



## PRESS RELEASE

# Addex Achieves Second Milestone in Parkinson's Disease Collaboration with Merck & Co., Inc.

### *Data Confirm Non-Dopaminergic Approach to Treating Parkinson's Disease*

**Geneva, Switzerland, 10 July 2008** – Allosteric modulation company Addex Pharmaceuticals (SIX:ADXN) announced today that the second preclinical milestone has been achieved in an exclusive collaboration and license agreement with Merck & Co., Inc. (through its affiliate Merck Sharp & Dohme Research Ltd). The collaboration is focused on developing an emerging type of drugs, called allosteric modulators, for treatment of Parkinson's disease and other undisclosed indications. Allosteric modulators have broad potential to address important therapeutic targets; this collaboration with Merck is focused on developing drugs that specifically activate the metabotropic glutamate receptor 4 (mGluR4). The preclinical study showed the desired non-dopaminergic activity profile after oral administration of mGluR4 positive allosteric modulator (PAM) in an animal model of Parkinson's disease.

"We are pleased that these preclinical data show such promise in the animal model used," said Emmanuel Le Poul, head of the CNS Business Unit at Addex. "This work is a further validation of the target and the strength of our collaboration, as both teams have contributed to this achievement."

"Innovative non-dopaminergic therapies represent a significant opportunity to address an important unmet medical need in Parkinson's disease patients," said Vincent Mutel, CEO of Addex. "We are proud that our allosteric modulation drug discovery and development platform has generated highly innovative products in Parkinson's disease in addition to other important indications with unmet medical need including: gastroesophageal reflux disease, migraine, schizophrenia and anxiety."

Addex will discuss the mGluR4 PAM collaboration and its clinical and preclinical stage allosteric modulator pipeline and discovery platform during its R&D Day on July 16, 2009. A webcast and recording of the Addex R&D Day will be made available at [www.addexpharma.com](http://www.addexpharma.com).

Addex will receive \$500,000 for achieving the second preclinical milestone. Addex received \$250,000 after achieving the first preclinical milestone during the first quarter of 2008. Under the terms of the agreement, first announced in December 2007, Addex received \$3 million upfront and is eligible for up to \$106.5 million in research, development and regulatory milestones for the first product developed for multiple indications. Additional milestones of up to \$61 million would be payable if a second and third product is developed. Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration. Merck is responsible for clinical development.

**mGluR4** may play an important role in Parkinson's disease, which is a debilitating movement disorder. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where dopaminergic treatments are no longer effective. There can also be debilitating side effects with dopaminergic treatments and many patients limit doses so their side effects will be less cumbersome. The recent success of surgical approaches suggests that bypassing the dopamine system may provide a more effective treatment strategy. It is believed that selective activation of mGluR4 is one way to do this and could correct the circuitry that modulates motor excitability. This has the potential to provide significant benefit in Parkinson's disease.

Published research\* shows that mGluR4 activators, like those in development at Addex, could work via two distinct mechanisms to alleviate symptoms of Parkinson's disease and, potentially, even slow the progression of the disease: 1) mGluR4 activation triggers a compensatory mechanism that may spare or potentiate the use of dopamine receptor activators; 2) mGluR4 activation may have a neuroprotective effect that helps to preserve the brain's dopaminergic neurons.

\**Nature Reviews Neuroscience*, Vol 6, Oct. 2005, pp 787-798

**Glutamate**, like dopamine and serotonin, is a key neurotransmitter in the human brain, an important signaling molecule involved in control of multiple brain functions ranging from motor control to mood. Although marketed drugs modulate specific receptors involved in both the dopaminergic and serotonergic systems, it has been difficult to develop drugs that can selectively target specific receptors of glutamate, which has many different receptors, some of which can cause serious side effects if improperly modulated.

Merck has been a pioneer in research on mGlu receptors and the metabotropic glutamatergic system for multiple indications. For example, research by Merck scientists provided the first evidence that mGluR4 activation has potential for treatment of Parkinson's disease. However, a remaining challenge has been to make drug-like molecules that activate mGluR4 in a specific fashion. Addex is a pioneer in developing allosteric modulators, truly selective small molecule drug candidates, for human health.

**Parkinson's disease** is a brain disorder characterized by movement disorders and other symptoms. It occurs when certain nerve cells (neurons) in a part of the brain called the substantia nigra die or become impaired. Normally, these cells produce a vital chemical known as dopamine. Dopamine allows smooth, coordinated function of the body's muscles and movement. When approximately 80% of the dopamine-producing cells are damaged, the symptoms of Parkinson's disease appear.

About 1.5 million Americans currently have Parkinson's disease, and about 60,000 new cases are diagnosed each year. Parkinson's is one of the fastest growing diseases, driven by the ageing population. Parkinson's disease drugs had global sales of around \$2.5 billion in 2005, which analysts believe could grow to \$3.8 billion by 2010.

Although no marketed products slow the disease progression, there are a number of medicines that effectively ease the symptoms. The medicines most commonly prescribed attempt to either replace or mimic dopamine. They can improve the tremor, rigidity and slowness associated with Parkinson's disease but they also can cause side effects like dyskinesia (involuntary movements) and eventually stop working, as the dopaminergic neurons continue to die.

**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. Both are important diseases for which existing products with limited efficacy 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 in multiple indications by large pharma competitors.

Our products and technology already have proven their value through our partnerships with four of the top 10 pharmaceutical companies in the world. Specifically, two separate agreements with Merck & Co., Inc., are focused on developing allosteric modulators as drugs to treat Parkinson's disease and schizophrenia, respectively. A third agreement with Ortho-McNeil-Janssen Inc. is focused on development of allosteric modulators to treat anxiety and schizophrenia. Finally, GlaxoSmithKline and Roche have made equity investments in Addex.

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