

*For immediate release*



## **IDEA AG reports data of a 12-month comparative study of the targeted analgesic Diractin<sup>®</sup> (ketoprofen in Transfersome<sup>®</sup> gel) versus naproxen and gives development update**

**Munich, Germany – November 5, 2008.** IDEA AG has recently presented results of a US phase III, 12-month clinical safety and efficacy study of Diractin<sup>®</sup> (ketoprofen in Transfersome<sup>®</sup> gel, formerly known as IDEA-033) in patients with osteoarthritis of both knees in comparison to oral naproxen (Study CL-033-III-05) at the American College of Rheumatology (ACR) Annual Scientific Meeting. This is the first time that 52-week efficacy and safety data comparing orally and locally applied NSAIDs is reported.

The multi-center, randomised, double-blind, double-dummy, active controlled study had enrolled 349 patients with osteoarthritis of both knees. Patients were either treated with 100 mg ketoprofen in Diractin<sup>®</sup> per knee applied epicutaneously twice daily, or with 500 mg oral naproxen twice daily over a treatment period of 12 months. The primary efficacy endpoints were the final change from baseline for the WOMAC pain subscale, the WOMAC physical function subscale and the final Subject Global Assessment of Response to Therapy.

The results of the intent-to-treat (ITT) analysis proved statistically non-inferiority of Diractin<sup>®</sup> versus oral naproxen for all three primary efficacy endpoints, i.e. pain, physical function and subject's global assessment of response to therapy. In the per-protocol (PP) analysis there is even a trend for superiority of the Diractin<sup>®</sup> group for both, pain ( $p = 0.0493$ ) and physical function ( $p = 0.0457$ ), as compared to oral naproxen.

Non-inferiority of Diractin<sup>®</sup> versus oral naproxen was also shown for secondary efficacy endpoints. No substantial differences were found for responder rates (according to

OMERACT-OARSI) in the Diractin<sup>®</sup> (77.1%) and in the oral naproxen group (81.2%). In addition, there were no substantial group differences with regard to the mean number of used rescue medication for the Diractin<sup>®</sup> (mean 0.09) and the oral naproxen group (mean 0.12).

In terms of safety, 51.2% of the patients treated with Diractin<sup>®</sup> experienced an adverse event in comparison to 61.6% of the patients treated with oral naproxen. 7.3 % of the patients treated with Diractin<sup>®</sup> showed gastrointestinal symptoms, whereas 10.9 % of the patients treated with oral naproxen suffered from gastrointestinal problems. Most treatment related adverse events related to the long-term use of Diractin<sup>®</sup> were dermal irritations.

Further data are expected at the end of 2008 from the European phase III, open-label, long-term safety and patient usage trial that had enrolled 487 patients, who were treated with Diractin<sup>®</sup> for up to 36 months (Study CL-033-III-01).

The data from both studies with Diractin<sup>®</sup> will be used in the new application to the EMEA for Community Marketing Authorisation of the product as well as for an US NDA, to be submitted in 2009.

**ENDS**

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***Notes to editors:***

IDEA is a privately held biopharmaceutical company with headquarters in Munich, Germany. The Company develops and commercialises non-invasive, targeted pain therapeutics, applied through the skin. The basis of the technology platform are proprietary carriers that are typically applied epicutaneously and can be engineered to achieve high drug concentration at or near the site of application on skin surface, diminish local or systemic adverse side effects, and often increase drug potency. In total over 100 patents from 9 patent families are protecting the core technology.

The Company's leading product is in the area of pain. Diractin<sup>®</sup> has significant sales potential in the peripheral pain market. In June 2007, SwissMedic approved use of 100 mg ketoprofen in Diractin<sup>®</sup> for the treatment of inflammation and pain related to osteoarthritis. The approval was based on the first pivotal European trial (CL-033-II-03), which demonstrated that both Diractin<sup>®</sup> and Celebrex<sup>®</sup> (celecoxib), improved pain comparably and progressively over the six-week study period and both were statistically superior to placebo. A much broader package had been submitted, in the form of a variation, to SwissMedic, from which label expansion is sought. The submitted package includes an 18-months interim analysis of a long-term, a multiple-dose, open label safety, compliance, and usage evaluation study (CL-033-III-01) with OA patients treated with Diractin<sup>®</sup>, a positive 3 month, placebo-controlled, phase III, OA efficacy and safety study (CL-033-III-02), and a 3 months extension (CL-033-III-02E) to the latter. Further clinical studies that remain to be submitted, or evaluated fully by various regulatory agencies, include the long term, 12 months, safety and efficacy study conducted in USA (CL-033-III-05) and the two ongoing clinical phase III studies. The results from an earlier phase III, US OA study with Diractin (CL-033-III-04) will be included only in the safety data package. In 2009, IDEA expects to submit a new Application for Community Marketing Approval for Diractin<sup>®</sup> to EMEA, and an NDA submission to the FDA.

IDEA's in-house capabilities range from formulation and small-scale (GMP) manufacturing work to clinical research.

For further technical information see IDEA's website at [www.idea-ag.de](http://www.idea-ag.de).

## **Background information:**

### **Osteoarthritis**

Osteoarthritis (OA), the clinical syndrome of joint pain and dysfunction caused by joint degeneration, affects more people than any other joint disease. It is one of the leading causes of disability, as by the age of 65 an estimated 85% of the population will have some degree of OA. Oral non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used to treat OA. Although effective, they cause serious adverse side effects, including gastrointestinal and cardiac problems, and kidney and liver abnormalities. Topical NSAIDs, which are marketed in the EU but have never been approved to date in the US, are seen as generally safer, but have only limited data available to prove their efficacy beyond a two-week treatment duration (Lin et al., BMJ 2004).

### **NSAID Market**

Worldwide sales of non-steroidal anti-inflammatory drugs (NSAIDs) are estimated to be €14 billion. Globally, approximately 30 million people take oral NSAIDs on a daily basis. NSAIDs, increasingly in combination with proton pump inhibitors (PPI) to manage the potential side effects, are also the gold standard for treating the majority of arthritic diseases and chronic pain. The main disadvantage is that all classical oral NSAIDs carry a risk of upper gastrointestinal (GI) side effects, with up to 30% of long-term NSAID users developing gastric ulcers, for example. Close to 20,000 osteoarthritis patients and 2,000 rheumatoid arthritis patients in the US alone die each year from GI complications associated with oral NSAID use. Newer, more selective NSAIDs (so-called COX-2 inhibitors) were developed to selectively inhibit only the COX-2 receptor, while sparing the COX-1 receptor, which are also inhibited by the unspecific NSAIDs. Until recently, COX-2 inhibitors were seen as a relatively safe arthritis treatment option. However, COX-2 inhibitors can also lead to serious adverse side effects, such as cardiovascular events, and may still cause bleedings in the lower GI tract. In 2004, Merck & Co. announced the world-wide withdrawal of Vioxx<sup>®</sup> (rofecoxib) and in 2005, Pfizer Inc. was requested by the FDA to withdraw Bextra<sup>®</sup> (valdecoxib). In April, 2007, the FDA issued a non-approval letter for Arcoxia<sup>®</sup> (etoricoxib) citing the need for additional data in support of the benefit-to-risk profile in order to gain approval. The FDA has mandated black-box warnings on all prescribed NSAIDs and similar labelling changes for comparable over-the-counter medicines.

### **Diractin<sup>®</sup>**

Diractin<sup>®</sup> contains a particularly potent, well-established non-steroidal anti-inflammatory drug in a Transfersome<sup>®</sup> based semisolid, creamy suspension in a water base. A Transfersome<sup>®</sup> is a novel, ultra deformable vesicle carrier designed to deliver drugs non-invasively through the skin barrier. With the correct formulation, Transfersome<sup>®</sup> carriers can also be used to target muscles and joints below the application site, as they are not cleared by the local cutaneous blood microcirculation. The resulting targeted drug delivery increases the product's efficacy by increasing local drug concentration and improve product safety by lowering systemic drug concentration in comparison with existing oral and topical NSAID formulations. IDEA hopes that Diractin<sup>®</sup> will become the first truly effective, and thus market leading, locally applied analgesic on the market for the long-term treatment of pain related to osteoarthritis. Diractin<sup>®</sup> should, moreover, give the medical community an effective and safe alternative for suppressing pain associated with soft tissue injuries.