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PRESS RELEASE

17 April 2007

Addex achieves statistically significant outcome in Phase IIa clinical trial with ADX10059 in Gastro-Esophageal Reflux Disease

Geneva, 17 April 2007 – Addex Pharmaceuticals announced today the successful completion of a Phase IIa proof of concept trial with its lead compound ADX10059 in patients with gastro-esophageal reflux disease (GERD), a highly prevalent condition with a significant unmet medical need. The study achieved its primary objective, the control of 24-hour esophageal pH, with statistical significance, and also showed statistically significant improvements in many of the secondary measures, including clinical symptoms of GERD. ADX10059 is also in clinical development in two other indications, migraine and anxiety.

Patients with GERD have a dysregulation of lower esophageal sphincter function, resulting in inappropriate relaxation of the sphincter muscle and causing reflux of stomach contents into the esophagus, particularly after meals and at night. Pre-clinical pharmacology studies have shown that metabotropic glutamate receptor 5 (mGluR5) inhibition reduces transient sphincter relaxation episodes, improves muscle tone of the lower esophageal sphincter, and prevents reflux of stomach contents into the esophagus. As ADX10059 is a selective mGluR5 negative allosteric modulator, it may have the possibility to reduce inappropriate esophageal sphincter relaxations and prevent reflux in man. Hence, a proof of concept study of the effect of this compound on gastro-esophageal reflux in patients with GERD was performed.

The single-blind, placebo-controlled, two-day study was performed in 24 male and female patients. The objectives were to evaluate the effect of ADX10059 on physiological measures of reflux, using continuous 24-hour pH recording in the lower esophagus, and on the occurrence of patient-recorded clinical symptoms of GERD. On Day 1 patients received placebo, while on Day 2 they received ADX10059 half an hour before each of three meals. The patients were unaware of the treatment sequence. Day 1 measurements were compared with Day 2 for each patient, who therefore acted as his or her own control. The effect of two different doses, 50mg or 250mg of ADX10059, was tested in the study.

ADX10059 at the dose of 250 mg three times daily demonstrated statistically and clinically significant effects on both the physiological measures and clinical symptoms of GERD (see table below). The primary endpoint, the percentage of time that esophageal pH was greater than 4 during the 24-hour period, was statistically significantly increased during ADX10059 treatment ($p = 0.014$). In addition, the duration of acid reflux episodes, determined by esophageal pH measurement, was significantly reduced throughout the 24-hour period ($p = 0.013$). Importantly, night time reflux, which is often poorly controlled by conventional acid-suppressing therapies and results in sleep disturbance and increased risk of esophageal damage, was also significantly reduced by ADX10059 ($p = 0.0021$).



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The benefits on the physiological measures of reflux were also seen clinically, as patients reported fewer and shorter episodes of GERD symptoms on the active treatment day. On the placebo treatment day, patients experienced an average of 7 symptomatic episodes each lasting an average of 14 minutes. These were reduced to an average of 2 episodes each lasting 5 minutes during treatment with 250mg ADX10059. The compound also appeared to show trends towards efficacy in some patients at the lower dose of 50mg three times daily, but the results for this group were more variable and were not statistically significant. Phase IIb trials in GERD are planned as a next step.

Efficacy summary: ADX10059 250mg t.d.s compared to placebo t.d.s.

Efficacy parameter	ADX10059 250mg t.i.d N = 11	Placebo t.i.d. N = 11	P value
% time pH>4 in 24h (Primary endpoint)	96.5	92.8	0.014
% time pH>4 nocturnal	96.3	90.3	0.0028
Total duration reflux pH<4 24h (min)	40	86	0.0132
Total duration reflux pH<4 nocturnal (min)	16.2	48.6	0.0021
No. symptomatic episodes	1.9	7.0	0.031
Duration symptomatic episodes (min)	5.2	13.9	0.031

Professor Jan Tack, Professor of Medicine at the Department of Pathophysiology, Gastroenterology Section of the University of Leuven, Belgium, commented: "In spite of the clinical successes of acid-suppressive therapy, there remains a significant unmet need in our ability to manage symptoms of GERD disease. To overcome limitations of acid-suppressive drugs, which eliminate only the acid component of reflux disease, drugs that inhibit reflux events are needed. These results, in keeping with previous animal studies, provide the first confirmation that mGluR5 inhibition is able to significantly reduce reflux events and symptoms in GERD patients. The magnitude of the effect on reflux time and symptoms suggest a potential for ADX10059 to become a major addition to our therapeutic options in GERD."

"ADX10059 is the first compound with this mode of action to have demonstrated significant therapeutic potential in GERD in man," said Dr Vincent Mutel, CEO of Addex. "Brought into clinical trials exactly 2 years after its discovery, it has the potential to become a breakthrough therapy in the management of this very common condition for which there is an important unmet medical need."



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About GERD

GERD is estimated to affect 15% of the adult population in the US. The proton pump inhibitors (PPIs) are the market leaders, with annual worldwide sales of approximately \$16 billion. Their mechanism of action in GERD is indirect, as they suppress gastric acid production rather than prevent relaxation of the lower esophageal sphincter. Approximately 20% of patients with GERD either do not respond or are inadequately controlled by PPIs. Hence there remains a significant unmet need in the market for drugs with an alternative non-acid-suppressing mode of action. There are currently no licensed medications which act specifically to normalize the dysregulated function of the lower esophageal sphincter, and Addex believes that ADX10059 has the potential to become a first-in-class treatment for GERD.

About Addex Pharmaceuticals

Addex Pharmaceuticals is an innovative pharmaceutical company that discovers and develops novel therapeutics that modulate the effect of natural activators on their specific targets, in particular G-Protein Coupled Receptors (GPCRs), in a non-competitive manner. The compounds are referred to as allosteric modulators and potentially offer advantages over conventional competitive agonist and antagonist compounds. This modulator principle is applicable to any GPCR, opening up a very wide variety of therapeutic opportunities. Addex is focusing its research and development on major indications with substantial unmet medical needs and significant commercial opportunities.

Addex has a portfolio of proprietary compounds in discovery and development for GERD, migraine, anxiety, smoking cessation, depression, pain, cognitive impairment, schizophrenia, Parkinson's disease, contraception and diabetes type 2. Addex's competence in drug development and its expertise in allosteric modulation were recognised through the establishment of a partnership for co-development of mGluR2 positive allosteric modulators for anxiety and schizophrenia with Johnson & Johnson in 2004.

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