



## PRESS RELEASE

### **PAION SEES IMPROVED PROBABILITY OF SUCCESS FOR PAIN DRUG M6G FOLLOWING SUCCESSFUL META-ANALYSIS OF CLINICAL DATA**

- Positive results from meta-analysis with M6G
- Wider therapeutic margin confirmed
- Re-launch of partnering activities

Aachen (Germany), Cambridge (United Kingdom), 3 November 2008 - The biopharmaceutical company PAION AG (ISIN DE000A0B65S3; Frankfurt Stock Exchange, Prime Standard: PA8, London AIM: PAI) today announces positive results from a meta-analysis of Phase II and Phase III data generated with morphine-6-glucuronide (M6G). According to PAION, applying the findings should improve the probability of success for the development program and will facilitate the planning of future studies. Accordingly, PAION is now re-launching the partnering process for M6G.

In spring 2007, a Phase III study with M6G was completed which demonstrated that M6G reduced pain as effectively as morphine, the current standard treatment for post operative pain. This study also showed a significant reduction in vomiting, a common side effect of morphine. However, while a marked and clinically relevant decrease in nausea was also shown, statistical significance was narrowly missed.

M6G was added to PAION's portfolio by way of the acquisition of CeNeS, which was successfully closed in June 2008. Following the transaction, and as planned, PAION initiated a meta-analysis of the clinical data in order to re-evaluate the study results obtained so far, and to gain a clearer view of the status of the M6G program.

A combined data analysis based on 769 patients from two Phase II studies and two Phase III studies has now been completed. The results confirm the analgesic effect of M6G and also reveal significant reductions in both vomiting and nausea, the pre-specified parameters of the meta-analysis, compared with patients treated with morphine. The p-values in this meta-analysis were 0.025 for nausea and 0.010 for vomiting and thus both reached statistical significance.

In parallel, modelling analyses have been conducted to simulate dose-response relationships and pharmacodynamic effects. The results support the product profile of M6G, both in terms of its analgesic properties and side-effect profile, and in addition reproduce the previously observed longer duration of action of M6G compared to morphine. Based on this model, PAION believes that even at increased doses M6G may be better tolerated than equi-analgesic doses of morphine.

Wolfgang Söhngen, CEO of PAION commented: *"As previously shown with Desmoteplase, which is now partnered with Lundbeck, a thorough analysis of clinical studies is a powerful tool, especially for studies which have failed at*

*first glance. The result of our current meta-analysis supports our thesis that M6G could make an important contribution to the improvement of pain management for patients requiring opioid analgesia. These new data allow us to now re-start the partnering process with a higher probability of success.”*

In summary, these new analyses support PAION's view that M6G has a wider therapeutic margin than morphine, with lower incidences of post-operative nausea and vomiting at equi-analgesic levels.

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### **About M6G**

Morphine-6-glucuronide (M6G) is an active potent metabolite of morphine which may offer therapeutic advantages over morphine, the current gold standard for the treatment of moderate to severe post-operative pain, in having an equivalent analgesic effect, but with a reduced tendency to cause side-effects such as nausea and vomiting. The substance was added to PAION's portfolio by acquiring CeNeS Pharmaceuticals in June 2008. Clinical trials have shown that M6G given intravenously can induce analgesia equivalent to morphine in the treatment of moderate to severe post-operative pain. These studies, along with those published in the scientific literature, suggest that M6G also induces less post operative nausea and vomiting compared with morphine, as well as less sedation and respiratory depression. Two Phase III trials have now been completed with M6G.

### **About PAION**

PAION is a biopharmaceutical company headquartered in Aachen, Germany. Since the acquisition of CeNeS Pharmaceuticals, which was completed in June 2008, the company has a second site in Cambridge, UK. The company is specializing in developing and commercializing innovative drugs for the hospital-based treatment of central nervous system (CNS) disorders and thrombotic/cardiovascular diseases, indications for which there is a substantial unmet medical need. PAION intends to further expand its portfolio of drugs by exploiting its core expertise in identifying high-potential compounds, licensing or otherwise acquiring them and advancing them through the clinical development and regulatory approval process. Where appropriate, particularly during the late stages of the clinical development and approval process and the commercialization phase, PAION seeks to collaborate with experienced partners.

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