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AB Science announces successful completion of futility test for masitinib in Alzheimer's disease

Independent Data Safety Monitoring Committee recommends continuation of phase 3 study based on review of current safety and efficacy data

Company to host web conference focused on masitinib in Alzheimer's disease

AB Science SA (NYSE Euronext – FR0010557264 – AB), a pharmaceutical company specialized in research, development and marketing of protein kinase inhibitors (PKIs), today announced the successful completion of a futility analysis related to the masitinib phase 3 trial for the treatment of mild to moderate Alzheimer's disease. Based on these results, the Independent Data Safety Monitoring Committee (IDMC) has recommended the continuation of the study.

Phase 3 status

The ongoing phase 3 trial is a double-blind, randomized, placebo-controlled study (AB09004) designed to assess the safety and efficacy of masitinib in patients with confirmed mild to moderate Alzheimer's disease. The treatment period is 24 weeks and masitinib is being given as an add-on therapy to cholinesterase inhibitor (donepezil, rivastigmine or galantamine and/or memantine). The main measures are the change in two commonly used clinical assessments: the effect on ADCS-ADL, which measures self-care and activities of daily living assessed, and the effect on ADAS-Cog, which measures the effect on cognition and memory. The study is intended to enroll about 600 patients.

The study was recently assessed as non-futile by the IDMC. A futility analysis tests the inability of a clinical study to achieve its efficacy objective. Therefore, a conclusion that a study is not futile suggests that a clinical study has the potential to achieve its stated efficacy objective. The IDMC analysis was performed after about one third of the patients were enrolled into the study and had reached the 24 week treatment duration period.

The study previously successfully passed all safety data reviews by the IDMC, indicating that there is no major or unexpected safety concern with masitinib in this patient population.

Previous establishment proof of concept

As a reminder, proof of concept for the evaluation of masitinib in Alzheimer's disease was established through a 35 patient double-blind, placebo-controlled phase 2 study. In this study, the rate of clinically relevant cognitive decline, according to the primary endpoint, ADAS-Cog response (increase >4 points), was significantly lower with masitinib treatment compared with placebo after 12 and 24 weeks (6% versus 50% for both; p=0.040 and p=0.046, respectively). Moreover, while the placebo treatment-arm demonstrated worsening mean ADAS-Cog, ADCS-ADL and MMSE scores, the masitinib treatment-arm reported improvements with statistical significance between treatment-arms at weeks 12 and/or 24 (respectively, p=0.016 and 0.030; p=0.035 and 0.128; and p=0.047 and 0.031). Adverse events occurred more frequently with masitinib treatment (65% versus 38% of patients); however, the majority of events were mild or moderate and transient. The phase 2 results were published in Alzheimers Res Ther. 2011 Apr 19;3(2):16. doi: 10.1186/alzrt75.

Scientific rationale

The potential therapeutic benefit of masitinib in Alzheimer's disease is linked to two possible mechanisms of action: the role of mast cells in neuroinflammation and regulation of the blood-brain-barrier (BBB) permeability; and the inhibition of the protein kinase Fyn, which is involved in Aβ signaling and Tau phosphorylation.

Neuroinflammation is thought to be a major contributor in the pathogenesis of Alzheimer's disease[1,2,3]. Mast cells release large amounts of proinflammatory mediators and therefore play an important role in sustaining the inflammatory network of the central nervous system. Furthermore; mast cells are found on both sides of the BBB and also have the ability to rapidly cross the BBB, thereby increasing their numbers in response to physiological stimuli. Given that the neural pool of mast cells is influenced by their ability to rapidly cross the BBB, inhibition of mast cells peripheral to the BBB could impact upon neurodegenerative disease outcome. Therefore, masitinib could be an effective drug in Alzheimer's disease because it blocks mast cells through the inhibition of the tyrosine kinases c-Kit and Lyn.

In addition to blocking mast cell activity, masitinib may exert an effect through its inhibition of the tyrosine kinase Fyn[4,5,6]. Alzheimer's disease is associated with the pathological aggregation of amyloid-beta (Aβ) plaques and tau-positive neurofibrillary tangles. Several lines of evidence implicate Fyn in the pathogenesis of Alzheimer's disease through its dual role in Aβ signaling and Tau phosphorylation. Masitinib, by inhibiting Fyn, could possibly disrupt the Aβ signaling cascade and modulate the phosphorylation of tau protein, thus and preventing neurofibrillary tangles.

Targeted population

The meta-analysis of epidemiologic studies indicates that between 5 and 10 million people suffer from Alzheimer's disease in the USA and Europe. Alzheimer's disease is the most common type of dementia among western countries, corresponding to about 60% of cases. Alzheimer's disease is already the sixth leading cause of all deaths in USA and the fifth leading cause among Americans over 65 years of age.[7,8,9] Worldwide, it is thought that there are more than 15 million people affected by Alzheimer's disease.[8]

Currently, there are only five products approved for the treatment of Alzheimer's disease, four of which belong to the pharmacological class of anticholinesterases, the fifth being an NMDA inhibitor. Therefore, this remains an area of significant unmet medical need. Accordingly, the FDA recently issued new guidance (21 CFR 149 314.510) that allows for the potential of conditional approval.

Web conference

AB Science will be hosting in the next few days a web conference focused on masitinib for the treatment of Alzheimer's disease. This event will feature key opinion leaders in the field of Alzheimer's disease treatment. Details will follow shortly.

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About masitinib

Masitinib is a new orally administered tyrosine kinase inhibitor that targets mast cells and macrophages, important cells for immunity, through inhibiting a limited number of kinases. Based on its unique mechanism of action, masitinib can be developed in a large number of conditions in oncology, in inflammatory diseases, and in certain diseases of the central nervous system. In oncology due to its immunotherapy effect, masitinib can have an effect on survival, alone or in combination with chemotherapy. Through its activity on mast cells and consequently the inhibition of the activation of the inflammatory process, masitinib can have an effect on the symptoms associated with some inflammatory and central nervous system diseases and the degeneration of these diseases.

About AB Science

Founded in 2001, AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a class of targeted proteins whose action are key in signaling pathways within cells. Our programs target only diseases with high unmet medical needs, often lethal with short term survival or rare or refractory to previous line of treatment in cancers, inflammatory diseases, and central nervous system diseases, both in humans and animal health.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine in Europe and in the USA. The company is currently pursuing thirteen phase 3 studies in human medicine in first-line and second-line GIST, metastatic melanoma expressing JM mutation of c-Kit, multiple myeloma, metastatic colorectal cancer, metastatic prostate cancer, pancreatic cancer, mastocytosis, severe persistent asthma, rheumatoid arthritis, Alzheimer's disease, progressive forms of multiple sclerosis, and Amyotrophic Lateral Sclerosis. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science website: www.ab-science.com.

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