Addex’s ADX48621 Effective in Preclinical Parkinson’s Disease Studies

Presented at the International Congress of Parkinson’s Disease and Movement Disorders

Geneva, Switzerland, 15 June 2010 - Allosteric modulation company Addex Pharmaceuticals Ltd (SIX:ADXN) today presented encouraging data from preclinical studies demonstrating the anti-Parkinson’s effects of ADX48621, a novel drug candidate that has completed three Phase I clinical trials.

Addex presented preclinical data at the 14th International Congress of Parkinson’s Disease and Movement Disorders held in Buenos Aires, Argentina showing that ADX48621 was effective in two well-established models of PD: the MPTP model of Parkinson’s disease levodopa induced dyskinesia (PD-LID) and the rat haloperidol induced catalepsy (HIC) model of PD symptoms. Addex previously disclosed that ADX48621, a negative allosteric modulator (NAM) of the metabotropic glutamate receptor 5 (mGluR5), was effective in these models and had achieved satisfactory pharmacokinetics, safety and tolerability in three separate Phase I clinical trials in a total of 130 healthy volunteers, including older subjects.

PD-LID develops in most PD patients after receiving levodopa for several years. It is a complication caused by dopamine replacement therapy (i.e. levodopa). The two main components of LID are chorea and dystonia. Chorea is manifest as sudden rapid uncontrolled movements (e.g. jerking). Dystonia is manifest as slow writhing type movements and sustained muscle contractions, which can be painful.

In the MPTP monkey model of PD-LID, ADX48621 (30 mg/kg) statistically and significantly inhibited LID. At this dose, ADX48621 almost abolished chorea and dystonia, the two major components of LID, without affecting the beneficial effects of levodopa as determined by disability scores.

In the rat HIC model of PD, ADX48621 decreased catalepsy time dose dependently, by 19% 43%, 53%, and 65% at 1, 3, 10 and 30 mg/kg, respectively, compared to vehicle control. There was a trend to efficacy at 3mg/kg, with statistical significance at 10 (p < 0.01) and 30 mg/kg (p<0.001). These data show that the minimal effective dose of ADX48621 was 10 mg/kg, with a corresponding plasma concentration of about 1700 ng/ml.

“We are very encouraged by these data, particularly the effect of ADX48621 on dystonia, a debilitating movement disorder in PD and also in other patients who do not have PD. To our knowledge, no other drug on the market or in development has demonstrated this level of activity in this primate model. Furthermore, the data from the HIC model indicate that, in the long-run, ADX48621 also could be tested as a treatment for the general symptoms of PD, potentially as a complementary drug that would allow doctors to optimize levodopa dosing,” noted Charlotte Keywood, chief medical officer at Addex. “There is currently no treatment approved for PD-LID and with the condition affecting so many people. We look forward to starting Phase II testing of ADX48621 in PD-LID and dystonia patients around the end of this year.”

Parkinson’s disease is a degenerative disease of the brain that often impairs motor skills, speech, and other functions. It is estimated that 60,000 new cases are diagnosed each year in the U.S., where more than 1.5 million people currently have PD. While the condition usually develops after the age of 65, 15% of those diagnosed are under 50. PD affects both men and women in almost equal numbers. Over time, generally several years, most PD patients treated with levodopa develop PD-LID.

mGluR5 inhibition reduces signaling activity of the neurotransmitter glutamate. Marketed blockbuster drugs treat multiple indications by targeting other types of neurotransmitter signaling, including selective serotonin reuptake inhibitors (SSRIs) used to treat depression and dopamine receptor inhibitors used to treat schizophrenia. The rationale for using mGluR5 inhibition in PD is that the loss of dopamine
producing cells leads to excess glutamatergic stimulation in the brain’s “striatopallidal pathway”. mGluR5 are found abundantly in the striatum and are implicated in the excess glutamate activity in Parkinson’s Disease. Research shows that inhibition of glutamate stimulation in this pathway has generated anti-Parkinsonian effects in animal models of PD and PD-LID and in humans with PD-LID.

Addex Pharmaceuticals (www.addexpharma.com) discovers and develops allosteric modulators for human health and is focused on validated therapeutic targets for diseases of the central nervous system, metabolic disorders and inflammation. Subject to the completion of Phase I testing and regulatory approvals, Phase II clinical trials are expected to start in 2010 in four indications for two lead products: ADX48621, an mGluR5 negative allosteric modulator (NAM), in dystonia and Parkinson’s disease levodopa-induced dyskinesia (PD-LID); and ADX71149, an mGluR2 positive allosteric modulator (PAM), in schizophrenia and anxiety. ADX71149 is licensed to Ortho-McNeil-Janssen Pharmaceuticals Inc. A third product, ADX71943, GABA-B receptor PAM with potential for chronic pain, is scheduled to enter Phase I testing around the end of 2010. In addition, Merck & Co., Inc. has licensed rights to two preclinical products: mGluR4 PAM for Parkinson’s disease and mGluR5 PAM for schizophrenia. Additional preclinical discovery stage programs include: mGluR2 NAM, GLP1R PAM, IL1R1 NAM and TNFR1 NAM. Roche Venture Fund and SR-One, corporate venture arm of GlaxoSmithKline, are investors in Addex.

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