



Addex Pharmaceuticals SA
12 Chemin des Aulx
1228 Plan-les-Ouates
Geneva, Switzerland
T +41228841555
F +41228841556
www.addexpharma.com

PRESS RELEASE

30 August 2006

Addex commences Phase II clinical trials programme with ADX10059

Geneva, 30 August 2006 – Addex Pharmaceuticals announced today the start of the Phase II development programme of its lead compound ADX10059. This announcement follows the successful completion of three Phase I trials, in over 100 healthy subjects, which demonstrated good tolerability of the compound across a broad dose range. The first Phase II study, which has started in Germany, evaluates the use of ADX10059 for the acute treatment of migraine. In the near future, two additional Phase II studies are scheduled to begin with this compound for the treatment of acute anticipatory anxiety and for the prevention of acid reflux in patients with gastro-oesophageal reflux disease (GERD).

The first study in migraine is a multicentre Phase IIa study, located at opinion leader sites in the UK and Germany. The design is a double-blind, placebo-controlled comparison of a single dose of ADX10059 with placebo, to treat a single moderate or severe (IHS Grade 2 or 3) migraine headache, in an outpatient setting. Standard efficacy outcomes will be used, with the primary efficacy variable being the proportion of patients pain-free (IHS Grade 0) 2 hours after dosing. The effect of ADX10059 on migraine headache pain, associated symptoms of migraine and functional disability will be graded in the 24 hours following dosing. Safety and tolerability will also be monitored.

ADX10059 is a potent, selective, negative allosteric modulator (NAM) of the metabotropic glutamate receptor 5 (mGluR5), implicated in anxiety, migraine and other CNS disorders. 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.

“The rapid advancement of our first product into Phase II attests to our development capabilities,” said Dr Vincent Mutel, CEO of Addex. “We hope to confirm ADX10059’s clinical potential as a first-in-class compound for the treatment of migraine.”

While anxiety, for which this pharmacological approach was clinically validated in a recent article co-authored by Dr. Mutel,⁽¹⁾ remains the primary indication being targeted by Addex, various animal pharmacology experiments have shown that glutamate is largely responsible for signal transmission in the neural circuit involved in migraine, and mGluR5 receptors are found at strategic points along the pathway.⁽²⁾



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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 the natural activator on its specific target, 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, severe spasticity, migraine, schizophrenia, smoking cessation, pain and Parkinson's disease. Addex's competence in drug development and its expertise in allosteric modulation were recognised by its recent collaboration with Johnson & Johnson.

For further information, please contact:

Christophe Lamps or Jonathan Leighton
Rochat & Partners
Tel: +41 22 786 54 55

Katia Spartalli
Addex Pharmaceuticals
Tel: +41 22 884 1555

Notes to the editor:

About Migraine

Migraine is a highly prevalent disorder that causes significant disability and loss of function with accompanying social and economic impact. Approximately 25 million Americans have migraine and the prevalence worldwide is about 12%. The market for acute and preventative treatments for migraine is estimated to reach \$3 billion worldwide by 2008. In the last ten years, acute treatment of migraine has been dominated by the vascular acting serotonin agonists (triptans), but increasing recognition of migraine as a neuronal rather than a vascular disorder highlights the need for drugs that target the fundamental process of the migraine attack, rather than the end symptoms. The mechanism of action of ADX10059 is very relevant to the pathophysiological processes involved in migraine and hence holds promise for the treatment of this condition.

About Anxiety

Anxiety comprises a spectrum of disorders including generalised anxiety, panic disorder, social phobia, post-traumatic stress disorder and obsessive compulsive disorder. It is a very common condition and the lifetime prevalence is approximately 20% for men and 30% for women. It is estimated that 490 million people worldwide suffer from some form of anxiety. Anxiety commonly accompanies other psychiatric



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disorders such as depression and addiction. The estimated market size for anxiety is approximately \$5 billion. There remains a considerable need for drugs with a novel mechanism of action to improve the effectiveness of treatment and to overcome the side effects of existing therapies, which limit patient use.

About GERD

GERD is a very common disorder with an estimated prevalence in the US of 30% of the adult population. The prescription market for GERD is worth several billion dollars and is dominated by the proton pump inhibitors and the histamine H2 receptor antagonists, some of which have become over-the-counter medicines. Most existing medications act to reduce gastric acid production, and there are no currently licensed medications which act specifically to improve lower oesophageal sphincter tone. ADX10059 has the potential to become an entirely novel and more physiologically relevant treatment for GERD.

References

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2. Ramadan NM (2003). The link between glutamate and migraine. *CNS Spectrums.* 8:446-449.