

*For immediate release*



**IDEA AG completes recruitment in two clinical studies with Diractin<sup>®</sup> (ketoprofen in Transfersome<sup>®</sup> gel), including the biggest German biotech study to date**

**Munich, Germany – December 19, 2008.** IDEA AG today announced completion of patients enrolment in one European and one US clinical study, both in the indication of osteoarthritis of the knee. The former, largest clinical study ever undertaken by a German biotech company, and the latter trial have enrolled together close to 2000 patients.

In the European, phase III, 12 week clinical study (CL-033-III-03) a total of 1402 patients were enrolled in 70 centres in Germany, UK, Poland, and the Czech Republic. The study is testing clinical efficacy and safety of two dosages (50 mg and 100 mg ketoprofen per application) of Diractin<sup>®</sup>, the first targeted analgesic gel for the long term, twice daily treatment of osteoarthritis (OA) of the knee. Comparators are the corresponding doses of locally applied placebo, oral Celebrex<sup>®</sup> (100 mg b.i.d.), and oral placebo.

In the US, phase III, 12 week clinical efficacy and safety study (CL-033-III-06), 555 patients were enrolled in 37 centres. The study compares the higher of the two Diractin<sup>®</sup> doses (100 mg ketoprofen per application) in osteoarthritis of the knee with placebo. The recruitment in US was so successful that it finished five weeks ahead of the schedule, proving efficient study conduct as well as physicians and patients interest in the product candidate.

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

Dr. Matthias Rother, IDEA's Executive Head of Medical Development commented:

*"I am extremely pleased with the studies progress to date. I therefore expect both studies also to finish on time, and to provide valuable insights into clinical safety and efficacy of Diractin<sup>®</sup>."*

**ENDS**

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

**IDEA AG**

Matthias Rother, MD, PhD, Head of Medical Development

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. In 2007, SwissMedic approved the use of 100 mg ketoprofen in Diractin<sup>®</sup> for the treatment of inflammation and pain related to osteoarthritis; the decision on a variation application in Switzerland is pending.

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 osteoarthritis patients treated with Diractin<sup>®</sup> for up to 36 months, a positive 3 month, placebo-controlled, phase III, osteoarthritis 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, osteoarthritis study with Diractin<sup>®</sup> (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 Alpharma Ireland Ltd., a subsidiary of Alpharma Inc., Bridgewater/New Jersey.

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.