



PRESS RELEASE

Addex Presents Data on ADX10059 at the Annual Meeting of the American Academy of Neurology

Data Suggests Glutamate Receptor “mGluR5” is Clinically Relevant for Migraine

Geneva, Switzerland, April 29, 2009 – Allosteric modulation company Addex Pharmaceuticals (SIX:ADXN) announced today the presentation of Phase IIa data on ADX10059, an mGluR5 negative allosteric modulator, which shows efficacy in treating acute migraine attacks and provides evidence that inhibition of this glutamate receptor subtype could play a role in stopping migraine attacks before they start. Data were presented at the 61st Annual Meeting of the American Academy of Neurology (Seattle, USA).

“Medication is available to prevent migraine but these treatments are often secondary uses of the drug and come with potentially limiting side-effects,” noted Dr. Peter Goadsby of the UCSF Headache Center and investigator in the study. “New therapies specifically developed for migraine prevention are urgently needed especially for the substantial proportion of migraine sufferers who have frequent attacks and have significant disability in their daily lives. Targeting mGluR5 signaling with ADX10059 is an interesting approach that is showing significant promise in early clinical evaluation.”

Preclinical experiments and small scale studies in migraineurs with drugs like ketamine, which acts on glutamate signaling through NMDA receptors (functionally related to mGluR5) and the NMDA antagonist memantine, suggest that mGluR5 could play a role in the “migraine circuit,” a positive feedback loop that generates the symptoms of a migraine attack. The initial step to test this hypothesis was Addex’ proof of concept study in acute treatment of migraine attacks.

In the Phase IIa trial of 129 migraine patients presented at ANN, significantly more patients taking ADX10059 than those taking placebo (16.7% vs 4.7%, respectively $p = 0.039$) were pain-free two hours after dosing. ADX10059 administration yielded better pain improvement than placebo at all time points up to two hours after treatment of a migraine attack. In addition, there were trends to superiority for ADX10059 over placebo for migraine pain improvement (mild or no pain) at all time points up to two hours post-dosing.

“The clinical trial data for ADX10059, presented here at AAN, proved the concept that by terminating acute attacks in some patients, mGluR5 inhibition plays a role in migraine pathophysiology. Now we are looking forward to the data from our ongoing Phase IIb migraine prevention study in the first half of 2010,” said Charlotte Keywood, chief medical officer.

In December 2008, Addex initiated a Phase IIb trial to study ADX10059 as a prophylactic agent in migraine. The 12-week trial will compare ADX10059 (25mg, 50mg or 100mg) versus placebo in migraine patients who suffer three or more attacks per month. Data from the migraine prevention trial are expected in the first half of 2010.

AAN Abstract P06.006: *Investigation of the Role of mGluR5 Inhibition in Migraine: A Proof of Concept Study of ADX10059 in Acute Treatment of Migraine* will be presented by Peter Goadsby, Director of the UCSF Headache Center, San Francisco, and Charlotte Keywood, Chief Medical Officer, Addex Pharma during Poster Session VI: Headache III in room 6E on Wednesday, April 29, 2009 4:00 PM. The authors are available for interviews prior to and during the conference.

Migraine is a condition distinguished by recurrent episodes of a characteristic headache, which can be accompanied by a variety of other symptoms such as nausea, and sensitivity to light and sound. The average migraine patient suffers 12 attacks a year. The International Headache Society estimates that about 25% of migraine patients have three or more attacks per month and could benefit from migraine prevention treatment. A migraine attack, which typically lasts about 24 hours but can range from 4-72 hours, has three distinct phases: the prodrome phase, when an array of individual warning signs - like blurred vision or tingling of the skin - may begin to appear; the headache phase; and the postdrome phase, when many patients report fatigue or other “hangover-like” symptoms. As migraine attacks are prolonged, many patients and especially those with frequent attacks, lose a significant amount of work and family time to suffering caused by the disease. Indeed, migraine is currently estimated to cost employers \$13 billion annually in lost productivity in the United States. Prevalence of migraine is estimated at 12% in the United States, where about

30 million people suffer from migraine. Given the role of glutamate in the pathophysiology of migraine, the future of migraine prophylaxis, may lie in modulating one of the receptors in the glutamate system, mGluR5.

mGluR5 inhibition: Research has shown that glutamate is the major neurotransmitter involved in the initiation and the propagation of the migraine circuit, a positive feedback loop that leads to pain and inflammation in the brain and hence migraine symptoms. mGluR5 is known to be expressed in key brain regions involved in the migraine circuit. Addex postulated that ADX10059 could interrupt the migraine circuit to abort an active attack and potentially prevent an attack from being triggered. ADX10059 has been shown by Addex to have a superior effect to placebo in acute treatment of migraine headache in Phase IIa testing. Inhibition of mGluR5 has therapeutic potential in multiple indications because mGluR5 is involved in a variety of functions in the central and peripheral nervous systems. In addition to migraine, mGluR5 inhibitors have achieved clinical proof of concept in separate studies in patients with gastroesophageal reflux disease (GERD), Parkinson's disease levodopa induced dyskinesia (PD-LID) and generalized anxiety disorder (GAD). Inhibition of mGluR5 also has potential in Fragile X syndrome.

*mGluR5 antagonists: Discovery, characterization and drug development, *Current Opinion in Drug Discovery & Development* 2008 11(5):655-665

Addex Pharmaceuticals (www.addexpharma.com) discovers and develops allosteric modulators for human health. Allosteric modulators are a different kind of orally available small molecule therapeutic agent, which we believe will offer patients better results than classical drugs. Our lead allosteric modulator product, ADX10059, has achieved clinical proof of concept and is in Phase IIb testing for the treatment of GERD and, separately, migraine headache. Both are important diseases for which existing products have established multi-billion dollar markets despite sub-optimal efficacy. ADX10059 is a first-in-class mGluR5 inhibitor, a therapeutic strategy that also is being pursued to treat multiple indications by large pharma competitors.

Our product pipeline and technology already have proven their value through our relationships with four of the top 10 pharmaceutical companies in the world. Specifically, in two separate license agreements with Merck & Co., Inc., we are developing positive allosteric modulators of mGluR4 and mGluR5 as drugs to treat Parkinson's disease and schizophrenia, respectively. A third agreement, with Ortho McNeil Pharmaceuticals Inc., a Johnson & Johnson company, is focused on development of positive allosteric modulators of mGluR2 to treat anxiety and schizophrenia. Separately, investment funds from Roche and GlaxoSmithKline have extended their validation of our technology, products and management by making significant investments in Addex.

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