



## PRESS RELEASE

# Addex ADX10059 Monotherapy is Effective on GERD Symptoms in Phase IIb Clinical Trial

Primary and Secondary Endpoints Achieved  
Webcast Today at 4pm CET (10am ET)

**Geneva, Switzerland, 16 November 2009** – Addex Pharmaceuticals (SWX:ADXN), the allosteric modulation company, announced that it achieved statistically significant efficacy on the primary endpoint, increasing the number of symptom free days in the Phase IIb trial of ADX10059 as a monotherapy in patients with gastroesophageal reflux disease (GERD), the cause of heartburn and other symptoms. ADX10059 is a first-in-class reflux inhibitor that works by reducing activation of the metabotropic glutamate receptor 5 (mGluR5) through negative allosteric modulation (NAM). This approach may lead to a new class of drugs that addresses the causes of GERD rather than just the symptoms.

Chief Medical Officer Charlotte Keyword said: "We saw the number of symptom free days increase by five-fold, an exciting and clinically meaningful effect for ADX10059 monotherapy. The magnitude of the effect, along with the tolerability profile, indicate that ADX10059 has potential to be a useful therapy for GERD management."

"Based on its marked efficacy in both reducing reflux and controlling symptoms in this study, I would be pleased to see ADX10059 tested in later stage trials as a monotherapy for GERD patients," said professor Frank Zerbib, head of gastroenterology at the University Hospital of Bordeaux and a leading expert on GERD. "Furthermore, the good tolerability seen with this modified-release formulation of ADX10059 was also a crucial part of these results, since GERD is a chronic disease where long-term therapy is needed in the majority of patients."

Vincent Mutel, CEO of Addex said, "These data confirm our belief in using this mechanism of action, mGluR5 inhibition, to treat GERD. Furthermore, we believe that the market potential for a product with the profile of ADX10059 is very significant. We look forward to further development of this molecule in GERD."

**Study ADX10059-204** was a double-blind, placebo-controlled, multi-center European Phase IIb trial in 103 GERD patients known to respond well to proton pump inhibitors (PPIs). There was a two-week baseline symptom evaluation period followed by two weeks of administration of ADX10059 120 mg twice daily. ADX10059 was used as a monotherapy so patients in the study did not use PPIs or other acid suppressant therapy during the baseline and study treatment periods. The primary clinical endpoint was the patient reported number of GERD symptom free days in week 2 of treatment compared to the last 7 days of baseline. Objective measures of the effects of ADX10059 on esophageal function and reflux events were made in a subset of 24 patients on the day before starting treatment and on the last day of treatment using impedance pH monitoring and esophageal manometry. Reflux events on impedance pH monitoring were the mechanistic primary variables.

ADX10059 significantly increased the mean number of GERD symptom free days in week 2 of treatment. At baseline the mean number of symptom free days was 0.46 in the ADX10059 group and 0.72 days in the placebo group. During treatment week 2 this increased to 2.5 days in the ADX10059 group and to 1.71 days in the placebo group ( $p = 0.0452$ )

In the subset of 24 patients who underwent mechanistic monitoring ADX10059 also achieved statistical significance in two mechanistic primary endpoints. ADX10059 significantly reduced total impedance measured reflux events and also acidic reflux events over the 24 hour monitoring period. In the ADX10059 treated group the mean number of total reflux events decreased by 26% from 64.9 at baseline to 47.9 on treatment compared to no change in the placebo group with a mean of 77.0 reflux episodes at baseline and 78.4 on treatment ( $p = 0.0342$ ). In the ADX10059 group the mean number of acidic reflux events in 24 hours decreased by 29% from 52.1 at baseline to 37.0 at end of treatment compared to a small increase in the placebo group with 55.7 episodes at baseline, and 59.7 at end of treatment ( $p = 0.0032$ ).

In addition to the primary efficacy endpoints, ADX10059 showed statistical superiority over placebo for a variety of secondary variables including an increase in heartburn free days, a reduction in sleep disturbance, a reduction in the requirement for antacid medication, an improvement in a GERD symptom patient reported outcome

questionnaire ( $p < 0.05$  for all measures). Finally patients also expressed a significant preference for ADX10059 treatment compared to placebo ( $p < 0.05$ ).

ADX10059 120 mg twice-daily given for two weeks was well tolerated and the tolerability profile seen is compatible with use in the treatment of GERD. Adverse events were reported more frequently for ADX10059 than placebo but in both treatment groups the vast majority was mild and none was described as severe. There were no significant changes in safety monitoring parameters.

Addex also announced today that enrolment has been completed in the second trial of ADX10059 in GERD patients. In the study ADX10059-205, the product is being used as an add-on therapy in patients who are partial responders to Proton Pump Inhibitors (PPIs), the standard therapy for GERD. Results are expected in January 2010. A third trial, where ADX10059 is being studied as a migraine prophylaxis in patients with frequent migraines is progressing as expected and data will be reported in the second quarter of 2010.

**GERD** is a chronic condition caused by stomach contents flowing back into the esophagus on a regular basis. The underlying cause of this is an abnormally functioning lower esophageal sphincter (LES) muscle that allows stomach contents to pass back into the esophagus too easily. GERD leads to painful symptoms like heartburn and can also damage the lining of the esophagus. It is a common disorder with prevalence at about 15% in the United States and between 10% and 25% in EU. Marketed GERD products work by reducing the acidity of the stomach contents but do nothing to reduce reflux events, so that in many patients symptoms of GERD persist.

**mGluR5 inhibition** in GERD aims to restore normal function and improve the tone of the LES muscle, thereby preventing reflux and addressing the cause of the disease. Indeed, ADX10059 has been shown by Addex to reduce reflux and reduce esophageal acid exposure in three separate clinical trials(1,2). Research has shown that mGluR5 inhibition improves LES function in animals. Reflux inhibitors are being recognized as potentially the next generation of GERD therapy because they address the cause of the disease and are complementary to marketed acid suppression therapies.

Inhibition of mGluR5 has therapeutic potential in multiple other indications because, as with other glutamate receptors, mGluR5 is involved in a variety of functions in the central and peripheral nervous systems(3). In addition to GERD, mGluR5 inhibitors have achieved clinical proof of concept in separate studies in patients with migraine headache(4), Parkinson's disease levodopa induced dyskinesia (PD-LID) and generalized anxiety disorder (GAD). Inhibition of mGluR5 also has potential in Fragile X syndrome, neuropathic pain and depression.

- (1) Keywood, C., et al., *GUT online* May 20, 2009 (free download: <http://bit.ly/2Rcu0k>)
- (2) Zerbib, F., et al., *Digestive Disease Week (DDW) 2009* (free download: <http://bit.ly/HjehE>)
- (3) Gasparini, F. et al., *Current Opinion in Drug Discovery & Development* 2008 11(5):655-665
- (4) Goadsby, P. et al., *American Academy of Neurology (AAN) 2009* (free download: <http://bit.ly/13aBkw>)

**Webcast and conference call today at 4pm CET (10am ET). Visit the Addex website for more information.**

**Addex Pharmaceuticals** ([www.addexpharma.com](http://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 a competitive advantage over 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. ADX10059 is a first-in-class mGluR5 inhibitor, a therapeutic strategy that also is being pursued in multiple indications by large pharma competitors.

Addex products and technology already have proven their value through our relationships with four of the top 10 pharmaceutical companies in the world. Specifically, under an agreement with Ortho-McNeil-Janssen Inc., a Johnson & Johnson company, ADX71149, a positive allosteric modulator (PAM) of mGluR2, is undergoing Phase I clinical testing and has potential for treatment of schizophrenia and anxiety. Under two separate agreements with Merck & Co., Inc., we are developing PAMs of mGluR4 and mGluR5 as drugs to treat Parkinson's disease and schizophrenia, respectively. In addition, GlaxoSmithKline and Roche have made equity investments in Addex.

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