NOVEL FORMULATION OF DICLOFENAC PROVIDES PAIN RELIEF AT LOWER DOSES

Data from Phase 2 Trial of Nano-formulated Pain Medicine Presented at World Congress on Osteoarthritis

Several NSAIDS Intended To Improve Safety and Tolerability Are Advancing in the Iroko Pharmaceuticals Pipeline

SAN DIEGO -- (September 15, 2011) -- A novel formulation of diclofenac provides pain relief at lower-than-standard doses during a Phase II clinical study as reported today at the 2011 World Congress on Osteoarthritis.[1] The Congress is organized by the Osteoarthritis Research Society International.

The diclofenac study is part of a multi-drug development program at Iroko Pharmaceuticals to use proprietary nanotechnology in re-formulating a large class of pain medicines called NSAIDs (non-steroidal anti-inflammatory drugs). Nano-formulations reduce drug particle size to enhance drug dissolution in the body.

The Iroko program aims to use the proprietary SoluMatrix™ technology to lower the dosing of NSAIDs, reduce systemic exposure by 20%, and thus improve their safety and tolerability while maintaining their effectiveness. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) both have advised that NSAIDs should be administered at the lowest effective dose for the shortest duration of time[2,3].

“Nano-formulations of NSAIDs may provide a new option for physicians as they balance efficacy and safety in treating pain,” said Dr. Allan Gibofsky, Professor of Medicine and Public Health at Weill Medical College of Cornell University. “Iroko’s results with nano-formulated diclofenac indicate this potential and merit larger-scale studies.”

Diclofenac in standard formulations is an NSAID that has long been used in various pain-relief indications including osteoarthritis. Standard, currently marketed formulations of diclofenac are typically prescribed in 25 mg and 50 mg doses.

In the Phase II study reported at the Congress, diclofenac in nano-formulated doses of 18 mg and 35 mg was compared to placebo. The primary efficacy endpoint was total pain relief as reported at intervals over 12 hours (TOTPAR-12) by patients with acute dental pain following third-molar extraction.[4] The improvement in pain relief associated with each of the two lower dose nano-formulations of diclofenac was highly statistically significant ($p<0.001$).

Also included in the study was the pain remedy celecoxib, at a dose of 400 mg. Although the study was not sized to show statistically significant differences between active drug treatments, both of the lower-dose nano-formulations of diclofenac showed numerically better scores than celecoxib by TOTPAR-12 assessment.

TOTPAR scores were also evaluated at eight hours and four hours. By those measurements as well, the nano-formulations of diclofenac showed statistically significant superiority to placebo and numerical superiority to celecoxib.

Another assessment used during the study was the time to onset of pain relief. This time was significantly shorter for all the active treatments than for placebo ($p<0.001$) and numerically shorter for both of the lower dose nano-formulations of diclofenac than for celecoxib.

Further data from Phase II clinical studies of nano-formulated NSAIDs under development by Iroko will be presented at another major medical conference this year.

Iroko has initiated several Phase III trials of nano-formulated NSAIDs manufactured using the proprietary SoluMatrix nano-technology platform of Iroko's partner, iCeutica. All these product candidates are designed for administration at lower doses without compromising onset of action and effectiveness, in keeping with the public-health advisories of the FDA and the EMA.

About Iroko Pharmaceuticals

Iroko, based in Philadelphia, is a pharmaceutical company focused on specialty therapeutic areas. The company acquires, develops and maximizes the potential of currently marketed products on a global basis through focused selling and marketing efforts and product lifecycle management activities including development of new formulations to improve patient treatment.

[1]A Phase 2 Study Evaluating the Efficacy and Safety of a Novel, Proprietary, Nano-formulated Oral Diclofenac

[2]Public Health Advisory – FDA Announces Important Changes and Additional Warnings for COX-2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDS). July 7, 2005.

[3]Opinion of the Committee for Medicinal Products for Human Use Pursuant to Article 5(3) of Regulation (EC) No 726/2004, for Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDS). October 18, 2006.

[4]In total, 202 subjects 18-50 years of age participated in this multisite, randomized, double-blind, single-dose, parallel-group study. All the study subjects had at least two third molars extracted and experienced moderate to severe pain within six hours after surgery. The subjects assessed baseline pain intensity at time zero before receiving either nano-formulated diclofenac 18 mg or 35 mg, celecoxib 400 mg, or placebo.

Detailed results appear in the following tables. In the first table, higher TOTPAR scores indicate better pain relief. In the second table, lower numbers indicate shorter time to pain relief, as measured in hours.

TREATMENT ARM	TOTPAR-12 Mean; SD	TOTPAR-8 Mean; SD	TOTPAR-4 Mean; SD
nano-formulated diclofenac 18 mg, N=49	17.8; 13.8[a]	14.3; 9.4[a]	8.2; 4.2[a]
nano-formulated diclofenac 35 mg, N=51	16.8; 12.8[a]	13.9; 8.8[a]	7.9; 4.3[a]
celecoxib 400 mg, N=51	14.6; 15.1[a]	11.2; 10.5[a]	5.7; 5.0[a]
placebo, N=51	5.7; 11.5	3.9; 7.2	2.1; 3.3

[a]*P*<0.001 compared with placebo

SD = standard deviation

ASSESSMENT	nano-formulated diclofenac 18 mg N=49 Mean±SE	nano-formulated diclofenac 35 mg N=51 Mean±SE	celecoxib 400 mg N=51 Mean±SE	placebo N=51 Mean±SE
Mean Time to First Perceptible Pain Relief (h)	0.6±0.05[a]	0.7±0.06[a]	1.2±0.17	1.6±0.19
Mean Time to Peak Pain Relief (h)	2.7±0.24[b]	2.9±0.32[c]	4.1±0.92	7.1±1.25

[a]*P*<0.001 compared with placebo
[b]*P*<0.01 compared with placebo
[c]*P*<0.05 compared with placebo
SE = standard error

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