlled Trial. THE PHYSICIAN AND SPORTSMEDICINE • ISSN – 0091-3847, June 2010, No. 2, Volume 38.*). In another published study, intra-articular injection of corticosteroids or hyaluronic acid demonstrated effect size of 0.32 or 0.34 compared with placebo at 12 weeks post treatment (*Bannuru et al., Annals of Internal Medicine. 2015; 162:46-54.*). “We are extremely encouraged by these early study results, which show the potential of topical XG004 as a non-oral, non-invasive treatment option for pain reduction and improvement in physical function and quality of life in osteoarthritis patients. Topical therapeutics are still the first line recommendation of various OA treatment guidelines for pharmacological management of OA.” said Leon Jiang, Chief Medical Officer at Xgene Pharmaceutical.

“There is a substantial need for innovative safer new treatment options for osteoarthritis, as many patients are unable to get sufficient relief with currently available medicines with intolerable side effects. We are pleased that the results from this trial showed the positive therapeutic effect of topical gel XG004, with the potential to be a better treatment option compared to the current therapies. Today’s data are a culmination of a persistent team effort within our organization and its collaborators. As fast-growing aging population continues to burden the healthcare systems across the globe, safer and cost-effective treatments will be needed for chronic pain. Xgene is proud to continue its efforts on this unique product aiming for various chronic pain conditions, moving forward with great confidence.” Said Gene Hsu, CEO of Xgene.



About the Study

The exploratory Phase 1b/2a OA study (NCT054540200) was a 1-week randomized, double-blind, placebo-controlled, single-center, parallel-group trial evaluating the safety and efficacy of topical administration of XG004 compared to placebo in patients with OA of the knee. The trial included an additional 1-week safety follow-up period following dosing completion. In the study, patients were enrolled with moderate to severe OA pain who had experienced inadequate pain relief with other treatment options for OA pain or were unable to take other pain medications. The patients were randomized to six treatment groups in a 3:1 ratio to receive 3 mL of 5% or 10% topical gel of XG004 qd, bid, tid or placebo over the 1-week period. Patient safety and tolerability was monitored as the primary endpoint. The exploratory efficacy of XG004 vs. placebo was measured by changes from baseline in the WOMAC Total score, Pain, Stiffness and Physical Function subscales, daily walking pain, sleep interference and the patient's Global Assessment of OA.

About Topical XG004

XG004, a novel molecule possesses dual functions of anti-inflammatory and anti-neuropathic pain therapeutic potential. It is a potential first-in-class, topical treatment being evaluated for OA pain. XG004 works by absorption through skin, followed by carboxyl esterase cleavage in the dermis to release two active drugs into the local tissues. By inhibiting local COXs enzymes and modulating peripheral $\alpha_2\delta$ subtype calcium ion channels simultaneously, XG004 is postulated to reduce inflammation in synovial membrane and knee joint and prevent pain signals produced by muscles and the skin from reaching the spinal cord and brain. Topical XG004 could minimize the gastrointestinal and central nervous systems side effects associated with these classes of drugs to improve side effects in a long term use.

PRESS RELEASE



About Xgene Pharmaceutical: Transforming Medicine for Better Lives

At Xgene, we apply new clinical findings, science and innovative technology to bring therapies to people to extend and significantly improve their lives. We strive for quality, safety and value in our new products. Our goal is to deliver the world's best medicine to patients worldwide. Xgene's drug discovery areas include pain and CNS diseases, finding treatments and cures to unmet medical needs. We collaborate with health care providers, governments, and local communities to identify patient needs and deliver reliable, affordable medicines around the world. Visit our website at www.xgenepharm.com.