



## PRESS RELEASE

### PHASE Ib STUDY ENDPOINT ACHIEVED WITH PAION'S SHORT ACTING ANESTHETIC/SEDATIVE CNS 7056

- CNS 7056 successfully provides sedation permitting diagnostic and therapeutic colonoscopy procedures
- Rapid onset and offset of effect confirmed
- Safety - good tolerability of CNS 7056 under procedural stress and with co-medication

Aachen (Germany), 28 October 2009 – The biopharmaceutical company PAION AG (ISIN DE000A0B65S3; Frankfurt Stock Exchange, Prime Standard: PA8) today publishes the headline data of the Phase Ib clinical trial assessing the new short-acting intravenous anesthetic/sedative CNS 7056 in volunteers undergoing colonoscopy.

The primary objective of the trial, to assess the feasibility of maintaining suitable sedation levels with CNS 7056 for 30 minutes during a colonoscopy procedure was met. As established in the first in man study, the onset and offset of sedative effect was rapid. There were no serious adverse events reported and no unusual findings were observed.

*"We are delighted about the results we received. They deliver further evidence for a unique profile in the lead indication procedural sedation. This growing market is in need of an agent that requires less resource consuming supervision and thus represents a great market opportunity," commented Dr. Wolfgang Söhnngen, PAION's CEO. „The data will be very helpful in fine tuning the dosage regimen for the Phase IIb study which is under active preparation. We are now looking forward to the outcome of the Phase IIa data. "*

#### **Notes to Editor**

##### **About the Phase Ib study**

The randomized, open, dose-escalating multiple dose Phase Ib study evaluated the sedation and recovery profile of CNS 7056 in two separate parts. A total of 51 volunteers (6 in Part 1 and 45 in Part 2) were enrolled.

The first part, reported on 11 May 2009, assessed the reversal of sedation induced with CNS 7056 by the benzodiazepine antagonist flumazenil in a double blind placebo controlled design. A single dose of flumazenil was able to reverse the effects of CNS 7056 within approximately 1.5 minutes in volunteers with deep sedation/loss of consciousness. Re-sedation after administration of flumazenil was not observed.

In the second part of the study 15 volunteers in each cohort received the following doses of CNS 7056 as in a dose escalation design:

- Cohort 1 - loading dose 0.04 mg/kg, plus top-up doses of 0.04 mg/kg
- Cohort 2 - loading dose 0.075 mg/kg, plus top-up doses of 0.04 mg/kg
- Cohort 3 - loading dose 0.10 mg/kg, plus top-up doses of 0.04 mg/kg

The doses were aimed to induce and maintain an adequate sedation level for 30 minutes – a duration which is required for a standard colonoscopy procedure including short interventions. Maintaining this sedation period was the main objective of the trial.

As all volunteers in Part 2 received 50 mcg fentanyl for analgesia prior to being sedated, the dose of CNS 7056 was selected, to take into account the known synergistic effects of fentanyl with benzodiazepines such as CNS 7056 on sedation.

The criteria for definition of a successful procedure included adequate sedation and completion of the colonoscopy without rescue sedation and lack of manual or mechanical ventilation. Overall, a successful procedure was achieved in 77 % of all subjects across all cohorts (34 of 44, one subject was not assessable due to technical reasons). In the higher dose groups (0.075 and 0.1 mg/kg loading dose) the success rate for sufficient sedation was 83 %. No rescue sedation was required in any subject and no subject required ventilation. The high rate of successful procedures achieved in this study gives a solid basis to refine the dose regimen for further development of the compound.

The rapid onset and offset of sedative effect established in the first in man and preclinical studies was again demonstrated. In the individuals who underwent the procedure, the mean time to reaching a level of sedation sufficient to commence the procedure after the first dose of CNS 7056 was 2 min and the mean time to recovery of full alertness after the last drug dose was 11 min.

The safety profile observed in this trial was as anticipated for a benzodiazepine. There were no serious adverse events reported and no unusual findings were observed.

Overall, there was good cardiovascular and respiratory stability at the doses of CNS 7056 studied.

###

#### **About CNS 7056**

CNS 7056 is a new short-acting sedative and general anesthetic that acts on GABA<sub>A</sub> receptors. CNS 7056 is a water-soluble, rapid and short-acting GABA<sub>A</sub> receptor modulator interacting with the benzodiazepine site. The clinical proof of concept study, reported in January 2009, showed that, after intravenous administration, CNS 7056 rapidly induces sedation. Importantly the sedative effects rapidly disappear after cessation of administration. The rapid offset of effect of the compound is due to its metabolism by esterase enzymes that are widely distributed throughout the body. Therefore, it is anticipated that CNS 7056 can be clinically developed as a sedative agent for day case procedures, the induction and maintenance of anesthesia and ICU sedation. PAION initiated partnering discussions in parallel to the Phase Ib and IIa studies that were initiated in April 2009 in order to accelerate the further development of CNS 7056 for territories outside Japan, where the compound is partnered to Ono Pharmaceuticals.

#### **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 specialized 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 has a "Search & Develop" business model, which is based on its core expertise in drug development. Where appropriate, particularly during the late stages of the clinical development, PAION seeks to collaborate with experienced partners.

**Contact**

Ralf Penner  
Director Investor Relations & Public Relations  
PAION AG  
Martinstrasse 10-12  
52062 Aachen – Germany  
Phone: +49 241 4453-152  
E-mail: [r.penner@paion.com](mailto:r.penner@paion.com)  
[www.paion.com](http://www.paion.com)

**Disclaimer:**

This release contains certain forward-looking statements concerning the future business of PAION AG. These forward-looking statements contained herein are based on the current expectations, estimates and projections of PAION AG's management as of the date of this release. They are subject to a number of assumptions and involve known and unknown risks, uncertainties and other factors. Should actual conditions differ from the Company's assumptions, actual results and actions may differ materially from any future results and developments expressed or implied by such forward-looking statements. Considering the risks, uncertainties and other factors involved, recipients should not rely unreasonably upon these forward-looking statements. PAION AG has no obligation to periodically update any such forward-looking statements to reflect future events or developments.