



PRESS RELEASE

Addex Partner Starts First-Ever Clinical Trial of an mGluR Positive Allosteric Modulator

Novel Approach Has Potential for Treatment of Multiple CNS Disorders

Geneva, Switzerland, 24 June 2009 – Allosteric modulation company Addex Pharmaceuticals (SIX:ADXN) announced today that its partner Ortho-McNeil-Janssen Pharmaceuticals Inc. (OMP) has started Phase I testing of ADX71149, a metabotropic glutamate receptor 2 (mGluR2) positive allosteric modulator (PAM). This product, which has potential to treat schizophrenia, anxiety, depression and other CNS disorders, is the first PAM of any mGluR subtype to enter clinical trials. Targeting mGluR2 with a PAM is a novel approach that may offer advantages over classical drug approaches. In reaching this milestone, Addex received a €1 million payment from OMP and remains eligible for additional development milestones and royalties.

Allosteric modulators are a novel class drugs that exert their effects on a specific receptor by interacting with a different site than the traditional binding site used by traditional “orthosteric” drugs and the body’s natural activators (i.e. endogenous ligands), glutamate in this case. Allosteric molecules afford modulation of receptors that is different than orthosteric drugs. Furthermore, Addex believes it can find specific drug-like allosteric modulators with more success than others have had with orthosteric drug discovery.

“We are proud to have been able, together with our partner, to discover and develop the first mGluR2 PAM to reach human beings,” said Vincent Mutel, CEO of Addex. “Because activating mGluR2 has been recognized as one of the most promising strategies for treating anxiety and more recently, schizophrenia, developing an allosteric modulator, like ADX71149, specifically targeting this brain receptor has been an exciting scientific endeavor and we are looking forward to seeing how differentiated this modulatory approach will be in humans.”

Note for editors: An orthosteric agonist binds at the same site on a receptor as the endogenous ligand, in this case, glutamate. Much like flipping a light switch on, endogenous ligands or orthosteric agonists, effectively turn receptors on, sending a message to the cell to perform a specific function. By contrast, an allosteric modulator binds at a different site on the receptor than the endogenous ligand. As a result, an allosteric modulator does not turn on/off a receptor but rather exerts its influence only when the endogenous ligand also is binding (i.e. the switch is turned on). Thus, allosteric modulators act much more like a dimmer than an on/off switch. Positive allosteric modulators increase the signal sent into the cell by the receptor, while a negative allosteric modulators (NAM) reduce it. This approach may prove advantageous because it allows the body to maintain control over the physiological on/off rhythm – something that no orthosteric drug has been able to emulate – while affording a new kind of therapeutic influence at disease mediating receptors.

Although no drug specifically targeting mGluR2 is marketed, a Phase II clinical study published in *Nature Medicine* in 2007 showed that an orthosteric mGluR2/3 agonist improved symptoms of schizophrenia with efficacy similar to a leading marketed drug for schizophrenia. Separately, a related orthosteric mGluR2/3 agonist has been shown to have efficacy in Phase II trials in patients with generalized anxiety disorder. Activation of mGluR2 also has been shown to be efficacious in multiple preclinical models of anxiety.

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 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 two of the top 10 pharmaceutical companies in the world. Specifically, the agreement, with OMP, is focused on development of mGluR2 positive allosteric modulators to treat anxiety and schizophrenia, and in two separate agreements with Merck & Co., Inc., we are developing allosteric modulators as drugs to treat Parkinson's disease and schizophrenia.

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