

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

Collaboration Targets a Non-Dopaminergic Approach to Treating Parkinson's Disease

Geneva, Switzerland – Allosteric modulation company Addex Pharmaceuticals (SWX:ADXN) announced today that the first preclinical milestone has been achieved in a recently announced 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 class of oral drugs, allosteric modulators, that target the metabotropic glutamate receptor 4 (mGluR4) for Parkinson's disease and other undisclosed indications.

"The achievement of this first preclinical milestone provides additional validation for the strategy of activating mGluR4 to treat Parkinson's disease" Vincent Mutel, CEO of Addex, said. "The speed with which the milestone was reached, within three months of signing the agreement, stems from our joint commitment to the project and the efforts of the excellent team involved in this collaboration."

Addex will receive \$250,000 for achieving the first preclinical milestone. 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 in Parkinson's disease

Parkinson's disease is a debilitating movement disorder. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where these treatments are no longer effective. There can also be debilitating side effects with current treatments and many patients limit doses so their symptoms are 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 mot or excitability. This has the potential to provide significant palliative 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.

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Targeting glutamate receptors

Like dopamine and serotonin, glutamate 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 target specific G protein coupled receptors in the glutamatergic system.

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 truly selective small molecule drug candidates targeting glutamate receptors and has disclosed allosteric modulator programs targeting mGluR5 and mGluR2.

About Parkinson's disease

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 Lehman Brothers forecasts 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.

About Addex

Addex Pharmaceuticals discovers and develops allosteric modulators, an emerging class of small molecule therapeutic agents. Allosteric modulation may offer more sophisticated ways to normalize biological signaling compared to classical orthosteric agonist or antagonist drugs. Allosteric, literally translated from its Greek roots, means: other site. Thus, allosteric modulators bind receptors at sites that are distinct from the binding sites of classical small molecule orthosteric agonist and antagonist drugs.

The most advanced drug candidate, ADX10059, a negative allosteric modulator (NAM) of metabotropic glutamate receptor 5 (mGluR5), recently demonstrated clinically and statistically significant efficacy in separate Phase IIa clinical trials in gastroesophageal reflux disease (GERD) patients and migraine headache patients.

The Addex allosteric modulation discovery and development platform has been additionally validated through collaborations with Merck & Co., Inc. and Johnson & Johnson.

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