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**PRESS RELEASE**

**19 December 2006**

## **Addex begins Phase IIa Proof of Concept Study on ADX10059 for Treatment of Acute Anxiety**

**Geneva**, 19 December 2006 – Addex Pharmaceuticals announced today the start of a Phase IIa proof of concept study on lead compound ADX10059 in patients with moderately severe dental anxiety. This is the third indication in a Phase IIa development programme in which ADX10059 is also being evaluated for acute treatment of migraine and for prevention of acid reflux in patients with GERD (gastro-oesophageal reflux disease). The latter two studies are being conducted in the UK, France and Germany, with results expected in the first quarter of 2007. ADX10059 successfully completed three Phase I trials in over 100 healthy subjects during the first half of 2006.

The multi-centre study, being carried out at specialist dental research centres in the UK, is a double-blind, placebo-controlled comparison of a single dose of ADX10059, to treat patients with moderately severe dental anxiety who are undergoing standard dental treatment. Efficacy variables include patient rating of anxiety during the procedure, using visual analogue scales and physiological measurements of stress. Effects on sedation will also be measured.

ADX10059 is intended as a non sedating alternative to benzodiazepines for the short term treatment of acute anxiety states; examples of which include acute stress disorder, fear of flying, acute social anxiety and fear of medical and dental procedures. Dental anxiety is an example of the latter condition and is a common disorder, affecting 7% to 10% of adult populations. The majority of sufferers have no other psychiatric problems, making the acute treatment of dental anxiety a useful paradigm in which to evaluate the anxiolytic potential of ADX10059, in the absence of confounding factors which might otherwise complicate the interpretation of drug effectiveness or tolerability.

ADX10059 is a potent, selective, negative allosteric modulator (NAM) of the metabotropic glutamate receptor 5 (mGluR5), a mechanism that has been clinically validated for the treatment of anxiety disorders. The compound Fenobam, which has a similar activity to ADX10059 on the mGluR5 receptors<sup>(1)</sup>, was shown to be an effective anti-anxiety therapy in controlled clinical trials. NAMs differ from classical, pure antagonists in that their inhibitory effects are non-competitive, meaning that they may achieve a pharmacological effect without the need to increase drug concentration, even in the presence of high concentrations of the natural ligand, glutamate. This novel mechanism offers the potential advantage of therapeutic activity with few side effects. In addition, ADX10059 does not have significant cross-activity or binding affinity to other mGluR or other CNS receptors, in particular serotonin, GABA and dopamine receptors.



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“In a short period of time, we have initiated Phase IIa trials of ADX10059 in three distinct indications,” said Dr Vincent Mutel, CEO of Addex. “In this trial we hope to confirm ADX10059’s potential as a novel, non-sedating acute treatment for anxiety.”

### **About Addex Pharmaceuticals**

Addex is an innovative pharmaceutical company engaged in the discovery and development of novel therapeutics for the treatment of Central Nervous System (CNS) disorders. The Company is developing new classes of drugs that modulate the effect of natural activators on their specific targets, in particular G-Protein Coupled Receptors (GPCRs). These compounds are referred to as allosteric modulators and potentially offer improved safety and efficacy over existing treatments, giving them a significant competitive advantage. Although at present Addex is focusing its activity on CNS targets, this modulator principle is applicable to any GPCR.

Addex has a portfolio of proprietary compounds in discovery and development for anxiety, Alzheimer’s disease, depression, GERD, severe spasticity, migraine, schizophrenia, smoking cessation, pain and Parkinson’s disease.

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### **References**

1. Porter R., Jaeschke G., Spooren W., Ballard-Yardy T., Prinssen E., Muehleemann A., Wichmann J., Kolezewski S., Buettelmann B., Viera E., Mutel V., Malherbe P. (2005) Fenobam: A clinically validated non-benzodiazepine anxiolytic is a potent, selective and non-competitive mGlu5 receptor antagonist with inverse agonist activity. *J Pharmacol Exp Ther.* 315:711-721.