



## PRESS RELEASE

# Addex: Better Tolerated Formulation of ADX10059 Reduces Acid Reflux

- ***Second trial showing mGluR5 inhibition reduces reflux in humans***
- ***Side effects dramatically reduced by formulation***
- ***Twice-daily oral dosing achieved***
- ***Doses selected for Phase IIb trials***
- ***Phase IIb GERD and migraine trials to start in 4Q08***

**Geneva, Switzerland, 10 September 2008** – Addex Pharmaceuticals (SWX:ADXN) announced clinical data showing that the modified release formulation of ADX10059 has improved commercial potential. Tolerability was dramatically improved while a statistically significant reduction in gastroesophageal reflux was achieved for the second time in clinical trials of this product. The novel formulation is appropriate for longer term twice-daily dosing in Phase IIb GERD and migraine prophylaxis studies scheduled to start in the fourth quarter of 2008. ADX10059 is a first-in-class negative allosteric modulator (NAM) of metabotropic glutamate receptor 5 (mGluR5).

CEO, Vincent Mutel, said: “These data show that the formulation of ADX10059 has greatly improved its commercial potential. The fact that ADX10059 has therapeutic potential in several indications, including GERD, migraine and possibly Parkinson’s disease, increases its chances of successfully making it to the market, thereby enhancing its attractiveness and mitigating development risks.”

Chief Medical Officer Dr. Charlotte Keywood said: “We are delighted to have developed a novel formulation which gives us very good tolerability and twice-daily dosing. The effect on reflux, taken together with previous clinical data in GERD patients, is encouraging with regard to the likelihood of demonstrating a clinical effect in Phase IIb.”

Professor Frank Zerbib head of gastroenterology at the University Hospital of Bordeaux and a leading expert on GERD added: “By using a special meal to provoke gastroesophageal reflux in asymptomatic volunteers, it has been shown that ADX10059 can decrease the occurrence of all types - both acid and weakly acidic - gastroesophageal reflux. These results confirm that mGluR5 represents a pertinent therapeutic target for the treatment of GERD.”

Although the unformulated ADX10059 active pharmaceutical ingredient (API) in capsule achieved in 2007 clinically and statistically significant effects in separate Phase IIa proof of concept trials for GERD and migraine, tolerability was suboptimal even though safety monitoring parameters were unaffected.

**Study ADX10059-104** was a two-part Phase I trial in 36 healthy subjects.

Part One was a single-dose, three-way crossover trial in 12 subjects where the pharmacokinetics, safety and tolerability of two modified release formulations of ADX10059 250 mg were compared to the original 250mg API filled capsules used in Phase IIa.

Part Two was a placebo-controlled, double-blind, multiple ascending-dose study of the pharmacokinetics, safety and tolerability of three different doses (50mg, 125mg and 250mg) of the modified release formulation given twice daily for 6 days. To support the selection of the optimal dose range for the Phase IIb studies, the pharmacodynamic effect of each dose was assessed using a clinical model of GERD, a reflux provocation test, which involves measuring reflux episodes using a gastroesophageal pH impedance probe in healthy volunteers following a high fat, large volume meal.

The primary objectives of Study 104 were met.

In Part One the selected modified release formulation was absorbed at a reduced rate while maintaining the total exposure achieved by the original API filled capsules. No adverse events were observed with the formulation selected for Phase IIb testing. In contrast, seven of 12 subjects taking the original ADX10059 250mg API in capsules experienced side effects like dizziness, drunk feeling and flushing.

In Part Two, statistically significant dose-dependent treatment effects were observed during the reflux provocation test for the percentage of total acid exposure ( $p = 0.0483$ ) and the post-prandial number of weakly acid reflux episodes ( $p = 0.0411$ ) compared to placebo.

In addition, statistically significant effects ( $p < 0.05$ ) were seen for the ADX10059 125 mg dose compared to placebo for impedance measured reflux, weakly acidic reflux, acid exposure percent, and bolus exposure percent. Statistically significant results ( $p < 0.05$ ) were seen for various pharmacodynamic measures with the 250 mg dose compared to placebo. Decreases in some reflux parameters were apparent for the 50mg dose group compared to placebo but these did not achieve significance.

**Study ADX10059-105** was a Phase I three-way crossover study in 15 healthy volunteers of the interaction of a single 250mg dose of the modified release formulation ADX10059 with food and with the proton pump inhibitor esomeprazole. Data from Study 105 show that neither food nor esomeprazole significantly altered the absorption of ADX10059.

The pharmacokinetics observed in Studies 104 and 105 confirmed satisfactory drug exposure with twice daily oral dosing. As in all previous studies, all safety monitoring parameters were unaffected by ADX10059.

### Conference Call & Webcast

Title: ADX10059 Studies 104 & 105 Clinical Results  
Date: 10 September 2008  
Time: 16:00 CET  
Dial-in numbers: +41 91 610 56 00 (Switzerland)  
+44 207 107 0611 (UK)  
+1 866 291 4166 (USA)

A live webcast and slides, as well as the webcast replay and transcript, will be available at [www.addexpharma.com](http://www.addexpharma.com).

### About Addex

Addex Pharmaceuticals discovers and develops allosteric modulators for human health. Allosteric modulators are an emerging class of orally available small molecule therapeutic agents that we believe will offer patients better results than classical drugs. Most marketed drugs bind receptors where the body's own natural molecular activators (i.e. endogenous ligands) bind, specifically to a key part of each receptor's anatomy called the "active site". In short, most drugs must out-compete endogenous ligands for the active site. By contrast, allosteric modulators are non-competitive because they bind receptors and modify their function even if the endogenous ligand also is binding it. In addition, because of this, allosteric modulators aren't limited to simply turning a receptor on or off, the way most drugs are. Instead, they act more like a dimmer switch, offering control over the degree of activation or deactivation, while offering the body the ability to maintain control over initiating receptor activation. Furthermore, the allosteric approach generally affords freedom to operate – even on well-known, clinically validated targets – because the intellectual property surrounding allosteric chemistry and the allosteric sites on receptors is most often un-exploited.

The Addex allosteric modulation discovery and development platform have been additionally validated through three separate product license or collaboration agreements with Merck & Co., Inc. and Johnson & Johnson as well as investments by Roche Ventures and SR One, the venture investment arm of GlaxoSmithKline.

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