Iroko Pharmaceuticals Receives FDA Approval for TIVORBEX™

New Lower Dose NSAID Marks Iroko's Second FDA Approval in Approximately Four Months

PHILADELPHIA, FEBRUARY 24, 2014 — Iroko Pharmaceuticals, LLC, a global specialty pharmaceutical company dedicated to advancing the science of analgesia, today announced that the U.S. Food and Drug Administration (FDA) has approved TIVORBEX™ (indomethacin) capsules, a nonsteroidal anti-inflammatory drug (NSAID), at 20 mg and 40 mg doses for the treatment of mild to moderate acute pain in adults[1].

TIVORBEX was approved at dosage strengths that are 20 percent lower than the 25 mg and 50 mg indomethacin products currently on the market[2]. FDA approval of TIVORBEX was supported by data from two Phase 3 multi-center, placebo-controlled trials that demonstrated significant improvement in pain relief in patients with post-surgical acute pain receiving TIVORBEX compared with patients receiving placebo[3].

"The FDA approval of TIVORBEX is another significant milestone for Iroko as it validates our strategic approach towards developing a suite of NSAID products that offer pain management at lower doses," said John Vavricka, President and CEO of Iroko Pharmaceuticals. "TIVORBEX is the second NSAID to be approved from Iroko's lower dose NSAID pipeline that uses proprietary SoluMatrix Fine Particle Technology™."

TIVORBEX contains indomethacin 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. In October 2013, FDA approved Iroko's ZORVOLEX™ (diclofenac) capsules, also developed using this technology, for the treatment of mild to moderate acute pain in adults. ZORVOLEX is now available at pharmacies in the U.S.[4]

"Based on recommendations from FDA and other professional organizations, physicians look for the lowest dose option that will provide the appropriate amount of relief for patients experiencing acute pain. I'm excited to see that Iroko is continuing to develop additional lower dose NSAIDs as potential

treatment options for my patients," said Roy D. Altman, M.D., Professor of Medicine, Rheumatology at the University of California at Los Angeles.

Systematic reviews of observational studies have shown that serious NSAID adverse events, including cardiovascular thrombotic events, myocardial infarction, stroke, gastrointestinal ulcers, gastrointestinal bleeds[5] and renal events such as acute renal failure[6] are dose related[7]. As such, the FDA and professional medical organizations including the American Heart Association, American Gastroenterological Association, and The American College of Rheumatology, recommend that NSAIDs be used at the lowest effective dose for the shortest possible duration of time consistent with individual patient treatment goals[8].

"Indomethacin has potent anti-inflammatory and analgesic properties, but, like other NSAIDs, it can also be associated with dose-related serious adverse events," said Dr. Clarence Young, Chief Medical Officer of Iroko Pharmaceuticals. "When available, TIVORBEX will allow healthcare professionals to have a lower dose formulation of this well-established NSAID."

"The last several months have truly been an exciting time for Iroko, with ZORVOLEX and TIVORBEX both approved by FDA," said Osagie Imasogie, Executive Chairman of the Board of Iroko Pharmaceuticals. "We look forward to continue advancing our SoluMatrix ® pipeline of products to offer patients and doctors novel lower dose NSAID options, in both the acute and chronic pain settings."

Important Safety Information about TIVORBEX

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.

TIVORBEX 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.

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

TIVORBEX 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 NSAIDs, including TIVORBEX. Physicians should measure transaminases (ALT and AST) periodically in patients receiving long-term therapy with TIVORBEX. TIVORBEX should be discontinued immediately if abnormal liver tests persist or worsen.

NSAIDs, including TIVORBEX, 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 TIVORBEX. 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. TIVORBEX 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. TIVORBEX 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 TIVORBEX in patients with advanced renal disease is not recommended.

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

Indomethacin may aggravate depression, and other psychiatric disturbances, epilepsy, or parkinsonism, and should be used with caution in patients with these conditions. Indomethacin may cause drowsiness; therefore patients should be cautioned about engaging in activities requiring mental alertness and motor coordination. Discontinue TIVORBEX if severe central nervous system (CNS) adverse reactions develop.

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

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

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

Most common adverse reactions in clinical trials (incidence ≥2%) include: nausea, post procedural edema, headache, dizziness, vomiting, post procedural hemorrhage, constipation, pruritus, diarrhea, dyspepsia, post procedural swelling, presyncope, rash, upper abdominal pain, somnolence, generalized pruritus, hyperhidrosis, decreased appetite, hot flush, and syncope.

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

Important Safety Information about ZORVOLEX

ZORVOLEX is indicated for the treatment of mild to moderate acute pain in adults.

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 higher than users of either drug alone.

Most common adverse reactions in clinical trials (incidence ≥2%) include: edema, nausea, headache, dizziness, vomiting, constipation, pruritus, flatulence, pain in extremity, 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. In addition to the Iroko products that are marketed worldwide, the company has a robust pipeline of investigational lower dose NSAID products being developed using iCeutica Inc.'s proprietary SoluMatrix Fine Particle Technology™. For more information, visit **www.iroko.com**.

Contacts:
Jessica Donnelly for Iroko Pharmaceuticals, LLC, 212-798-9819
Kate de Santis, Iroko Pharmaceuticals, LLC, 267-546-1682

###

[1] TIVORBEX Prescribing Information, pg. 1
[2] TIVORBEX Prescribing Information, pg. 17
[3] TIVORBEX Prescribing Information, pg. 20
[4] ZORVOLEX Prescribing Information, pg. 1
[5] Rahme E et. al. (2001 Aug). Cost of prescribed NSAID-related gastrointestinal adverse events in elderly patients. Br J Clin Pharmacol. 52(2): 185-192.
[6] Annual Review of Medicine, Nonsteroidal Antiinflammatory Drugs and Renal Function. Vol. 35: 411-428. DOI: 10.1146/annurev.med.35.020184.002211.
[7] Risser A. (2009 Dec). NSAID Prescribing Precautions. Am Fam Physician. 80(12):1371-1378.
[8] 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).