

*For immediate release*



**IDEA reports results from a prospective 3 years phase III study of Diractin<sup>®</sup> (ketoprofen in Transfersome<sup>®</sup> gel)**

**Munich, Germany – April 2, 2009.** IDEA AG today announced positive results of a long-term, open-label, Phase III study in joint-pain, musculoskeletal pain (including lower back pain), stiffness, or soft tissue inflammation, presented at the 9<sup>th</sup> European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis.

The open-label study (CL-033-III-01) evaluated the safety, efficacy, compliance, and usage of the targeted analgesic Diractin<sup>®</sup> (ketoprofen in Transfersome<sup>®</sup> gel) applied on the skin for a treatment period of up to 36 months. The study enrolled 487 patients with joint/musculoskeletal pain or soft tissue inflammation (342 with knee osteoarthritis (OA), 75 with OA of other joints, 44 with muscle pain or tendopathies, and 26 with back pain). Patients were allowed to use up to 110 mg ketoprofen in Diractin<sup>®</sup> b.i.d. for up to two application areas. The patients were allowed to modify the dosage of the epicutaneously applied product over the treatment period of up to 36 months.

Relative to the initial pain level, 77.7% of patients reported pain reduction >30%, 59.1% notified pain reduction >50%, and 28% experienced pain reduction >80%. Such reductions ameliorated the patients' quality of life in all measured categories, mainly due to pain improvement. The treatment related adverse events (AE) were mainly transient, mild to moderate, dermal reactions, of which erythema was most frequent. No reported serious AE was considered drug related by the assessing investigator; no treatment related effects on safety laboratory parameters or vital signs were observed; no phototoxic reactions were reported. All measured ketoprofen concentrations in plasma were very low, in the range of 30 µg L<sup>-1</sup>. Altogether, 292 patients used Diractin<sup>®</sup> for at least 24 weeks (6 months) and 216 for at least 48 weeks (12 months). Average daily usage of the study medication was around 170 mg of ketoprofen in Diractin<sup>®</sup>.

IDEA plans to include the study results in a new application to the EMEA, to gain the Community Marketing Authorisation for Diractin<sup>®</sup>, as well as for an NDA submission in the USA. Both are scheduled for the second half of 2009.

Matthias Rother, M.D., IDEAS's CMO commented:

*"There are limited options for medical treatment of chronic pain states like in osteoarthritis. Treatment of patients at higher risk like elderly patients or patients with gastro-intestinal or cardiovascular risk factors including those using concomitantly low dose aspirin present a particular challenge. We know that usage of the current gold standard - oral NSAID's including the Cox-2 inhibitors, for certain patients to be prescribed in combination with a proton pump inhibitor - cause adverse events related to systemic drug exposure. Those obviously could be reduced by local application. However, conventional topical NSAID formulations face scepticism about their efficacy for use in indications that require long term application like OA and only very few long-term studies have been published. It was good to observe that Diractin® was safe and well tolerated in the hands of investigators for treatment periods of up to 36 months. Obviously, efficacy measures in the framework of an open label study without a control group need to be treated with some caution. But it is reassuring that results of this study were in line with the results of the long-term randomized, double-blind controlled studies."*

**ENDS**

***For further information, please contact:***

**IDEA AG**

Matthias Rother, MD, PhD, Chief Medical Officer

Tel.: +49 (174) 1789457

Prof. Gregor Cevc PhD, CEO

Tel.: +49 (172) 8386267

***Notes to editors:***

IDEA is a privately held biopharmaceutical company with headquarters in Munich, Germany. The Company develops and commercialises non-invasive, targeted therapeutics, applied through the skin. The basis of its technology platform is proprietary carriers, the Transfersome<sup>®</sup> vesicles, which are typically applied on the skin. The carriers can be engineered to achieve high drug concentration at or near the site of application, diminish local or systemic adverse side effects, and often increase drug potency. Over 110 patents from 9 patent families were issued to IDEA to date, protecting its core technology.

The Company's leading product is in the area of pain. This product, Diractin<sup>®</sup>, a ketoprofen in the Transfersome<sup>®</sup> gel, has an excellent market potential for treatment of peripheral pain. SwissMedic approved the use of 100 mg ketoprofen in Diractin<sup>®</sup> for the treatment of inflammation and pain related to osteoarthritis.

The existing Swiss approval is based on the first pivotal European study which demonstrated that both Diractin<sup>®</sup> and Celebrex<sup>®</sup> (Pfizer) improved pain comparably over six-week treatment period, being both statistically superior to placebo. IDEA more recently reported the data from a 12 month comparative study that proved non-inferiority of Diractin<sup>®</sup> in comparison with oral naproxen (2-times 500 mg daily) for all three primary efficacy endpoints, i.e. pain, physical function, and subject's global assessment of response to therapy; the per-protocol analysis even revealed a trend for superiority of the Diractin<sup>®</sup> group for both pain ( $p = 0.0493$ ) and physical function ( $p = 0.0457$ ) in comparison with oral naproxen. The available clinical data package furthermore includes results of a long-term, open-label, safety and efficacy study with OA patients treated with Diractin<sup>®</sup> for up to 36 months, a positive 3 month, placebo-controlled, phase III, OA efficacy and safety study, and a 3 months extension to the latter. Two clinical phase III, 3 month studies with the product, one in Europe and one in the USA, are ongoing. The results from an earlier US phase III, OA study with Diractin (CL-033-III-04) will be included into the safety data package only. IDEA expects to submit a new Application for Community Marketing Authorisation for Diractin<sup>®</sup> to EMEA in 2009.

Diractin<sup>®</sup> is partnered for the US market with a subsidiary of Alpharma Inc., which was recently acquired by King Pharmaceuticals Inc. (Bristol, TN, USA).

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 the most commonly used drugs for OA treatment. Although effective, they can cause serious adverse side effects, including gastrointestinal and cardiac problems, and kidney and liver abnormalities. Topical NSAID gels, which are now in the EU markets for several decades, were only approved in the US recently (end of 2007), for the 4 times 4 g daily application. Such products are generally perceived as being safer than oral drugs, but if used less frequently and/or at a lower dose have only limited data available to prove their efficacy beyond a two-week treatment duration (Lin et al., BMJ 2004).

### **NSAID Market**

The estimated worldwide sales of non-steroidal anti-inflammatory drugs amount to €14 billion. Globally, approximately 30 million people take oral NSAIDs daily. 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 problems. 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 usage. Oral NSAIDs are thus increasingly combined with proton pump inhibitors (PPI) to manage the potential gastrointestinal side effects. More selective NSAIDs (so-called COX-2 inhibitors) were moreover developed to inhibit selectively the COX-2 receptor merely, while sparing the COX-1 receptor which is also inhibited by the unspecific NSAIDs. Until recently, COX-2 inhibitors were seen as a relatively safe therapeutic 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); 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 before an 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. The Transfersome<sup>®</sup> is a novel, ultra deformable vesicle carrier designed to deliver drugs non-invasively through the skin. With the correct formulation, the Transfersome<sup>®</sup> carriers can 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 and sustained drug deposition increases the product's efficacy by increasing the local drug concentration. It also improves the product safety, by lowering systemic drug concentration in comparison with more conventional oral and topical NSAID formulations. IDEA believes that Diractin<sup>®</sup> will become the first truly effective locally applied analgesic on the market for the long-term treatment of pain related to osteoarthritis. Diractin<sup>®</sup> could moreover give the medical community an effective and safe alternative for suppressing pain associated with soft tissue injuries.