



Iroko Pharmaceuticals' Submicron NSAIDs Demonstrate Efficacy at Lower Doses in Studies in Patients with Acute and Chronic Pain

Results from Phase 3 Submicron Indomethacin and Diclofenac Studies Being Presented at American Academy of Pain Medicine Annual Meeting and World Congress on Osteoarthritis

PHILADELPHIA, April 11, 2013 — [Iroko Pharmaceuticals, LLC](#), a Philadelphia-based pharmaceutical company focused on the development and commercialization of innovative therapeutic products, is presenting positive Phase 3 data from its investigational submicron non-steroidal anti-inflammatory drug (NSAID) pipeline at two medical meetings. These presentations summarize the results of studies of lower dose submicron indomethacin in patients with post surgical pain, and lower dose submicron diclofenac in patients with osteoarthritis pain. Both studies met their primary endpoints of providing significant pain relief compared with placebo.

“Currently available formulations of NSAIDs are associated with significant risk for adverse events, which increases with dose and duration of use,” said Alan Gibofsky, Professor of Medicine and Public Health at Weill Medical College of Cornell University. “Lower dose options that reduce the amount of medication in a patient’s bloodstream, while preserving efficacy and onset of action, may be a valuable addition for physicians.”

Data from the Phase 3 multi-center submicron indomethacin study demonstrated that lower dose indomethacin provided significant improvement in pain relief as measured by a visual analog scale (VASSPID-48) in patients with post-surgical acute pain. These data are being presented at the 29th Annual Meeting of the American Academy of Pain Medicine (AAPM) in Ft. Lauderdale. New data from the submicron diclofenac Phase 3 study showed osteoarthritis patients treated with investigational, lower dose submicron diclofenac experienced a significant reduction in pain compared with placebo as measured by the mean change from baseline in the Western Ontario and McMaster Universities Arthritis Index (WOMAC®) pain subscale at week 12. These data will be presented at the 2013 World Congress on Osteoarthritis, being held April 18-21 in Philadelphia.

“Our goal at Iroko is to address the significant unmet need in pain management by bringing new therapeutic options to patients and physicians that allow for lower systemic exposure,” said John Vavricka, President and CEO of Iroko Pharmaceuticals. “Our multiple Phase 3 data presentations reinforce the potential of submicron NSAIDs to provide effective pain relief at lower doses in a variety of pain models.”

About the Phase 3 Submicron Indomethacin Study in Post Surgical Acute Pain

Four hundred and sixty two adult patients with moderate to severe pain enrolled in a multi-center, double-blind, placebo- and active- controlled study following bunionectomy surgery. Patients were randomized to receive either investigational lower dose submicron indomethacin (40mg three times daily or twice daily, or 20mg three times daily), celecoxib (400mg loading dose; 200mg twice daily), or placebo. Statistically significant overall decreases in pain intensity were demonstrated for submicron indomethacin 40mg three times daily (509.6, $P<0.001$), 40mg twice daily (328.0, $P=0.046$), 20mg three times daily (380.5, $P=0.017$), compared with placebo (67.8). Although there was some evidence of analgesia for celecoxib (279.4), it did not achieve statistical significance compared with placebo. Some evidence of pain control was observed as early as 30 minutes in the submicron indomethacin 40mg three times daily (2.9) and 40mg twice daily (2.6) groups compared with placebo (0.2). The most common adverse events were generally similar across treatment groups and included nausea, post-procedural edema, dizziness, and headache.

About the Phase 3 Submicron Diclofenac Study in Osteoarthritis

The lower dose submicron diclofenac study was a 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. Participants were randomized to submicron diclofenac 35mg three times daily or 35mg twice daily, or placebo. Lower dose submicron diclofenac (35mg) administered three times daily in people with osteoarthritis met its primary endpoint of significant reduction in pain as measured over 12 weeks using the WOMAC. Patients receiving submicron diclofenac experienced a mean reduction in WOMAC pain subscale score at 12 weeks vs. baseline that was 11.6 points greater than those receiving placebo (44.1 vs. 32.5; $P=0.0024$). There was numerical evidence of pain improvement with submicron diclofenac 35mg twice daily that was 6.5 points greater than placebo (-39.0 vs. 32.5; $P=0.0795$),



although this did not achieve statistical significance. The most common adverse events were similar across treatment groups and included diarrhea, headache, nausea, and upper respiratory tract infection.

“These studies are among many we have initiated with the aim of providing new, lower dose, therapeutic options for patients and physicians,” said Clarence Young, M.D., Chief Medical Officer at Iroko Pharmaceuticals. “The results of these studies increase our understanding of the therapeutic potential of our submicron NSAID pipeline, especially in chronic conditions like osteoarthritis where people may require long-term NSAID treatment.”

A third Phase 3 study, also being presented at AAPM, showed that patients treated with lower dose submicron diclofenac (18mg and 35mg), experienced early and sustained significant pain relief as measured by the visual analog scale (VASSPID-48). These data were also presented at the 54th Annual Meeting of the American Headache Society in 2012. Iroko announced in March this year that the U.S. Food and Drug Administration has accepted for review the New Drug Application for lower dose submicron diclofenac with a proposed indication of treatment of mild to moderate acute pain in adults.

“We now have results from three Phase 3 studies from our lower dose submicron NSAID franchise, which is an important step toward our goal of becoming a leading provider of novel pain management solutions,” said Osagie Imasogie, Iroko Chairman and Senior Managing Partner of Phoenix IP Ventures.

About Lower Dose Submicron NSAIDs

The risk of adverse events, including ulcers, gastrointestinal bleeds¹, and cardiovascular events² associated with currently marketed NSAIDs is higher among patients receiving higher doses of NSAIDs and longer duration of treatment³. Iroko is at the forefront of the development of lower dose submicron NSAIDs – new drug products based on existing NSAIDs – that are designed to potentially provide effective pain relief at lower doses than existing commercially available oral drug products. These lower dose submicron NSAIDs are being developed by Iroko, using iCeutica Pty Ltd’s proprietary SoluMatrix™ technology, licensed to Iroko for exclusive use in NSAIDs. The SoluMatrix™ technology alters the pharmacokinetic absorption properties of NSAIDs by reducing drug particles to finer particles that are at least 10 times smaller than standard oral NSAID formulations, thereby enhancing drug dissolution and promoting absorption.



About Iroko Pharmaceuticals, LLC

Iroko is a pharmaceutical company focused on the development and commercialization of innovative therapeutic products. The company acquires, develops and maximizes the potential of currently marketed products on a global basis through focused selling and marketing efforts and development of new drug products based on existing NSAIDs. In addition to Iroko's marketed products which are marketed in 48 countries, the company has a robust pipeline of late-stage NSAID submicron product candidates using the proprietary SoluMatrix™ platform. These submicron NSAIDs are being developed using iCeutica Pty Ltd's SoluMatrix™ technology, licensed to Iroko for exclusive use in NSAIDs. For more information, visit www.iroko.com.

About Phoenix IP Ventures

A fully-integrated Private Equity and Venture Capital Fund which specializes in life sciences, principally in the pharmaceutical sector, the Firm acquires intellectual property protected assets that meet its criteria for value maximization. Phoenix IP Ventures works in collaboration with major players in the financial community to scale its own proprietary investments in transactions identified and managed by the Firm.

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¹ 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.

² Howes LG. (2007 Oct.) Selective COX-2 inhibitors, NSAIDs and cardiovascular events – is celecoxib the safest choice? Ther Clin Risk Manag, 3(5), 831-845.

³ Risser A. (2009 Dec). NSAID Prescribing Precautions. Am Fam Physician. 80(12):1371-1378.