Iroko Pharmaceuticals Gains FDA Approval of ZORVOLEX® for Management of Osteoarthritis Pain

New Indication in Chronic Pain Marks Company's Third FDA Approval in Less Than a Year

PHILADELPHIA, August 25, 2014 — Iroko Pharmaceuticals, LLC, a global specialty pharmaceutical company dedicated to advancing the science of analgesia, announced today the United States Food and Drug Administration (FDA) has approved ZORVOLEX® (diclofenac) capsules, a nonsteroidal anti-inflammatory drug (NSAID), for the management of osteoarthritis pain. This marks the second indication for ZORVOLEX, approved by FDA in October 2013 for the treatment of mild to moderate acute pain in adults[1].

"Given the dose-related adverse events associated with NSAIDs as a class and the widespread use of NSAIDs for osteoarthritis, we are delighted to gain approval for our first SoluMatrix® NSAID for the management of osteoarthritis pain," said Dr. Clarence Young, Chief Medical Officer of Iroko Pharmaceuticals. "Iroko has already made great strides to help fill the need for low dose NSAID options in patients with acute pain and we are continuing to expand our portfolio to also address chronic pain indications."

ZORVOLEX was developed to align with recommendations from FDA and several professional medical organizations that NSAIDs be used at the lowest effective dose for the shortest possible duration consistent with individual patient treatment goals[2]. ZORVOLEX is the first FDA-approved low dose NSAID developed using proprietary SoluMatrix Fine Particle Technology™ and is now available by prescription. ZORVOLEX contains diclofenac as submicron particles that are approximately 20 times smaller than their original size. The reduction in particle size provides an increased surface area, leading to faster dissolution.

"Expanding the use of ZORVOLEX beyond acute pain to osteoarthritis pain, a chronic condition, is a testament to Iroko's continued commitment to developing a low dose NSAID portfolio to address a broad range of unmet patient needs," said John Vavricka, President and CEO of Iroko Pharmaceuticals. "This second approval for ZORVOLEX continues to lay the groundwork for our future portfolio, which utilizes a new approach to pain management."

The approval of ZORVOLEX for the management of osteoarthritis pain was supported by data from a 12-week, multi-center, randomized, double-blind, parallel-group, placebo-controlled trial that enrolled 305 patients, aged 41-90 years, with osteoarthritis of the hip or knee. Half of the patients were between the ages of 61-90. Participants were randomized to ZORVOLEX 35mg three times daily or 35mg twice daily, or placebo[3]. The Supplemental New Drug Application (sNDA) also included data from a 12-month open-label safety study that enrolled 602 patients[1].

"NSAIDs continue to be an integral part of the management for osteoarthritis, the most common type of arthritis[4], and their use is likely to increase as the U.S. population continues to age and the incidence of osteoarthritis rises[5]," said Dr. Roy Altman, Professor of Medicine in Rheumatology at UCLA. "The approval of ZORVOLEX is a welcome and meaningful advance and is the first SoluMatrix® NSAID option approved by the FDA for osteoarthritis pain."

About ZORVOLEX

ZORVOLEX was developed to align with recommendations from FDA and several professional medical organizations that NSAIDs be used at the lowest effective dose for the shortest possible duration consistent with individual patient treatment goals[2]. ZORVOLEX is the first FDA-approved low dose NSAID developed using proprietary SoluMatrix Fine Particle Technology™ and is now available by prescription. ZORVOLEX contains diclofenac as submicron particles that are approximately 20 times smaller than their original size. The reduction in particle size provides an increased surface area, leading to faster dissolution. For more information, visit **www.ZORVOLEX.com**.

ZORVOLEX is indicated for the management of mild to moderate acute pain and osteoarthritis pain.

Important Safety Information about ZORVOLEX

Cardiovascular Risk

Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with

duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

ZORVOLEX is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk

NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

ZORVOLEX is contraindicated in patients with: a known hypersensitivity to diclofenac or its inactive ingredients; a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs.

ZORVOLEX should be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Elevation of one or more liver tests may occur during therapy with ZORVOLEX. Physicians should measure transaminases (ALT and AST) periodically in patients receiving long-term therapy with ZORVOLEX. ZORVOLEX should be discontinued immediately if abnormal liver tests persist or worsen.

NSAIDs, including ZORVOLEX, can lead to the new onset or worsening of existing hypertension, which may contribute to the increased incidence of cardiovascular events. Blood pressure should be monitored closely during treatment with ZORVOLEX. NSAIDs may diminish the antihypertensive activity of thiazides, loop diuretics, ACE inhibitors and angiotensin II antagonists.

Fluid retention and edema have been observed in some patients taking NSAIDs. ZORVOLEX should be used with caution in patients with fluid retention or heart failure.

Long-term administration of NSAIDs can result in renal papillary necrosis and other renal injury. ZORVOLEX should be used with caution in patients at greatest risk of this reaction, including the elderly, those with impaired renal function, heart failure, liver dysfunction, and those taking diuretics and ACE inhibitors. Treatment with ZORVOLEX in patients with advanced renal disease is not recommended.

Anaphylactoid reactions may occur in patients with the aspirin triad or in patients without prior exposure to ZORVOLEX and should be discontinued immediately if an anaphylactoid reaction occurs.

NSAIDs can cause serious skin adverse events such as exfoliative dermatitis, Stevens - Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. ZORVOLEX should be discontinued if rash or other signs of local skin reaction occur.

Starting at 30 weeks' gestation, ZORVOLEX and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur.

Concomitant administration of diclofenac and aspirin or anticoagulants is not generally recommended because of the risk of increased GI bleeding that is higher than in users of either drug alone.

Most common adverse reactions in clinical trials (incidence ≥2%) include: edema, nausea, headache, dizziness, vomiting, constipation, pruritus, diarrhea, flatulence, pain in extremity, abdominal pain, sinusitis, alanine aminotransferase increased, blood creatinine increased, hypertension, and dyspepsia.

ZORVOLEX capsules do not result in an equivalent systemic exposure to diclofenac as other oral formulations. Therefore, do not substitute similar dosing strengths of other diclofenac products for ZORVOLEX.

Please see full **Prescribing Information** for additional important safety and dosing information.

For more information, visit **www.ZORVOLEX.com.**

About Iroko Pharmaceuticals, LLC

Iroko is a global specialty pharmaceutical company, based in Philadelphia, dedicated to advancing the science of analgesia. The company develops and globally commercializes pharmaceutical products. Iroko is at the forefront of the development of SoluMatrix® NSAIDs – new low dose drug products based on existing NSAIDs – using iCeutica Inc.'s proprietary SoluMatrix Fine Particle Technology™ exclusively licensed to Iroko for NSAIDs. ZORVOLEX is the first SoluMatrix® NSAID and is available in pharmacies; a second was approved by FDA in February 2014. For more information, visit **www.iroko.com**.

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[1] ZORVOLEX Prescribing Information.

[2] U.S. Food and Drug Administration. Public Health Advisory – FDA Announces Important Changes and Additional Warnings for COX-2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).

[3] Gibofsky, A., et al. Efficacy and safety of low-dose submicron diclofenac for the treatment of osteoarthritis pain: a 12 week, phase 3 study. Current Medical Research Opinion. 2014 Aug 6:1-11.

[4] The Burden of Musculoskeletal Diseases in the United States: Arthritis and Related Conditions. Chapter 4; 2011. http://www.boneandjointburden.org/pdfs/BMUS_chpt4_arthritis.pdf.

[5] Fine, Michael. Quantifying the Impact of NSAID-Associated Adverse Events. The American Journal of Managed Care, 2013. http://www.ajmc.com/publications/supplement/2013/A467_Nov13_NSAID/A467_Nov13_Fine_S267.